ISHBT

INDIAN SOCIETY OF HEMATOLOGY & BLOOD TRANSFUSION

HAEMATOCON 2024 NAGPUR

GENETIC CALLIGRAPHY, CORRECTING THE CODE

HEMATOLOGY ONCOLOGY SOCIETY, NAGPUR

65th Annual Conference of Indian Society of Haematology & Blood Transfusion

07th - 10th November 2024 at Hotel Centre Point, Nagpur

ABSTRACTS

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Content

Dr J C Patel Award Paper Presentations JCP-1

Feasibility of High/Intermediate Dose Ara-C consolidation following Azacytidine - Venetoclax Induction Therapy in Previously Untreated Adult Acute Myeloid Leukemia Patients Unfit for Intensive Chemotherapy - A Pilot Study

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Background

Acute myeloid leukemia (AML) predominantly affects the elderly, posing challenges in treatment due to comorbidities and age-related factors. Azacitidine and venetoclax have shown promising results in older or unfit AML patients. However, the feasibility and efficacy of consolidative therapy with high/intermediate-dose cytarabine (HIDAC/IDAC) following azacitidine and venetoclax induction in this population remain unexplored. Cytarabine consolidation remains relevant in most of the low-middle income countries, as bone marrow transplantation is not always feasible.

Methods

This ambispective non-randomized interventional study was designed to evaluate the feasibility and outcomes of azacitidine and venetoclax induction followed by HIDAC/IDAC consolidation in previously untreated, unfit AML patients. Consolidation with HIDAC/IDAC was offered to those achieving remission. Primary objectives included overall survival (OS) and progression-free survival (PFS), while secondary objectives encompassed comparison with continuous azacitidine and venetoclax therapy and barriers to administration of HIDAC/IDAC consolidation.

Results

During the study period, out of 151 AML patients admitted, 47 deemed unfit for intensive chemotherapy received azacitidine and venetoclax (AZA-VEN) induction therapy, with 75% presenting baseline infections. Twenty-two patients achieved remission, of whom 9 received HIDAC/IDAC consolidation, while 13 continued AZA-VEN therapy. With a median follow-up of 14 months, the median OS was 24 months in the Aza-Ven group and not reached in the Aza-Ven-HI/IDAC group (P=0.9840). The MRD negativity rate in the Aza-Ven-HI/IDAC group increased from 33% to 45%, while in the Aza-Ven group it rose from 15% to 31%. The relapse rate was 44% in Aza-Ven-HI/IDAC (median time=9 months) vs. 31% in Aza-Ven (11 months). The main reason for not administering HI/IDAC was higher age/multiple comorbidities.

Conclusion

Among unfit treatment naive AML patients, who achieve remission with AZA-VEN, there was no significant difference in OS and PFS between those treated with HIDAC/IDAC consolidation and those receiving continuous AZA-VEN therapy.

Dr J C Patel Award Paper Presentations JCP-2

Utility of flow cytometry combined with fine needle aspiration cytology in extramedullary hematolymphoid lesions – a cross-sectional study

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Background

The utility of FNAC in diagnosing and subclassifying hematolymphoid lesions is less established. Thus, flow cytometry can be used as an adjunct to FNAC.

Aims and Objective

To assess the diagnostic accuracy of fine needle aspiration cytology

combined with flow cytometry in confirming and categorizing hematolymphoid lesions in

comparison with the gold standard.

Material and methods

This was a cross-sectional study. All patients with suspected

hematolymphoid lesions (both nodal and extranodal lesions) and reactive lesions were enrolled in the study. Combined FNAC/FCM diagnosis was compared with the gold standard, either biopsy, cell block, or flow cytometry of peripheral blood/bone marrow aspirate.

Results

The study included 67 suspected lymphoma cases and 67 reactive cases.

Twenty-nine cases yielded non-contributory flow cytometry findings. In the lymphoma

group, 10/67 cases were extranodal. 4 out of 67 cases had discordant findings between FNAC and FCM. 5/56 cases had discordant findings between combined FNAC/FCM and the gold standard. We were able to subclassify according to WHO based on morphology alone (FNAC) in 11/67 cases and in 34/67 cases based on combined FNAC/FCM. Of 67 reactive cases, five cases had discordant findings between FNAC and flow cytometry. Diagnostic sensitivity and specificity of combined FNAC/FCM was 86.7% and 98.4%, respectively. Non-contributory FCM was attributed to significant cells/ necrosis/ NLPHL/ metastasis/Castleman disease/ technical problem.

Conclusion

Combining FCM with FNAC enhances diagnostic accuracy and helps subclassify lymphoma. In future, this can replace excision biopsy, especially in recurrent cases.

Key words : Fine needle aspiration cytology (FNAC), flow cytometry (FCM), hematolymphoid lesions, extranodal

Dr J C Patel Award Paper Presentations JCP-3

Integrated pediatric intensive care and hematopoietic stem cell transplantation service improves the peri- transplant survival in children.

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Background

Peri-transplant is a critical period which is associated with a myriad of complications that require pediatric intensive care unit (PICU) referral. PICU outcomes have been historically poor post hematopoietic stem cell transplantation (HSCT), especially when associated with inotrope support, invasive ventilation and renal replacement therapy. The study aimed to assess the outcomes of PICU referral in children undergoing HSCT.

Patients & Methods

A retrospective analysis was performed, of children between 1 to 18 years of age who underwent HSCT between 2016 to 2023. A Clinical Deteriorating Event (CDE) was defined as an unplanned transfer to the ICU or requiring ICU-level intervention on the floor. The reason for PICU referral, place of intervention, cause for the CDE, and requirement of respiratory, renal, and cardiac support were noted. The study period was divided into two 4-year intervals to assess change over time, 2016- 2019, and 2020- 2023.

Results

In an 8-year period, a total of 934 HSCTs were performed, with 272 patients requiring PICU referral. A total of 415 CDEs were recorded. CDEs for PICU referrals were hypotension (43%), disproportionate tachycardia (42%), respiratory distress (26%), hypertension (22%), altered sensorium (8%), seizures (7.4%), and major bleeds (7.3%). Overall peri-transplant survival was 73.8% (n = 201/272). Comparing the two study intervals, 2016 – 2019 and 2020 – 2023, the survival of patients on mechanical ventilation had improved from 4.5% to 27.5% ($p = 0.005$) and from 39.4% to 55.9% ($p = 0.11$) among those who received inotropes. Patients with three organ dysfunctions had worse outcomes. Disproportionate tachycardia [OR 0.19 CI 95% (0.06 – 0.64); $p = 0.008$], hypotension [OR 0.177 CI 95% (0.04 – 0.84); $p = 0.029$] and acute GVHD [OR 28.46 CI 95% (3.66 – 221); $p = 0.001$] were significant risk factors for peri-transplant mortality as per multivariate analysis.

Conclusion

Integrated care with the PICU team is the first step towards improving survival in these critically ill children. With timely intervention on the floors for CDEs and protocol-driven care in the PICU, we have demonstrated an increase in overall survival over the past four years and would recommend similar team-based care for units catering to children.

Key words: PICU; HSCT; children; survival; outcome

Dr J C Patel Award Paper Presentations

JCP-4

Outcome of Low Dose Azacitidine in Patients of Lower Risk Myelodysplastic Syndromes

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Introduction

Myelodysplastic syndromes (MDS) are clonal haematopoietic stem cell disorders characterised by dysplasia leading to cytopenias and a high probability of progression to acute myeloid leukaemia (AML). In 2004, the US Food and Drug Administration approved the hypomethylating drug azacitidine for the treatment of MDS.

Rationality of the study

Most strategies in lower-risk MDS (LR-MDS) have focused on improving transfusion requirements or are only active in a small subset of patients. Given the poor prognosis of a fraction of LR-MDS patients, strategies that could alter the natural history and improve overall survival are needed. Hypomethylating agents like azacitidine are an emerging option in improving overall survival in lower risk MDS. There is scarcity of this data in our population, so this study will assess the responses of low dose azacitidine in patients of LR-MDS.

Aims and Objectives

Overall objective was to assess the responses of low dose Azacitidine in patients of lower risk myelodysplastic syndromes

Primary specific objective of the study was to assess the overall response (complete response, partial response, marrow complete response, hematological improvement, stable disease, failure), and secondary specific objectives were to assess transfusion dependency, overall survival, and ECOG performance status.

Materials and Methods

This was a prospective observational study of 20 LR-MDS cases over a study period of 18 months **(January 2023 – June 2024)** in the Department of Hematology, Nil Ratan Sircar Medical College and Hospital, Kolkata, India. All patients received subcutaneous azacitidine at 75 mg/m2 for three days in every four weeks for six cycles and were followed up for another six months.

Results

The median age was 53.5 years, with 65% (n = 13) of the study population being in the 41-60 years age group. Male: female ratio 1.85:1.

As per WHO 2016 classification, six patients (30%) had MDS-SLD (single lineage dysplasia), 11 patients (55%) had MDS-MLD (multilineage dysplasia), two patients (10%) had MDS-RS-SLD (ring sideroblast-single lineage dysplasia), and one patient (5%) had MDS-EB1 (excess blasts 1).

Five patients (25%) were in the low-risk, and 15 patients (75%) were in the intermediate-risk IPSS-R category. Good cytogenetics was present in 16 patients (80%), and four patients had intermediate cytogenetics (20%). Normal cytogenetics was present in 60% of patients, followed by Del 12q in 15% of patients. Del 7q and Gain 8 were each present in 10% of patients. One patient had Del 20q (5%).

At the end of the study period, 11 patients (55%) showed an overall response. Four patients (20%) showed a complete remission, three patients (15%) showed partial remission, four patients (20%) showed marrow complete remission, and 11 patients (55%) showed haematological improvement.

By using the paired t test, it was found that the mean deviation rise of hemoglobin (1.52 g/dl) and absolute neutrophil count (630.55/cmm) at 6 months was higher compared to baseline (P value ≤ 0.05).

By using an independent T test, it was observed that a better overall response was achieved among patients with a higher baseline platelet count (mean ± standard deviation = 157000 ± 104035.57) (P value ≤ 0.05).

Coming to ECOG performance status, 62.5% of the patients had improvement in ECOG status after six cycles of low-dose azacitidine.

At baseline, 18 patients with LR-MDS (90%) were transfusion dependent. After 6 cycles of low-dose azacitidine therapy, 10 out of 18 patients (55.6%) were transfusion-independent. Myelosuppression and infections were observed in 35% and 25% of the patients, respectively.

One-year overall survival was 95% (n = 19). The Kaplan-Meier curve for survival analysis was done with a single intervention, which showed one death at 8 months (due to intracerebral hemorrhage) among 20 participants. Estimated mean survival time was 11.8 months

Discussion and relevance to Indian context:

Study	Azacitidine duration of therapy per 28-day cycle (Days)	Number of azacitidine cycles	ORR (%)	OS (%)
Jabbour E et al (2017)	3	9	49	100
Musto P et al (2010)	5	7	45.9	71
Filic et C (2013)	5	8	47	72
Falantes J et al (2015)	7	8	40.7	62
Present study	3	6	55	95

Table 1: Comparison of the results/outcome of the present study with different other studies published in literature

Conclusions

Azacitidine can be a cost-effective treatment for transfusion-dependent LR-MDS, particularly in an emerging market and mid-income economic country like India. An overall response and one-year overall survival were achieved in 55% and 95% of the patients, respectively. Transfusion independence and improvement in ECOG performance status were achieved in 55% and 62.5% of the patients, respectively, at the end of the study period. Azacitidine is a safe drug with only minor adverse effects. The present study had a couple of limitations. The current study included only a limited number of patients, and six cycles of azacitidine were given in this study with short-term follow-up. Studies with a larger number of patients and a longer duration of follow-up are required to understand the effectiveness and duration of low-dose azacitidine in patients of LR-MDS patients to achieve a sustainable overall response.

Dr J C Patel Award Paper Presentations

JCP-5

Highlighting clinical utility of digital MLPA in detecting genomic lesions in pediatric B-ALL along with correlation of ploidy abnormalities with FISH and or DNA ploidy index

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Introduction

Current study was planned with an aim to compare and evaluate the clinical utility of Digital MLPA in detecting genomic lesions and correlate the ploidy abnormalities with FISH and or DNA ploidy index in pediatric B-ALL.

Materials & Methods

Pediatric B-ALL (0-12 years) cases were prospectively enrolled and underwent primary genetic abnormality testing by FISH, DNA index-based ploidy and targeted NGS. In addition, all cases were analysed for CNAs using Digital or conventional MLPA and data was analyzed using Coffalyser.Net and normalized dosage quotient (DQ) scores calculated.

Results

A total of 207 pediatric B-ALL cases were enrolled over 2-year period. The median age was 4.2 years with M:F ratio 1.7:1. A primary genetic abnormality was noted in 87% (181/207) cases with high hyperdiploidy being the most common (31%). The overall CNA frequency was 54% (112/207) with CDKN2A/2B deletion being most common (28.5%). DigitalMLPA was performed for 185 cases; data from FISH and DNA index-based ploidy revealed: 141 (76%) had a primary genetic abnormality, while 44 (24%) were negative. DigitalMLPA identified additional genetic abnormalities in 8/44 (18%) cases, including DUX4-r (4 cases), PAX5-amplification/ITD (2 cases), CRLF2-P2RY8 (1 case), and ETV6 RUNX1-like (1 case). Two samples did not yield digitalMLPA data, hence the concordance of digitalMLPA with ploidy abnormalities accounts for 46% (84/183) and concordance of digitalMLPA with copy number abnormalities accounts for 58% (106/183).

Conclusion

The study clearly shows there is a good concordance of digitalMLPA with FISH and DNA index-based ploidy. However, the cost and turnaround time of utilizing digitalMLPA as robust method to detect CNAs should be worked out before implementing it as a routine clinical testing in B-ALL cases.

Benign Hematology-laboratory (BHL) OP-BHL-1

Development of a Client Server Architecture Based, Multiuser, Graphical Flow Cytometry Analysis Software with Higher Dimensional Clustering Capabilities: A Make in India Initiative

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Introduction

Flow cytometric software is limited by their adherence to a specific platform or operating system. The chief difficulty in developing a platform independent, client-server architecture based analyser is the transfer of large flow cytometry standard (FCS) files - with millions of events - over a network.

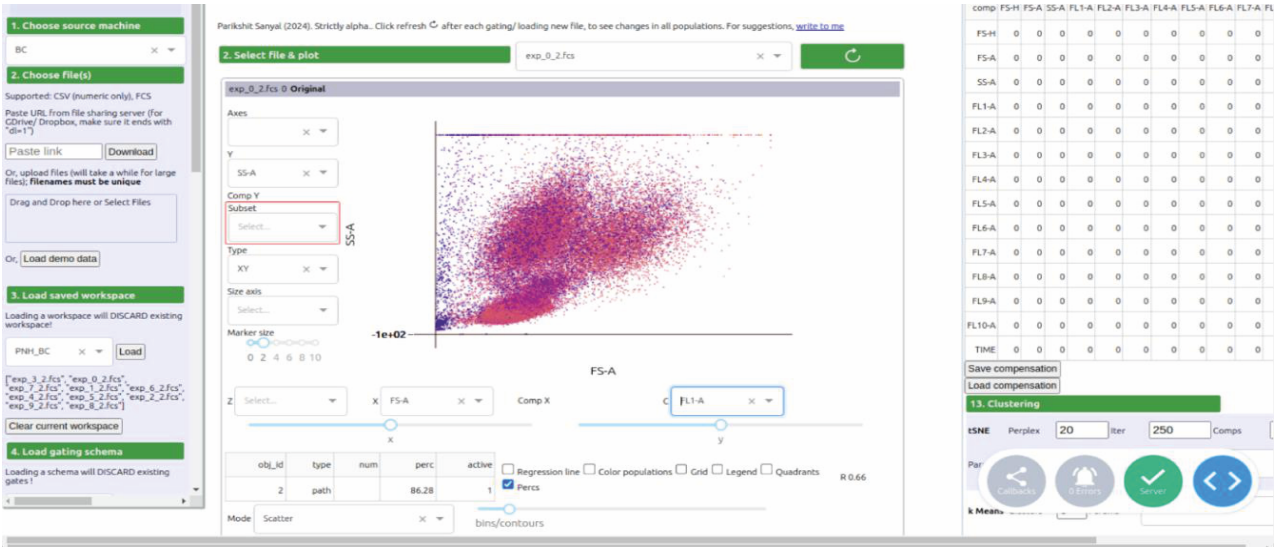
Aims & Objectives

To develop a flow cytometric analysis software which can be run remotely from a browser on client-server mode and can transfer large quantities of event data over a network through clustering/ dimensionality reduction.

Materials & Methods

Pramā, the analysis software, was built with the Dash web application platform on the Python programming language. The sequential gating model – standard for flow cytometry analysis software - has been fully implemented. Multiple files can be analysed at a time, and geometric gates (ellipses, rectangles, polygons and histogram gates) work as expected. Standard plotting modes such as scatter, density and contour have been added. Effectively, a linear workflow was created for analysis of flow cytometric data similar to industry standard flow cytometric analysis software, but inside a browser. Next, options to to reduce data/ dimensions for to-and-fro transfer over a network were implemented. In addition, several machine learning algorithms have been included: a k-means clustering algorithm, t-distributed stochastic neighbourhood embedding (tSNE) & prinicpal component analysis (PCA) - to reduce the entire dataset to lesser dimensions. Lastly, we added options to save gating schemas and workspaces so that experiments can be retrieved later.

We validated Pramā by comparison with industry standard software such as Kaluza (Beckman Coulter). Ten (10) anonymised samples from multicolor flow experiments, recovered from the archives of the laboratory, were analysed with both Industry standard software and Pramā.



Result

More than 98% concordance was achieved between Pramā and industry standard software. In addition, the n-dimensional k-means clustering algorithm displayed the ability to reduce the dataset without loss of information, as well as automatically segment cell populations close to their biologic characteristics. Three (03) hematopathologists have independently reviewed Prama and assessed its usability as satisfactory.

Conclusion

Pramā shows promise as an independent, browser based flow cytometric analysis software that can be implemented on a client-server basis for an entire laboratory/ hospital.. However, before implementing Pramā in a flow cytometry laboratory, extensive testing and validation studies are required.

Benign Hematology-laboratory (BHL) OP-BHL-2

HLA-DR Expression in T Cell Subsets in Hemophagocytic Lymphohistiocytosis

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Introduction

T lymphocytes play a crucial role in the pathogenesis of Hemophagocytic lymphohistiocytosis (HLH), with Human Leucocyte Antigen-DR (HLA-DR) expression on T cells serving as a key marker of immune activation. Increased HLA-DR expression indicates hyperactivation of T cells, contributing to the cytokine storm and tissue damage characteristic of HLH.

Aims & Objectives

To compare surface activation marker HLA-DR on various T cell subsets in patients of HLH and healthy children and to establish diagnostic cut-offs to differentiate between them.

Materials & Methods

Retrospective observational study which included patients of primary HLH (n=18), secondary HLH (n=13) and healthy controls (n=31) aged less than 16 years. The FCS files from screening ten color panel of children suspected of inborn error of immunity (IEI) and healthy controls which included expression of HLA-DR were retrieved from the archives of a National Research Institute. HLA-DR expression on different T lymphocyte subsets was analyzed and compared between HLH patients and healthy controls using unpaired two-tailed t-test. Receiver Operating Characteristic (ROC) curves were used to establish diagnostic cut-offs.

Result

HLA-DR expression was significantly higher on various T cell subsets in HLH patients compared to healthy controls. Lack of increased HLA-DR expression on T cell subsets effectively excluded HLH with high specificity. Notably, HLA-DR expression on the T helper memory subset was significantly different between primary and secondary HLH ($p=0.03$).

Conclusion

Elevated HLA-DR expression on T cell subsets is a distinguishing feature of HLH. These findings highlight the potential of HLA-DR expression as a diagnostic and prognostic marker in HLH.

Benign Hematology-laboratory (BHL) OP-BHL-3

An Observational Study on The Variability of Nutritional Status and its Impact on Outcomes in Recipients of Haematopoietic Stem Cell Transplant

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Introduction

Various factors like the underlying disease, conditioning regimens, infections and graft versus host disease lead to malnutrition in recipients of Hematopoietic Stem Cell Transplant. Malnutrition in turn leads to increased risk of transplant-related complications, prolonged hospitalisation, increased cost of treatment and higher incidence of morbidity and mortality.

Aims & Objectives

The present study aims to study the variability of nutritional status during the pre-and post-transplant period, factors influencing the same and the impact of malnutrition on transplant outcomes.

Table 1: Weight percentage and calorie intake difference at various time points

Day	n	Mean % weight change from baseline	Mean difference in calorie intake from baseline
Day 0	50	-1.8	-335
Day +7	49	-3.4	-441
Day +14	47	-5.11	-389
Day +21	46	-6.87	-229
Day +30	22	-7.65	-209
Day +60	21	-7.6	-78.9

Materials & Methods

This was a prospective and retrospective observational study in the department of Clinical Haematology at Christian Medical College, Ludhiana. Baseline demographic and transplant details were collected for all the patients. Weight and average calories consumed were checked at different time points post-transplant. Other parameters, including documented infections, mucositis, acute GVHD, length of hospital stay, and non-relapse mortality, were also assessed for their correlation with nutritional status.

Result

A total of 50 subjects (26 prospective and 24 retrospective) were analysed. Majority (62%) had normal baseline nutritional status. Mean percentage weight change showed a declining trend post-transplant with maximum change at Day+30 (-7.65%). Maximum decline in mean calorie intake was seen on Day +7 (-441 Kcal, -29%) (Table 1). Repeated measures ANOVA test showed a significant change in weight from baseline till Day +60 ($p<0.001$); and calories till Day +14 ($p<0.001$). Weight loss at Day +60 was significantly higher in patients with viral infections (-14.7% vs -5.4%, p-value: 0.03). Similarly, change in calorie consumption from baseline at Day 0 (-30.4% vs 9.9%, p-value<0.001), Day +21 (-24.5% vs +16.5%, p-value<0.01) and Day +60 (-12% vs 26.2%, p-value: 0.02) was significantly higher in patients with bacterial infections. No statistically significant association was seen between nutrition and incidence of mucositis, GVHD and overall survival.

Conclusion

Early intervention aimed at better enteral and parenteral nutrition in the peri-transplant transplant period can help in minimizing the weight loss and calorie deficit which can improve the outcomes and quality of life of the transplant recipients.

Benign Hematology-laboratory (BHL) OP-BHL-4

A Retrospective Study of the Clinical Outcomes of Extracorporeal Photopheresis in Patients with Steroid Refractory or Dependent Graft-versus-host Disease

Yash Shailesh Patel
Uday Kulkarni, Aby Abraham, Biju George,Vikram Mathews,Anu Korula,Sushil Selvarajan

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Introduction

There is paucity of real-world data on the use of extracorporeal photopheresis (ECP) for treatment of graft-versus-host-disease (GVHD).

Aims & Objectives

To describe the clinical outcomes of ECP in patients with steroid refractory or steroid dependent GVHD at our centre.

Materials & Methods

We conducted a retrospective analysis using hospital records of patients who were treated with ECP between 1.4.2023 to 10.9.2024. One cycle ECP constituted of 2 consecutive day procedure once a week. Response assessment was done at the end of 1 month.

Result

During the study period, 12 patients were treated with ECP. Median age of patients was 25 years (7 to 58 years), 50% were males. 11 had acute GVHD and one had chronic GVHD. Median duration between start of steroids and ECP in steroid-refractory acute GVHD was 12 days (6- 14). All patients with acute GVHD had Grade IV disease, ten were steroid-refractory and one was steroid-dependent. Five of them responded, one had no response, and response was not assessable in the remaining five. Of the responders, 3 achieved complete response (CR) and 2 achieved partial response (PR). They received 4 cycles before assessment except one who received 3 cycles, achieved CR and stopped subsequently due to financial constraints. The patient with no response received 3 cycles, following which she developed cytopenia, Candida sepsis and expired. 5 patients were not assessable as three of them expired after 1 cycle of ECP (due to GVHD and infective complications), one patient took discharge against medical advice due to worsening of GVHD. One patient is still undergoing treatment (3 cycles completed). Maintenance ECP (one session every fortnightly) was continued in one patient with CR and one patient in PR. The patient with chronic GVHD had steroid dependent severe GVHD with multiple organ involvement. He was treated with one cycle every 2 weekly for 5 cycles, achieved PR, continued maintenance ECP for 4 more cycles and achieved CR. He is currently well at 15 months of follow up.

Conclusion

ECP in another available option for patients with steroid-refractory or dependent GVHD though cost constraints limit wider access.

Benign Hematology-laboratory (BHL) OP-BHL-5

Real World Data on The Use of Extracorporeal Photopheresis for the Treatment of Graft Versus Host Disease

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Christian Medical College, Vellore

Introduction

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TABLE 1 – BASELINE AND DEMOGRAPHIC DATA OF PATIENTS TREATED WITH STEROID REFRACTORY OR STEROID DEPENDENT GVHD TREATED WITH ECP

Patients, n	12
Sex, male(%)	6(50%)
Median age in years	25 (7 to 58)
Disease, n	
MDS(Myelodysplastic syndrome)	3
AML(Acute myeloid leukemia)	2
ALL(Acute lymphoblastic leukemia)	2
CML(Chronic myeloid leukemia)	1
VSAA(Very severe aplastic anemia)	2
Adrenoleukodystrophy	1
Beta thalassemia major	1
Donor type, n	
Matched related	4
Matched unrelated	4
Haplo-identical	4
Type of GVHD, n	
Acute	11
Chronic	1
Acute GVHD grade, n(%)	
Grade IV	11(100%)
Number of organs involved in Acute GVHD, n(%)	
1	4(36.4%)
2	7(63.6%)
Organs involved in Acute GVHD, n	
GUT	4
GUT and Skin	6
GUT and Liver	1
Steroid status in Acute GVHD, n(%)	
Steroid refractory	10(90.9%)
Steroid dependent	1(9.1%)
ECP cycles in acute GVHD prior to 1st assessment, n	
1	4
3	3
4	3
Response assessment after 1 month in acute GVHD, n	
Complete response (CR)	3
Partial response (PR)	2
No response(NR)	1
Not assessable (NA)	5
Number of organs involved in Chronic GVHD, n(%)	
4	1(100%)
Chronic GVD severity, n(%)	
Severe	1(100%)
Organs involved in chronic GVHD, n	
Liver + Lung + Skin + Eyes	1
Steroid status in Chronic GVHD, n(%)	
Steroid dependent	1(100%)
ECP cycles in Chronic GVHD prior to 1st assessment, n	
5	1
Response assessment at 3 months in chronic GVHD, n	
PR	1
Patients treated with maintenance ECP, n	
Acute GVHD	2
Chronic GVHD	1
Time between onset of GVHD and start of ECP (in steroid refractory acute GVHD), n	
<7 days	1
8 to 10 days	2
11 to 13 days	5
>=14 days	1
Immunosuppressants within 2 weeks of ECP (for steroid refarctory aGVHD), n	
Ruxolitinib	9
Sirolimus	5
Etanercept	6
Basiliximab	2
Median counts before starting ECP(Range)	
Hb(in g%)	10.2(8.1 to 13.2)
WBC(per cumm)	6900(4200 to 26200)
Platelet(per cumm)	57000(3000 to 420000)
Complications with ECP, n	
Catheter related thrombosis	1
Catheter related blood stream infection	1
Infective complications with concomitant immunosuppressants, n	
Clostridium difficile	4
CMV reactivation	6
Blood culture positive	3
Lowest WBC counts within 1 month of starting ECP in cells/cumm, n	
<=500	4
501 to 1000	2
1001 to 2000	4
2001 to 4000	2
Median duration of follow up of surviving patients (Range)(in months)	6 (1 to 15)
Cause of death, n	
Infection	2
Both GUT GVHD and infection	3

fortnightly) was continued in one patient with CR and one patient in PR.

The patient with chronic GVHD had steroid dependent severe GVHD with multiple organ involvement. He was treated with one cycle every 2 weekly for 5 cycles, achieved PR, continued maintenance ECP for 4 more cycles and achieved CR. He is currently well at 15 months of follow up.

Conclusion

ECP is another available option for patients with steroid-refractory or dependent GVHD though cost constraints limit wider access.

Benign Hematology-laboratory (BHL) OP-BHL-6

Donor Specific Antibodies in Haploidentical Hematopoietic Stem Cell Transplant – A Retrospective Study

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Introduction

Haploidentical hematopoietic stem cell transplant (Haplo-HSCT) is used for patients with hematological diseases lacking a matched sibling or unrelated donor. One limitation is the presence of donor-specific antibodies (DSA) in recipients, which can delay engraftment and cause graft failure.

Aims & Objectives

To define demographic characteristics of patients undergoing DSA estimation and tabulate underlying diseases. To report DSA incidence and significant titers. To formulate strategies to tackle significant DSA.

Materials & Methods

We retrospectively analyzed patients referred for Haplo-HSCT between 2022 and 2024. Data on demographics, primary disease, and DSA estimation were collected. DSA levels were measured using a multiplex assay and reported as median fluorescence intensity (MFI). MFI > 1000 was considered positive; MFI > 5000 indicated desensitization need.

Result

Thirteen patients were included: 6 males (46.15%) and 7 females (53.84%); 12 pediatric (92.30%) and 1 adult (7.70%). MFI ranges noted in patients for different donor categories were: Class I DSA: 190-4213 (average: 1389.89) Class II DSA: 179-6195 (average: 2433.89). DSA titers: Male donors (n=8): Class I 190-3628 (average: 1420.87); Class II 179-6195 (average: 2469.12). Female donors (n=11): Class I 276-4214 (average: 1367.33); Class II 186-5335 (average: 2408.27). Maternal donors (n=9): Class I 276-4213 (average: 1500.44); Class II 186-5335 (average: 2836.22). Paternal donors (n=5): Class I 190-3628 (average: 1924.6); Class II 179-6195 (average: 3468.20). Sibling donors (n=4): Class I 267-829 (average: 548); Class II 537-3782 (average: 1367.75). Out of 13 patients, 5 (38.46%) were positive for Class I DSA, none with MFI > 5000, and 7 (53.84%) were positive for Class II DSA, with 3(23.07%) patients having MFI > 5000, necessitating desensitization.

Conclusion

Patients had comparable DSA titers against male and female donors, with higher titers against paternal donors. Sibling donors had the lowest titers. Significant DSA titers were found in 23.07% of patients, requiring desensitization

Benign Hematology-laboratory (BHL) OP-BHL-7

The Role of Cytogenetic Aberrations on Risk Assessment and Prognosis in Myelodysplastic Syndromes

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Introduction

Myelodysplastic Syndromes (MDS) are a heterogeneous group of clonal hematopoietic stem cell disorders characterized by ineffective hematopoiesis, peripheral blood cytopenias, and a heightened risk of progression to acute myeloid leukemia (AML). This study analyses cytogenetic abnormalities in MDS patients and their impact on prognosis and treatment.

Aims & Objectives

The study aims to evaluate the frequency of cytogenetic abnormalities, age distribution, gender prevalence, clinical parameters, prognostic risk scores, treatment modalities, and survival outcomes in MDS patients. The key objectives include assessing the impact of cytogenetic profiles on prognosis and identifying effective treatment strategies.

Materials & Methods

134 MDS patients were analyzed using conventional karyotyping and FISH to detect chromosomal abnormalities. Patients were stratified using the IPSS-R, and survival outcomes were analyzed with Kaplan-Meier methods. Statistical correlations between age, cytogenetic abnormalities, and clinical parameters were evaluated using mixed-model ANOVA.

Result

Out of 134 MDS patients, 68 (50.7%) were cytogenetically positive and 66 (49.3%) were negative. The most prevalent abnormalities among cytogenetically positive patients included del(5q) in 22 (16.4%) patients, 7/del(7q) in 19 (14.2%), trisomy 8 in 7 (5.2%), del(20q) in 6 (4.5%), complex abnormalities (>3) in 7 (5.2%), and other abnormalities in 7 (5.2%). The cohort comprised 84 (62.7%) males and 50 (37.3%) females, with a mean age of 60 years. Significant correlations ($p < 0.001$) were found between age and clinical parameters such as bone marrow blast percentage, hemoglobin, platelet count, and absolute neutrophil count. Patients with cytogenetic abnormalities had a mean Leukemia-Free Survival (LFS) of 3±1.8 years and Overall Survival (OS) of 3.3±1.9 years. OS was highest in patients with Y chromosome deletions (5.3 ± 1.4 years), followed by 5q deletions (4 ± 0.5 years). Azacitidine and Decitabine resulted in lower hazard ratios (1.7 and 1.9, respectively), indicating improved survival outcomes.

Conclusion

Cytogenetic profiles are vital prognostic factors in MDS, significantly influencing survival outcomes. This study underscores the importance of comprehensive cytogenetic profiling combined with clinical parameters for personalised treatment. Combining hypomethylating agents with other therapies offers promising survival benefits. Future research should integrate molecular genetic techniques involving NGS to elucidate MDS pathogenesis further and improve treatment strategies.

Benign Hematology-laboratory (BHL) OP-BHL-8

Haematopoietic Stem Cell Transplantation in Inherited Bone Marrow Failure Syndromes: A Tertiary Care Center Experience

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Introduction

Inherited bone marrow failure syndromes (IBMFS) are genetic disorders characterized by cytopenias and increased malignancy risk. Hematopoietic stem cell transplantation (HSCT) is a key treatment option, but outcomes can vary significantly due to complications like opportunistic infections and hemorrhage, which are common in IBMFS patients.

Aims & Objectives

This study aims to document

- Demographic and clinical profile
- Transplant characteristics- including donor type, stem cellsource and dose, conditioning regimens, and GVHD Prophylaxis
- Transplant related complications – including GVHD, infections , graft failure, secondary malignancy

Materials & Methods

STUDY TYPE: Retrospective observational study

STUDY POPULATION: Patients diagnosed with IBMFS who underwent HSCT

STUDY CENTRE: Advanced Centre for blood and Marrow transplant,Department of Clinical Haematology,Madras Medical College,Chennai ,Tamilnadu

STUDY DURATION: AUG 2022 to AUG 2024.

INCLUSION CRITERIA: Patients with diagnosed IBMFS who underwent HSCT

EXCLUSION CRITERIA: Aplastic anaemia patients with mutations which are not associated with IBMFS.

Data were collected on Demographics, Clinical Diagnosis, Transplant characteristics and related complications

Result

Analyzed 16 patients who underwent transplantation for IBMFS.The cohort consisted of 8 males and 8 females with a median age of 5-25 years.

DIAGNOSIS: A total of 11 patients had Fanconi Anemia,3 had Dyskeratosis congenita and 2 were diagnosed with rarer forms of IBMFS: Braddock-Carey syndrome (KIF mutation) and Bone Marrow Failure syndrome-2 (ERCC6L2).

TRANSPLANT CHARACTERISTICS:Matched sibling donors (43%), matched unrelated donors (37%), and matched related donors (18%) were used, all with reduced-intensity conditioning.In the cohort 69% received cyclosporine and methotrexate for GVHD prophylaxis. 31% of patients switched to sirolimus due to acute kidney injury.

COMPLICATIONS:Acute GVHD(Grade 3) &chronic GVHD occurred in 18% patients

One patient turned HBsAgpositive.Three patients (18%) tested positive for BK virus and CMV reactivation with no primary graft failure reported

MORTALITY:4 patients succumbed to their disease

CAUSES:Intracranial hemorrhage(D +5),Fungal pneumonia and multi-organ dysfunction (D +6),Squamous cell carcinoma of the tongue (D +668)and AML transformation (D +210)

Conclusion

This study emphasises the critical need for early transplant, optimized conditioning regimen, donor selection, monitoring for transplant related complications for achieving long-term survival in IBMFS patients.

Benign Hematology-laboratory (BHL) OP-BHL-9

Design, Fabrication, And Characterization of A Paper-Based Microfluidic Device For Serum Multi-Nutrient Assay By Colorimetry

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Introduction

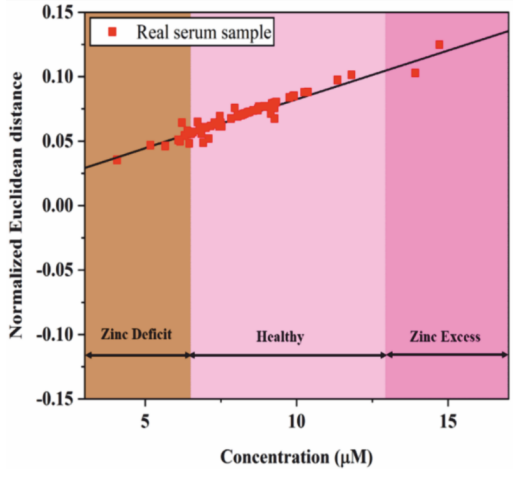
Rapid screening became an indispensable element of community health care, especially in resource-constrained environments. Micronutrient deficiency has emerged as a substantial public health concern and among them Zinc and magnesium are considered essential elements for both mental and physical functioning. Herein, we attempt to develop, for the first time, a multiplexed device for the detection of zinc and magnesium for a combined population-wise mapping of the micronutrients.

Aims & Objectives

This study involves the fabrication of a paper-based microfluidic device for the quantitative determination of zinc and magnesium in blood serum for different physiological levels. The hydrophobic barriers needed for these devices are fabricated using commercial desktop printers. The images of the reaction zones are captured using a mobile phone camera and the intensity of the digitized image are correlated to the concentrations.

Materials & Methods

1. Whatman grade 1 filter paper is used for the paper-based microfluidic device with hydrophobic barriers fabricated in the form of spotting wells using an HP LaserJet Pro 400 series printer.
2. The wells are soaked with 3 µL acetate buffer (6.3 M, 4.5 pH) to maintain an acidic environment. The wells are allowed to dry in ambient conditions for 30 mins before spotting them with 1 µL of 1.95 mM dithizone.
3. Dithizone reacts with zinc in stoichiometric proportions to form pink-colored zinc dithizonate and the color intensity systematically changes with the zinc concentration.
4. We have initially standardized the process with aqueous solutions of ZnCl2 over the physiological concentration range (i.e., 5-25 µM) with an increment of 2 µM, followed by zinc in artificial plasma to formulate calibration curves and then real blood serum samples are tested. 4 µL real blood serum are spotted in the µPAD and allowed to react and dry for 30 mins.



5. We have designed an automated image analysis application program in the MATLAB platform.

Result

1. An average absolute error of 5.06% suggests the potential of the μPAD in serum zinc assay with a resolution of 2 μM to differentiate between the healthy and zinc deficient population groups.

2. Sensitivity and specificity of the device are found to be 95% and 76%, respectively. Moreover, the method is also found to be 97

Conclusion

The method is straightforward, rapid, cost-effective, and does not require any complex equipment or fabrication protocol. Thus, its potential in point-of-care testing is worthy of further clinical trial.

Benign Hematology-laboratory (BHL) OP-BHL-10

Unacceptable Results for Microscopic Peripheral Smear Examination – A Participating Laboratory Analysis

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Introduction

Peripheral smear (PS) a basic morphological, qualitative, subjective test. Its external quality assessment (EQA) requires specific alternate method interlaboratory comparison as per ISO 15189:2012. Z or Q score cannot be applied for this test. Unacceptable or outwith consensus result (numerical or non-numerical) value not in agreement with other peer group subjects. Such results root cause analysis needs to be done.

Aims & Objectives

Root cause analysis unacceptable results of peripheral smear. Assess performance of laboratory.

Materials & Methods

EQA results of 10 years from January 2014 to June 2024 reviewed retrospectively, data collected for PS diagnosis. Every year there are four surveys of EQA programme. A Romanwasky stained PS, relevant history, hemoglobin value, total leucocyte count and platelet count are disclosed to all participants enrolled in EQA. The red blood cell morphology, differential count of white blood cells and provisional diagnosis is submitted by the participating laboratory. Acceptable, partially accepted or unaccepted method is used to define the performance of laboratory. EQA report reveals the final diagnosis.

Result

78 PS EQA survey results of the laboratory and final diagnosis report were analysed. Of 450 participating laboratories 8-10% laboratories do not submit the result. The most common diagnosis encountered was chronic myeloid leukaemia (CML) followed by acute leukaemia (AL), hereditary spherocytosis (HS), chronic lymphatic leukaemia (CLL), thalassemia respectively.

For 6 (7.69%) surveys were partially acceptable, two (2.56%) unacceptable, one (1.28%) not submitted. The laboratory reported HS and thalassemia as haemolytic anaemia, unacceptable result was acute leukaemia whereas the final diagnosis was pancytopenia/MDS.

Overall performance of laboratory is 96.15%.

Conclusion

Microscopic examination of PS involves various cells, types of erythrocytes, white blood cells and its precursors, platelets and parasites. Overall performance of laboratory is 96.15%. CML and AL were used in most surveys to assess the reviewer performance. Standard terminologies need to be used by participating laboratory, with the guidance of EQA provider. Without clinical or instrument data, peripheral smear as a standalone test can clinch the diagnosis and benefit patient treatment. Hence EQA builds confidence in the reporting pathologist.

Benign Hematology-laboratory (BHL) OP-BHL-11

Bone Marrow Metastases in Solid Nonhematological Malignancies and Rank Ligand (Rankl) Expression

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Introduction

Bone marrow (BM) is one of the common metastatic sites of solid malignancies, commonest being that from breast, prostate, lungs, gastrointestinal tract, and even unknown primaries. Receptor activator of nuclear factor kappa-B ligand (RANKL) and its receptor RANK, involved in osteoclastogenesis and bone remodelling, are postulated to be the two key molecules in tumor cell proliferation, angioinvasion, and homing to BM stromal microenvironment. However, literature on RANK/RANKL immunoexpression by cancer cells in the BM is sparse and this warrants further study.

Aims & Objectives

To describe the clinico-hematological characteristics of bone marrow metastases (BMM) from solid malignancies and highlight RANKL expression by immunohistochemistry (IHC).

Materials & Methods

Immunohistochemical expression of RANKL on BM trephine biopsies was retrospectively analyzed in a series of cases with BMM and correlated with clinical, hematological, and BM morphological features.

Result

BM metastases were reported among 34 subjects over the last eight years (2016-2024) [M/F:21/13), median; 53 years (25 -78)]. Cancers from unknown primaries (32.4%), GIT (23.5%), breast (17.6%), prostate and lungs (11.8

Conclusion

RANKL expression might play a crucial role in BM metastasis in solid cancer and alteration of BM stromal microenvironment.

Benign Hematology-laboratory (BHL) OP-BHL-12

Immunophenotypic Profile in A Pediatric Patient Mimicking Malignant Lymphoproliferative Disorder

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Background

There are overlaps in the symptoms of malignant and non-malignant hematological disorders specially in pediatric population. The reactive/non-malignant lesions include lymphoid leukemoid reaction due to viral illness (EBV, Hepatitis, CMV etc) that closely clinically mimic that of malignant disorder and fall under differential diagnosis of acute lymphoblastic leukemia. The pathological findings of EBV induced IM may mimic lymphomatous spread or leukeimas. We present a case of 12-year-old child who presented with fever, pain abdomen on and off, peri orbital puffiness, distended neck veins and lymphadenopathy.

Case Presentation

A 12 year old male presented to the hematology OPD with complaints of fever, pain abdomen on and off, peri orbital puffiness, distended neck veins and lymphadenopathy. He was admitted with the clinical suspicion of acute leukemia. A peripheral smear study showed lymphocytosis with atypical lymphocytes and leucocytosis of (42,700/ µl). Ancillary hematological work up was done for BMA, BMB and sample for Immunophenotyping by flow cytometry was received. Immunophenotyping was done by flow on BD FACS lyric analyzer.

Diagnosis

Flow cytometry for Immunophenotyping was done in flow lab (FACS lyric) analyzer, where CD45/SSC graph revealed majority of gated population 90%. CD3+ out of which CD8+ T Cells increase, and CD4 cells were reduces, altering CD4/CD8 ratio (1:10) indicating proliferation of CD8+, T Cells. There was weak CD5 [removed]down regulation of CD5 cells) and strong HLA DR as well as CD38 expression. The Cells were negative for CD16, CD19, CD34 and CD56. EBV viral load testing was done and revealed 32,000 copies. Based on FCM results, final diagnosis infectious mono nucleosis was given.

Treatment

The patients of IM do not need specific treatment. Only supported therapy, prednisonole and anti-viral is given in acute cases. In our patients, symptomatic treatment for fever and prednisonle was given. The patient is doing fine now.

Follow-up

The patient was kept on follow-up with serial monitoring of blood counts and recovered within 1 month. The patient is doing well now.

Conclusion

Careful Clinico-pathological correlation is needed in the interpretation of Immunophenotypic results with EBV-IM to avoid erroneous diagnosed of LPD and hence can prevent hazardous treatment. In our case Immunophenotyping result guided to EBV infection that was confirmed by viral load studies.

Benign Hematology-laboratory (BHL) OP-BHL-13

Borderline HbA2 Levels: Are We Missing Something?

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Introduction

HbA2 levels are crucial in detection of beta thalassemia trait (BTT). However, there is a lack of unified cut off value for HbA2 to diagnose BTT. There exists a discrepancy among laboratories in different parts of the world, and even within our country. The cut off levels of HbA2 vary from ≥3.5% to ≥4.0, being in use for classifying individuals as BTT. Some studies have recommended that laboratories need to establish their own cut offs based on regional differences and ethnic populations. Thus, interpreting 'Borderline HbA2 values', especially inantenatal settings is a challenging task.

Aims & Objectives

To test for common beta thalassemia mutations (IVS-1-1 and IVS-1-5) in subjects with borderline HbA2 values (3.2-3.9%).

Materials & Methods

83 random subjects with borderline HbA2 values ranging from 3.2 to 3.9% on HPLC were selected for the study. DNA was extracted from

these blood samples using Qiagen column based method and stored at -80 degree Celsius. These samples were tested for two common beta thalassemia mutations: IVS-I-5(G>C) and IVS-1-1 (G>A) by Beta thalassemia Real Time polymerase chain reaction (PCR) kit (Helini).

Result

A beta globin gene mutation was identified in 38/67 subjects (56.7%) with borderline HbA2 levels ranging from 3.2-3.9%. PCR run showed a reaction failure in 19.2% (16/83) subjects. 36/62 (58%) cases showed mutation for IVS-1-1 (G>A), while IVS-I-5 (G to C) was mutated in 4/60 (6.6%) subjects. Of these 2/67 cases were negative for wild type IVS-1-1 (G>A) suggesting a homozygous mutation profile. A total of 24/62 (30.7%) cases with IVS-1-1 mutation in the beta globin gene, had HbA2 values in the range of 3.5-3.9%.

Conclusion

The results of this study highlight the prevalence of common beta thalassemia mutations (IVS-1-1 and IVS-I-5) in individuals with borderline HbA2 values. If a cut off of HbA2 ≥4% is used (as recommended by the NHM), we could be missing cases falling in the borderline category. Hence, mutational analysis should be advised in the setting of borderline HbA2 levels, particularly in screening of antenatal couples at risk.

Benign Hematology-laboratory (BHL) OP-BHL-14

Likelihood of Identifying a HLA-Matched Related or Unrelated Donor for Indian Patients Seeking Stem Cell Transplantation

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Sureka Rajendran, Ambily Sivadas, Kanaga Ganesan, Rubika Elumalai, Karthikeyan Ganesan, Maniraj Ramalingam, Ankur Chaturvedi, Nagarajan.M. Phani, Chirayu Padhiar, Prakash Sadashiv Gambhir.

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Introduction

Hematopoietic Stem Cell Transplantation (HSCT) is a critical therapeutic procedure for treating many life threatening haematological malignant and non-malignant disorders. Donor selection is one of the most critical factors in the success of allogeneic stem cell transplantation. Matching the human leukocyte antigen (HLA) types between the donor and recipient is key to reduce the risk of transplant rejection and complications like GVHD. Both related and unrelated donor can have a HLA match and this varies based on the race/ethnicity.

Aims & Objectives

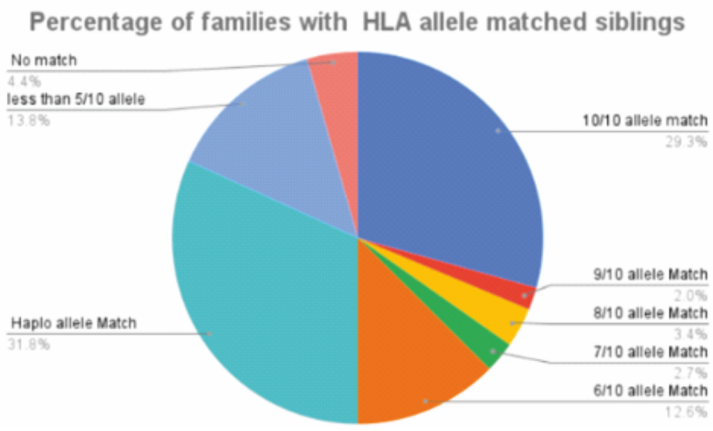
The objective of this study is to determine the likelihood of finding HLA-matched related and unrelated donors for Indian patients requiring HSCT. Additionally, the study aims to explore HLA diversity of Indian population and factors that necessitate race/ethnicity-specific donor registries.

Materials & Methods

High-resolution HLA typing for HLA-A, -B, -C, -DR, and DQB1was performed using Miafora NGS Flex5 Kit (Immucor, Inc.) and the haplotype frequencies were estimated by expectation-maximization algorithm via Arlequin software (version 3.5.2.2). Matching probabilities for 10/10 and 9/10 unrelated donors were calculated using 30,027 cord blood samples collected across India, modelled into six regional. For related donors, 406 Indian families were analyzed to determine the percentage of HLA-matched siblings.

Result

The chances of finding a 10/10 allele HLA-matched sibling donor were 29.3%, while the likelihood of finding a haploidentical sibling donor was 31.8%, leaving 4.4% of families with no HLA allele match (Fig:1) The search for unrelated donors indicates that, on average, 17.88% of the Indian population (refraining northeast population) can find a 10/10 HLA allele-matched donor. The South Indian population at the lowest match rate of 15.64% whereas the highest match rate of 22.24% was in the East Indian population, supported by a registry size of 30,000. To achieve a 50% match rate for Indian patients with the registry size would need to increase to 500,000.



Conclusion

This study highlights the challenges and opportunities in finding HLA-matched donors for Indian HSCT patients. While many families can access HLA-matched siblings, there is a pressing need for larger adult donor registries to improve the chances of finding 10/10 allele-matched unrelated donors. The low likelihood of fully matched unrelated donors due to underrepresentation and genetic diversity necessitates exploring haploidentical transplants and cord blood as alternatives

Benign Hematology-laboratory (BHL) OP-BHL-15

Utility of Neutrophil Lymphocyte Ratio (NLR) and Platelet Lymphocyte Ratio (PLR) as Biomarkers of Inflammation in Type II Diabetes Mellitus

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Introduction

Type II Diabetes mellitus (DM) is a chronic disease with high morbidity and mortality characterized by hyperglycemia due to impairment of insulin secretion, cellular resistance to insulin or both. It is known that chronic inflammation has a significant role in development and progression of diabetes mellitus as well as in the pathogenesis of micro and macrovascular complications. Neutrophil to Lymphocyte ratio (NLR) and Platelet to Lymphocyte ratio (PLR) are new inflammatory biomarkers studied widely in Type II diabetes mellitus. Their normal ranges (NLR and PLR) are 1.9 ± 0.6 and 91.77 ± 26.95 respectively.

Aims & Objectives

To analyze NLR and PLR in type II diabetes mellitus patients with/without complications.

Materials & Methods

A total of 176 patients with type II diabetes mellitus were included in this study over a period of one year. Venous blood samples were collected in K2EDTA and white blood cell count, absolute counts for neutrophils, lymphocytes and platelets were recorded using DxH hematology analyzer and NLR and PLR were calculated. Results were categorized in two groups- Diabetes with/without complications. Results were analyzed and categories were compared using Kruskal -Wallis and Mann Whitney U tests.

Result

Among the total of 176 patients of type II diabetes mellitus (with /without complications), 134 patients (76.1%) showed raised NLR ($p < 0.001$) and 127 patients showed raised PLR ($p<0.002$). NLR in the category of type II diabetes mellitus with complications was higher than that of without complications ($p<0.001$). Comparison of different categories of type II diabetes mellitus complications also showed statistical significance in NLR ($P<0.003$) but not with respect to PLR($p<0.16$).

Conclusion

This study showed increase in NLR and PLR in type II DM with/without complications. NLR and PLR tests are beneficial inflammatory markers in chronic inflammatory conditions like diabetes mellitus. This study highlights the prognostic utility and significant association of both of these parameters in type II diabetes mellitus.

Benign Hematology-laboratory (BHL) OP-BHL-16

Reference Interval for Coagulation Parameters in Non-Pregnant and Pregnant Women

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Introduction

Normal pregnancy is associated with major changes in many aspects of hemostasis, unlike healthy non-pregnant women. These changes help to maintain placental function and prevent excessive bleeding during delivery. So, the reference intervals (RI) of coagulation screening tests based on non-pregnant healthy women cannot be applied to pregnant women as they may interfere with accurate diagnosis or effective treatment during pregnancy.

Aims & Objectives

(1) To determine the RI of coagulation parameters in normal pregnant women.

(2) To compare them with normal non-pregnant women.

Materials & Methods

Settings: This study is conducted in the Department of Pathology, GMCH Nagpur from February to July 2024.

Participants: It includes ANC patients from Gynaecology OPD as well as IPD patients. A total of 250 healthy pregnant women of reproductive age group (First trimester 130 cases, third trimester 120 cases) and 150 healthy non-pregnant women were included. Patients having pregnancy related complications like PIH, Eclampsia, Gestational diabetes mellitus, any coagulopathy, or patients on any drugs are excluded from study

Variables: Prothrombin time (PT), Activated partial thromboplastin time (APTT), Fibrinogen, and D-dimer were performed on the Sysmex CS-1600 Coagulometer.

Statistical analysis: Results were expressed as Mean and Standard deviations. Student's t-test was performed and P < 0>

Result

The RI for PT, APTT, Fibrinogen, D-dimer at first trimester were 9.6-12.9 sec, 27.3-38.8 sec, 250-490 mg/dl, 0.05-0.95 µg/ml respectively, for third trimester were 9.3-11.9 sec, 25.4-35.4 sec, 340-590 mg/dl, 0.13-1.70 µg/ml and for non-pregnant women were 11.5-13.5 sec, 27.3-42.9 sec, 200-400 mg/dl, <0.5 µg/ml respectively.

Conclusion

After extensive research, so far, no study has been conducted in central India. Our study presents RIs for the central India population that can be adopted by other laboratories after proper validation and also help clinicians make early diagnosis and treatments.

Benign Hematology-laboratory (BHL) OP-BHL-17

Bone Marrow Granulomas - Insights and Implications

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Introduction

Granulomas in the bone marrow are unusual findings associated with various disorders. Though the morphological findings are not characteristic of a disease, their presence is related to various disorders. This study reviewed bone marrow cases over a period of 07 years.

Aims & Objectives

The present study aims to evaluate the incidence and the spectrum of underlying causes of granuloma in bone marrow.

Materials & Methods

A retrospective study was conducted in Department of Pathology and Laboratory Medicine at AIIMS, Jodhpur, Rajasthan over a period of seven years analyzing clinical details and laboratory investigations of patients which revealed granulomas on bone marrow examination.

Result

We identified 46 cases among 2949 bone marrow biopsies, representing an incidence of 1.5% in the series. Median age of the patients was 41.76 years. Male: female ratio was 1.3:1. Fever (37 cases, 80%) was the most common presenting accompanied with unexplained weight loss. Lymphadenopathy was seen in 19 cases (41%), hepatosplenomegaly in 18 (39%), hepatomegaly in 2 (4%) and splenomegaly in 6 (13%). Hematological evaluations revealed 19 cases (41%) with pancytopenia, 25 (54%) with anaemia, 04 (9%) with leukocytopenia, 2 (4%) with leucocytosis and 15 (33%) with thrombocytopenia. Identified etiologies included tuberculosis in 11 cases (24%), including 2 HIV-positive patients, EBV infection in 3 (6%), Hodgkin's lymphoma in 3 (6%), NHL in 1 HIV-positive patient (2%), SLE in 1 (2%), Angioimmunoblastic T-cell lymphoma in 1 (2%), candida in 1 case (2%). For 7 cases (15%), including one with disseminated granulomas, the cause remained undetermined despite extensive work-up.

Conclusion

Bone marrow aspiration and biopsy are essential for diagnosing granulomatous lesions, significantly aiding in cases of pyrexia of unknown origin or unexplained pancytopenia and anemia in immunocompetent patients.

Benign Hematology-laboratory (BHL) OP-BHL-18

Strategies For Small Laboratories That Are Economical in Terms of Internal Quality Control

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Introduction

Convectional quality control (QC) methods for hematology analyzers includes performing precision with commercial control materials and setting accuracy by using calibrators. Peer group analysis, i.e., participation in proficiency testing (PT) program, also adds to the accuracy check. These involves cost and may not be feasible for small laboratories. By developing predictive models of alternate QC approaches (AQA) based on retrospective analysis, this study aims to proactively identify systemic errors (SE) by using patient's samples. Preliminary results indicate its feasibility and potential to enhance instrument performance monitoring. Further work may be needed to validate its effectiveness in real-world medical settings. The AQA includes duplicate testing, inter-instrument comparison, moving average analysis, retained sample testing, etc. Here patient's sample is used instead of commercially procured QC materials, thus making this a cost-effective approach.

Aims & Objectives

To study the performance of a hematology cell counter by using AQA using a patient's sample.

Materials & Methods

In the ongoing process of >10 years, which involved >30,000 patient samples run on two calibrated cell counters (Advia 2120i), a study involving a data size of six months was done to evaluate the effectiveness of AQA for detecting SE. A QC protocol for the AQA and their acceptability limits was developed by our laboratory in reference to NABL112, a specific criteria guideline. Statistical evaluation includes mean, standard deviation (SD), % coefficient of variation (CV) for precision testing, ±2 SD of the mean bias for duplicate testing, linear regression analysis for inter-instrument comparison, and 3% of the target mean as the upper limit and lower limit for moving average analysis.

Result

From the total runs in six months, SE detected by duplicate testing was 15.9%, with the maximum root-cause finding associated with daily maintenance; inter-instrument comparison was 4.5%, where maximum times RBC flow cell cleaning was the root-cause; SE detected with moving average analysis was 1.2%, with the root-cause findings of a skewed patient population. The retained sample testing detected 8.3% errors with root-causes associated with errors in storage conditions.

Conclusion

Alternate QC methods help in the detection of systemic errors in a very cost-effective manner in hematology cell counters. Thus, mini laboratories may adopt these QC approaches for better practice.

Benign Hematology-laboratory (BHL) OP-BHL-19

Prevalence Of KIR-B Haplotype and KIR Alloreactivity in Donors of Haploidentical Hematopoietic Cell Transplantation: A Single Center Study from India

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Introduction

Alloreactive KIR-B haplotypes mediate potent anti-tumor and anti-microbial effects and can improve the prognosis of haploidentical hematopoietic cell transplantation (HHCT) but there is paucity of this data in the Indian population.

Aim and objectives

We aimed to evaluate the prevalence of KIR-B haplotypes and their alloreactivity in HHCT donors at our center.

Methods

A total of 119 individuals (haploidentical donors, (n=93); and patients, n=26) from 26 families were included in this study. The KIR genotyping of the donors and HLA-B, as well as HLA-C genotyping of donor-recipient pairs, was done by polymerase chain reaction with sequence-specific primer genotyping assay. The KIR B-content score of donors was calculated using the online donor KIR B-content group calculator of the Immuno Polymorphism Database (IPD)(www.ebi.ac.uk/ipd/kir/donor_b_content). The alloreactivity of KIR was determined using an online KIR ligand matching calculator of IPD (www.ebi.ac.uk/ipd/kir/matching/ligand).

Results

Haploidentical donors were siblings and parents in 64% and 36% of cases, respectively. The prevalence of KIR-A (A/A) and KIR-B haplotype (B/A or B/B) in donors was 21% (20/93) and 79% (73/93), respectively. The KIR-B content score was 0 in 21% (20/93), 1-2 in 66% (61/93), and 3-4 in 13% (12/93) of donors. Accordingly, donors were classified as better/best in 77% (20/26) and neutral in 23% (6/26) of screened families. The KIR alloreactivity was absent in 44% (41/93) of donors while it was present in the recipient-versus-donor direction in 21% (20/93), the donor-versus-recipient direction in 23% (21/93) and both directions in 12% (11/93) of donors.

Conclusion

Our study shows that over two-thirds of donors have KIR-B haplotype and over two-thirds of families have killer-B content based better/best donors but KIR alloreactivity in GvH direction in approximately one-fourth of donors highlights the feasibility of alloreactive KIR-B haplotype-based selection of suitable donors for HHCT.

Benign Hematology-laboratory (BHL) OP-BHL-20

Experience of New Born Screening for Hemoglobinopathies at Tertiary Care Center in Vidarbha Over 18 Months : Identifying Challenges and Solutions

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Introduction

Hemoglobinopathies are the most common monogenic disorders in India posing a significant health burden. The purpose of newborn screening for hemoglobinopathies is to identify clinically significant disorders and provide early intervention and education before complications. However non availability of newborn phlebotomist and HPLC analyzer capable to process dried blood spot at most centers restrict availability of Newborn screening (NBS) to wider population.

Aims & Objectives

1. To estimate the diagnostic accuracy of HPLC of capillary sample using collection kit against cord blood HPLC on widely available variant II HPLC analyzer
2. To describe spectrum of hemoglobinopathies in newborn over 18 months.

Materials & Methods

Prospective observational study conducted in Department of Pathology at AIIMS Nagpur on 163 samples over the period of 18 months from February 2023 to August 2024. In initial 100 samples, universal screening was done to compare the efficacy of the cord blood sample and the heel prick sample. Additional targeted 63 newborns were screened later when one of the parents had hemoglobinopathy trait. Patients having prior blood transfusion were excluded from the study. HbA2, HbF and other hemoglobin variants were quantified by HPLC method on Bio-Rad Variant II hemoglobin analyzer.

Result

Considering cord blood as the gold standard method in this study, the diagnostic efficacy of capillary samples collected using capillary collection kits for detection of hemoglobinopathy has 93% sensitivity and 99% specificity. (n=100) There was good concordance in both samples in quantification of Hb A, F and variant Hb using kappa statistics.

The spectrum of hemoglobinopathies were studied in 163 cases. Out if these cases, 17.17% diagnosed as sickle cell trait, 1.22

Conclusion

HPLC is the recommended testing modality for NBS. Using capillary samples collected with bio rad collection kit we could provide accurate report with reliable quantification on routine HPLC analyzer Bio rad Variant II. We could by pass need of phlebotomy in newborns and analyzer capable of processing dried blood spot (DBS) sample. As expected in Vidarbha region, Sickle was the most common hemoglobinopathy detected in our cohort.

Benign Hematology-laboratory (BHL) OP-BHL-21

Comparing The Diagnostic Accuracy of Detecting Red Blood Cells in Urine Using Light Microscopic Examination, Phase Contrast Microscopic Examination and an Automated Urine Analyser

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Introduction

Hematuria is an important indicator of disease process. Cause of hematuria can be attributed to a wide range of pathological conditions involving renal, urinary tract and many systemic diseases, which all together can be categorised into glomerular and non glomerular diseases. Variations in red cell morphology can be used as an aid to localise the site of bleeding. In glomerular diseases, red cells undergo morphological alterations to form dysmorphic cells. Presence of isomorphic red cells indicate non glomerular etiology. Light microscopic examination, phase contrast microscopy and many automated techniques classify red cells on the basis of these parameters. The present study looks forward to compare the diagnostic capabilities of newly introduced modalities against the time tested gold standard phase contrast microscopy in detecting glomerular hematuria.

Aims & Objectives

This study aims to observe the clinicopathological profile with patients with hematuria and analyse the morphology of dysmorphic erythrocytes as well as calculate their percentage using light microscopy, phase contrast microscopy and automated urine analyser.

Materials & Methods

A cross-sectional analytical study was conducted at Himalayan Institute of medical sciences with a total of 60 patients diagnosed with gross/ microscopic hematuria as well as patients with suspected glomerular pathology for phase contrast analysis and with positive dip stick analysis for hematuria.

Result

The analysis for presence of hematuria detected majority of patients with 3+ hematuria. The 60 samples were analysed for the presence of dysmorphism which was further categorised into glomerular and non-glomerular etiology based on the percentage of dysmorphic red cells. Attempts were also made to find the better diagnostic modality among the three in triaging cases with glomerular and non-glomerular pathology.

Conclusion

To analyse the diagnostic accuracy of microscopy and automated urine analayser (Urinalysis Hybrid-FUS-1000) in detecting dysmorphic red cells in urine, the study was done for a period of 12 months employing 60 samples. The population varied from all age groups. The final diagnosis by phase contrast microscopy was considered as the gold standard.

Benign Hematology-laboratory (BHL) OP-BHL-22

Comparison of Immature Platelet Fraction (IPF) Between Normotensive and Pre-Eclamptic Pregnant Females

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Introduction

Pre-eclampsia (PE) is a multisystemic disorder characterized by elevated blood pressure and proteinuria, manifesting after the 20th week of gestation. The condition is associated with endothelial dysfunction, leading to platelet activation and increased platelet consumption, which stimulates thrombopoiesis in the bone marrow. Immature platelet fraction (IPF) is a key indicator, representing the percentage of immature platelets relative to total platelets in peripheral blood. This study aims to evaluate the predictive value of IPF and other platelet indices—mean platelet volume (MPV), platelet distribution width (PDW), and platelet large cell ratio (PLCR)—in diagnosing PE.

Aims & Objectives

The study has three primary aims: 1) to compare IPF levels between normotensive and pre-eclamptic pregnant women; 2) to analyse other platelet parameters (platelet count, MPV, PDW, PLCR) in both groups; and 3) to correlate these parameters with the severity of pre-eclampsia.

Materials & Methods

This cross-sectional observational study was conducted over one year at a tertiary care hospital. We analysed and compared platelet count, IPF, MPV, PDW, and PLCR between 35 pre-eclamptic patients and 35 normotensive pregnant women. We further compared these parameters among patients with mild and severe PE.

Result

The study found that mean IPF ($p = 0.007$), MPV, and PLCR were significantly higher in pre-eclamptic subjects compared to normotensive counterparts. Moreover, these parameters were elevated in severe PE compared to mild PE, with IPF showing a p value of 0.033. Notably, IPF emerged as the best predictor of PE, with a cut-off value of >6%.

Conclusion

This study underscores the significance of platelet dynamics in pre-eclampsia and highlights the potential of using automated blood analyses of platelet parameters, particularly IPF, as a reliable tool for diagnosing and assessing the severity of PE. These findings may enhance clinical management and monitoring of at-risk pregnant women.

Benign Hematology-laboratory (BHL) OP-BHL-23

Antiphosphatidylserine/Prothrombin (APS/PT) IgG : A Surrogate Marker for Lupus Anticoagulant?

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Introduction

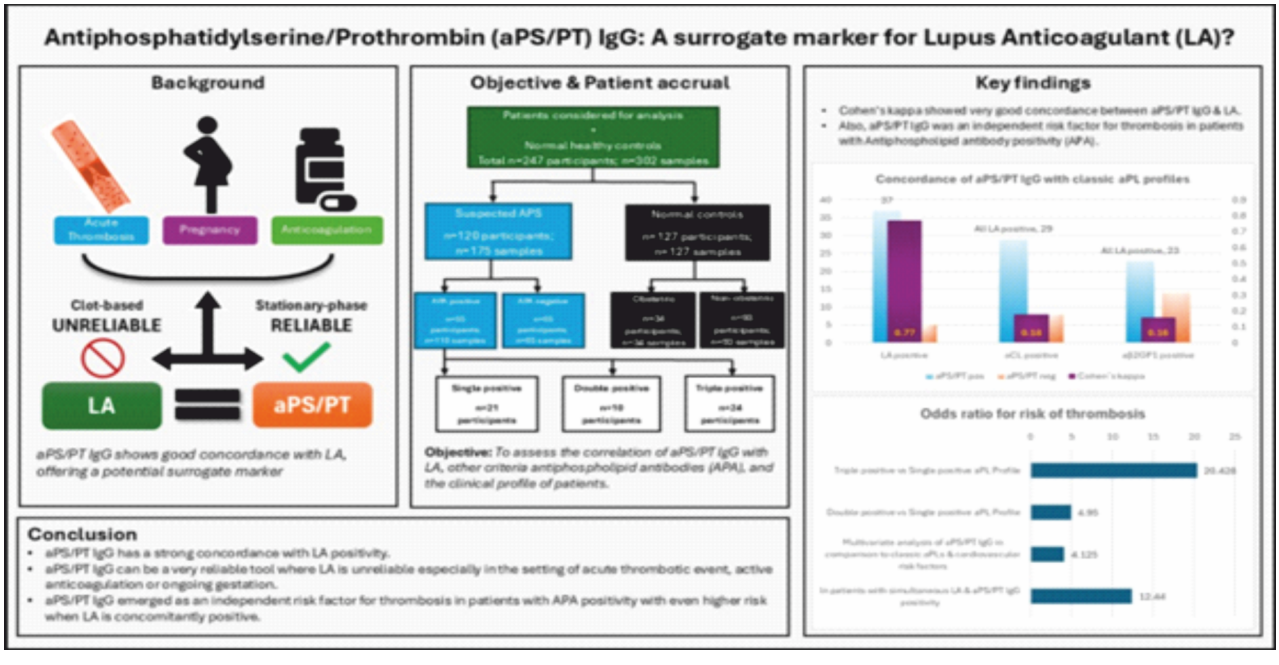
Lupus anticoagulant (LA), a clot-based assay, is unreliable during acute thrombotic events, active anticoagulation, or pregnancy—conditions where its detection is crucial for classifying patients as APS, especially without aCL and aβ2GPI positivity or for identifying triple positivity. Anti-phosphatidylserine/prothrombin antibodies (aPS/PT) have shown good concordance with LA.

Aims & Objectives

To assess the correlation of aPS/PT IgG with LA, other criteria antiphospholipid antibodies (APA), and the clinical profile of patients.

Materials & Methods

We enrolled 55 patients meeting APS laboratory criteria (APA+) and 65 with clinical suspicion but negative for laboratory criteria, totalling 120 patients. aPS/PT IgG titers were measured using the QUANTA Lite kit. Samples from 127 healthy controls established the aPS/PT IgG positivity cut-off. LA, aCL, and aβ2GPI were also assessed in all patients.



Result

Significant concordance of aPS/PT IgG with LA was observed, with a Cohen's kappa of 0.77 in APA-positive patients and 0.91 in the entire cohort. ROC analysis showed an AUC of 0.842, with an optimal cut-off near that of healthy controls. Median aPS/PT IgG titers were significantly higher in LA-positive patients (146.42 U/L vs. 12.20 U/L). aPS/PT IgG demonstrated 100% specificity and PPV for LA detection at a cut-off >39 U/L. Additionally, aPS/PT IgG was the only independent risk factor for thrombosis (OR 4.125), particularly in LA-positive patients (OR 12.44).

Conclusion

The significant concordance of aPS/PT IgG with LA, its high specificity and PPV, suggests its utility in patients with unreliable LA. aPS/PT IgG also indicates a higher thrombosis risk, making it a key prognostic factor.

Benign Hematology-laboratory (BHL) OP-BHL-24

HBA1c Through Capillary Electrophoresis, as a Tool to Recognize Hemolytic Anemias and Hemoglobinopathies

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Introduction

HbA1c has been one of the standard assays to screen and/or monitor Diabetes mellitus. The assay performed through Capillary Electrophoresis technology will also provide data on abnormal hemoglobin fractions and clue for Hemolysis and shortened red cell survival.

Aims & Objectives

1. To identify the minor hemoglobinopathies through detection of abnormal hemoglobin bands and quantification of HbA2
2. To identify Hereditary Hemolytic anemia through low HbA1c value of less than 4.5%
3. To identify other Hemolytic anemias through low HbA1c values.

Materials & Methods

Study duration spanning from, March 2023 to August 2024. A total of 293168 samples were analyzed for HbA1c, through capillary electrophoresis, Sebia Capillarys Tera 3, included in preventive health check.

Result

Out of 293168 samples,

1. 2616 were of Beta Thalassemia minor
2. 1945 were of other minor hemoglobinopathies consisting of variant band.
3. 230 were of Delta-Beta Thalassemia spectrum
4. Low A1c was noted in 445 patients of which
   (A) 18 were of red cell membrane pathology - Hereditary Spherocytosis
   (B) 11 were other hereditary hemolytic anemia
   (C) 43 samples had isolated indirect bilirubinemia.
   (D) CKD, CLD comprised of 205 cases
   (E) 50 cases comprised of Megaloblastic anemia, Immune hemolytic anemia, Thalassemia Intermedia and post transfusion.
   (F) 16 cases remained unidentified due to lack of other data
   (G) 98 cases were physiological(A1c between 4 to 4.5 only with normal red cell morphology, liver and renal function)
5. 8 Cases of CLL and CML were recognized as the migration was improper

Conclusion

HbA1c through Capillary electrophoresis gives information on Hemoglobin fractions, through which carriers of minor hemoglobinopathy can be identified.

HbA1c value less than 4.5 is quite rare in a healthy individual and this can be utmost clue for diagnosing hereditary hemolytic anemias with mild to moderate clinical presentation.

Carriers of Hereditary Hemolytic anemia can thus be identified and with appropriate family screening can be counseled.

Benign Hematology-laboratory (BHL) OP-BHL-25

BAMBO : Empowering Segmentation with an Annotated Bone Marrow Biopsy Dataset

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Introduction

Bone marrow examination plays a critical role in diagnosing and treating hematologic and other diseases. Current methods rely on visual assessments by pathologists, which are inherently subjective, leading to inaccuracies. Thus, there is a scope for artificial intelligence tools to improve accuracy by providing consistent and objective measurements. However, the absence of publicly available, standardized, high-quality datasets hinders progress in developing such tools.

Aims & Objectives

This work aims to address the lack of annotated bone marrow biopsy datasets and introduces a comprehensive dataset of semantically segmented and annotated biopsy images.

Materials & Methods

We present a comprehensive Bone Marrow Biopsy (BaMBo) dataset consisting 185semantic-segmented bone marrow biopsy images, specifically designed for the automated calculation of bone marrow cellularity. Our dataset comprises high-resolution, generalized images of bone marrow biopsies, each annotated with precise semantic segmentation of different hematological components. These components are divided into 4 classes: Bony trabeculae, adipocytes, cellular region and Background (BG). The annotations were performed with the help of two experienced hematopathologists that were supported by state-of-the-art Deep Learning (DL) models and image processing techniques. We then used our dataset to train a custom U-Net based DL model that performs multi-class semantic segmentation of the images (Dice Score: 0.831± 0.099).

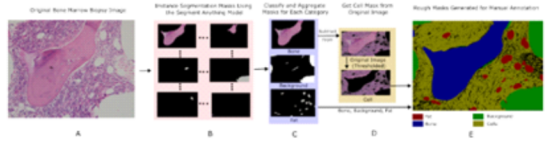

Figure 3: Flowchart representation of generating rough automated annotations by SAM, SVM and image processing. A: Original BMT image. B: Generating unclassified segmentation objects using SAM on basis of visual distinction betwen various parts of image. C: Classification of segmentation objects into masks by SVM on the basis of feature vector of colors,texture and shape. D: Generation of cell mask by first using color thresholding to seperate non-white part from original image and subtracting bone mask from it to obtain aproximate cell mask. E: Stitching together all 4 masks and obtaining rough annotations.

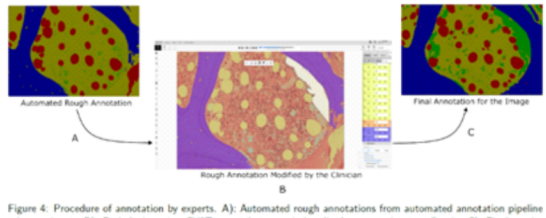

Figure 4: Procedure of annotation by experts. A): Automated rough annotations from automated annotation pipeline taken as input. B): Pathologist using CVAT remotely to precisely edit the annotation to refine it. C): Final precise annotation to be taken as ground truth (Colors and the respective classes are: yellow: cells, green: background, blue: bone, red: fat)

Result

The model demonstrated strong performance in segmenting various parts of a biopsy, facilitating further diagnostics. The segmentation masks allowed accurate cellularity estimation, validating the effectiveness of the BaMBo dataset with segmentation object classification accuracy of 96%

Conclusion

This open-source dataset is publicly available and addresses critical gaps in the availability of high-quality, annotated images essential for the training of machine learning models focused on automated bone marrow diagnostics.

Benign Hematology-laboratory (BHL) OP-BHL-26

Significance of Emerging Inflammatory Haematological Ratios and Distribution Widths in Type 2 Diabetes Mellitus

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Introduction

Diabetes mellitus (DM) is a metabolic disorder characterized by chronic hyperglycaemia and insulin resistance. Emerging predictive inflammatory markers, such as Neutrophil-Lymphocyte Ratio (NLR), Monocyte-Lymphocyte Ratio (MLR), Platelet-Lymphocyte Ratio (PLR), Red cell Distribution Width (RDW) and Platelet Distribution Width (PDW) can be readily assessed during routine haematological analysis, facilitating early detection of DM and its complications.

Aims & Objectives

To determine the diagnostic utility of NLR, MLR, PLR, RDW, and PDW in Type 2 DM patients.

Materials & Methods

This case-control study was conducted over 6 months and involved 100 Type 2 DM patients and 100 healthy non-diabetic individuals. A complete blood count, fasting blood sugar (FBS), and glycated haemoglobin (HbA1c) levels were measured using automated analyzers. Statistical analysis was performed using tests like the Kruskal-Wallis and Spearman's correlation coefficient in the Statistical Package for the Social Sciences version 21.0 software.

Result

The mean age of the participants was 45.75 years. Among the diabetics, 35% of patients had complications. A statistically significant difference (p=0.01) was observed in the mean MLR and PLR among controls and diabetics with and without complications. The PLR exhibited a statistically significant negative correlation with FBS and HbA1c ($r = -0.24$, $p = 0.01$). NLR and MLR did not correlate significantly with either FBS or HbA1c. Further, receiver operating characteristic curve analysis revealed that PLR had the highest predictive value for Type 2 DM (AUC: 0.6254), while MLR is the most effective predictor of DM complications (AUC: 0.6591). No significant difference was observed in RDW across the groups, however, PDW showed a statistically significant positive correlation with HbA1c ($r = 0.63$, $p = 0.01$).

Conclusion

PLR and PDW exhibited a potential for detecting DM while MLR emerged as a marker for DM complications. This underscores the pivotal utility of using these ratios and distribution widths as key indicators alongside glycaemic indices such as FBS and HbA1c in monitoring DM progression and anticipating associated complications.

Benign Hematology-laboratory (BHL) OP-BHL-27

Detection of Circulating Tumour Cells in The Blood Using EPCAM and Cytokeratin in Colorectal Carcinoma by Flowcytometry

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Introduction

Colorectal Carcinoma (CRC) is the third most common cancer and the second leading cause of cancer related deaths in the world with an estimated number of 1.8 million new cases & about 881,000 deaths worldwide in 2018.

Liquid biopsy is a non-invasive method for detecting, analyzing & monitoring cancer by examining body fluids. It includes circulating tumor cells (CTCs), cell-free nucleic acids & exosomes. CTCs are tumor cells that detach from the primary tumor & circulate in the bloodstream or lymphatic system & potentially initiate metastasis in distant organs. However, the low concentration of CTCs in blood makes them difficult to detect. Flow Cytometry is an effective way to detect CTCs.

Aims & Objectives

To detect circulating tumour cells in the blood using EpCAM and Cytokeratin in Colorectal carcinoma by flow cytometry & to correlate CTCs with TNM staging and clinicopathological parameters.

Materials & Methods

A prospective study conducted after IEC approval included 22 patients with mean age of 47.6 years & M:F of 1:2.14.

The most common presentations were, pain abdomen (100%) & cachexia (86.3%).

The current study employed flow cytometry for the detection of CTCs in CRC patients with Three Laser Ten Color Navios Flow Cytometer. Enrichment methods included density gradient centrifugation & red cell lysis. CTCs with positive immunostaining for EpCAM, CK, CD24, CD34, CD44 & negative immunostaining for CD45 were noted.

Result

CTCs detection rate was 86.4% with a range of 0-13. EpCAM, CK, EpCAM+CK, EpCAM+CD44 & CK+CD44 markers showed significant p-values with sensitivity, specificity, PPV & NPV as shown in the table.

	EpCAM	CK	EpCAM+CK	EpCAM+CD44	CK+CD44
p-Value	0.01	0.041	0.008	0.016	0.016
Sensitivity	68.17%	63.64%	50.00%	63.64%	63.64%
Specificity	100.0%	100.0%	100.0%	100.0%	100.0%
Positive Predictive Value	100.0%	100.0%	100%	100.0%	100.0%
Negative Predictive Value	41.67%	38.46%	31.25%	38.46%	38.46%

CD44 positivity was higher in advanced disease stages.

The present study is in conjunction with existing literature, although detection rates were lower, possibly due to methodology differences. These findings highlight the potential of specific markers in CTC detection & their correlation with disease stage. In the current study 45.5% patients underwent palliative treatment, 45.5% underwent abdomino-perineal resection, 4.5% patient died & 4.5% were lost to follow up. TNM staging revealed T3 as the most common stage (18.2%). stage IIIB was the most common stage as per UICC. Although no statistically significant correlation was found between CTCs and TNM or UICC stages, higher T-staged cases demonstrated increased CTCs. Histological grading revealed moderately differentiated as the most common variant (59.1%).

Conclusion

EpCAM and CK are reliable and sensitive marker however, EpCAM being the more sensitive marker while 100% specificity in both EpCAM and CK.

Benign Hematology-laboratory (BHL) OP-BHL-28

Spectrum of Haemoglobinopathies in Antenatal Women in a Tertiary Care Centre

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Introduction

Anemia is a major public health problem in developing countries and is a cause of serious concern. It is also one of the most encountered medical disorders during pregnancy. Iron deficiency anemia is the most common nutritional deficiency anemia in India. The other major cause is due to "Haemoglobinopathies" - the inherited disorders of hemoglobin. Haemoglobinopathies are divided into two main groups as Thalassemia syndromes and the structural hemoglobin variants. High performance liquid chromatography (HPLC) is widely used as the diagnostic modality for diagnosis of various hemoglobin disorders. It is important to identify the haemoglobinopathies in the pregnant females to prevent birth of thalassemia major child which has a huge socio-economical burden on family and society.

Aims & Objectives

Aim : To determine the carrier state of haemoglobinopathies in ANC cases.

Objectives:

1. To assess prevalence of (mainly beta thalassemia) in ANC cases based on Mentzer index.
2. To confirm the diagnosis for haemoglobinopathies by Hemoglobin HPLC.
3. To correlate haemoglobinopathies findings with HPLC findings.

Materials & Methods

A retrospective study conducted with the aim of analyzing the prevalence of haemoglobinopathies in antenatal cases in a tertiary care hospital. Total 2007 cases were studied from the data obtained for last five years (January2019-December2023). Their complete blood count (CBC) and HPLC reports were retrieved from the software.

Result

Results- A total of 2007 antenatal cases were included in this study. Complete blood counts and HPLC analysis were studied. The most common abnormal haemoglobinopathies detected were beta (β) thalassemia trait 105 (5.23%) cases followed by sickle cell trait 7 (0.34%). Other Haemoglobinopathies include Heterozygous for HbD Punjab, Heterozygous delta beta thalassemia and other rare hemoglobin variants which were seen in 5 (0.24 %) cases. Normal HPLC pattern was seen in 1890 (94.17%). Mean HbA2 was 4.9% in Beta thalassemia trait cases. Mean MCV was 65.0 fl and mean RDW was 18.8%. Seven cases were of Heterozygous sickle Hemoglobin. Mean sickle hemoglobin was 37.2% in these cases.

Conclusion

Beta Thalassemia trait is the most common haemoglobinopathies detected followed by Heterozygous sickle hemoglobin cases in ANC patients, underscoring their significant prevalence in the population. Identifying the abnormal hemoglobin is crucial for genetic screening programs, especially in regions where hemoglobin disorders are endemic. Antenatal screening programme and timely intervention is an effective strategy to control clinically significant major haemoglobinopathies in the offsprings.

Benign Hematology-laboratory (BHL) OP-BHL-29

Expression of CD45RO And CD45RA By Flowcytometry in Paediatric Primary Immunodeficiency Case and its Correlation with Molecular Pathways Using RAG1 And TREC Genes

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Introduction

Primary immunodeficiencies (PIDs) are genetic disorders that impact the development or function of the immune system, making individuals susceptible to infections, autoimmune conditions, and malignancies. The International Union of Immunological Societies (IUIS) has classified 406 PIDs related to defects in 430 genes. There are >1 million PID patients estimated in India. Diagnosing PIDs is a major challenge due to limited access to diagnostic technologies and wide range of atypical presentations. Flow cytometry has emerged as a vital tool in immune system assessment, offering insights into various disorders. However, confirmation of diagnosis typically requires genetic defect identification.

Aims & Objectives

To study expression of CD45RO and CD45RA in suspected cases of Primary Immunodeficiency Disease by Flowcytometry and its correlation with molecular pathways.

Materials & Methods

It was a prospective study done during December 2023-August 2024. All suspected cases of IEI less than two years of age were enrolled based on warning signs. 3ml EDTA peripheral blood sample was subjected for flowcytometry after complete blood cell counts using three laser ten colour flowcytometer NAVIOS and automated Haematology analyser XN 1000i respectively, 3 ml sample was collected for immunoglobulin assay as well in plain vial.

Result

These patients aged 8 days-2yrs were studied in 3 cohort groups 0-6 month (11), 6month-1year (6) & 1-2 years of age (3), with M:F of 1.85:1, presented with failure to thrive (20/20), fever (15/20), recurrent diarrhoea (7/20) & sepsis (7/20). History of consanguinity in the parents was seen in 30% of patients. Absolute no of T, B & NK cell subsets were reduced in 25%, 30% & 25 cases respectively. B cell lymphopenia seen in 36.4% in <6 month age group & 66.7% in 1-2 yr age with significant p value of 0.03. Mean value of CD45RO+ T cells were 316.5, 724.17 & 1710 in respective age group with significant p value of 0.001. Further, classified into T-B+NK+ (1/20), T-B+NK- (1/20) & T-B-NK- (3/20). 1/20 case was SCID. Serum immunoglobulin levels were also analysed. 1/20 case & 6/20 case were positive for RAG1 gene & TREC gene by NGS analysis

Conclusion

PID has a significant health burden, and is not well understood entity a very high index of suspicion with complete workup including immunoglobulin assay , flowcytometry and molecular study is the mainstay for management and to be done in all suspected cases.

Benign Hematology-laboratory (BHL) OP-BHL-30

Prognostic Correlational Study of Hemoglobin Indices with Rising MELD Scores

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JNMC Sawangi, Wardha

Introduction

Liver cirrhosis is a chronic condition associated with changes in blood parameters such as anemia, leukopenia and thrombocytopenia.Its causes are varied.Relationship between blood parameters and prognostic markers such as model for end stage liver disease (MELD) sodium score are helpful for knowing long term outcomes.

Aims & Objectives

To assess the correlation between hemoglobin and MELD sodium score in liver cirrhosis patients.

Materials & Methods

A total of 50 patients diagnosed with liver cirrhosis were enrolled over a duration of 6 months after taking written informed consent.After taking detailed history and clinical evaluation patients underwent routine blood investigation and were assessed with severity of anemia along with calculation of MELD sodium score.

Result

Out of 50 patients studied , males contributed 80% & females 20% with male to female ratio being 4:1.Alcohol was found to be the commonest etiology followed by hepatitis B.The most common age group affected was 41 to 60 years.MELD Sodium score was found to be more than 15 in 42 patients and less than 15 in 8 patients.Mean hemoglobin was 7.9.The correlation coefficient between hemoglobin and MELD score was -0.170 and was statistically significant, establishing that hemoglobin levels decrease with increasing severity of liver cirrhosis.

Conclusion

The study concluded that the level of hemoglobin varies inversely with increasing severity of liver disease so level can be used for initial assessment.To determine whether hemoglobin levels can be used to predict mortality and assess the severity of liver cirrhosis in individuals, a larger prospective trial is required.

Benign Hematology-laboratory (BHL) OP-BHL-31

AI-Driven Differentiation of nRBCS, Lymphocytes, and Blast Cells for Precision in Hematological Disorders

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Introduction

In India, pathologists frequently face challenges in differentiating between normal and abnormal cells, particularly with less advanced and affordable automated cell counters. These counters struggle to distinguish nucleated red blood cells (nRBCs) from lymphocytes, especially in splenectomized patients, leading to diagnostic errors in hematological disorders. Artificial intelligence (AI) and deep learning technologies hold promise for addressing these challenges, and improving the precision of diagnostics.

Aims & Objectives

This study aims to leverage deep learning models to classify four critical bone marrow cell types—Erythroblast, Proerythroblast, Myeloblast, and Lymphocyte—enhancing diagnostic precision and overcoming the limitations of both manual examination and automated systems.

Materials & Methods

We used a dataset of 68,420 expert-annotated bone marrow cell images (Train: 47,845 images, Validation: 10,252 images, Test: 10,253 images) from 945 Leukemia & Lymphoma patients. The ResNet-50 and MobileNet V2 models were trained to classify these four cell types, and performance was evaluated using metrics such as accuracy, loss, and classification reports.

Result

The ResNet-50 model achieved a test accuracy of 90.18%, with the following classification report:

Myeloblast: Precision 0.84, Recall 0.82, F1-Score 0.83

Erythroblast: Precision 0.94, Recall 0.94, F1-Score 0.94

Lymphocyte: Precision 0.90, Recall 0.93, F1-Score 0.91

Proerythroblast: Precision 0.70, Recall 0.63, F1-Score 0.66

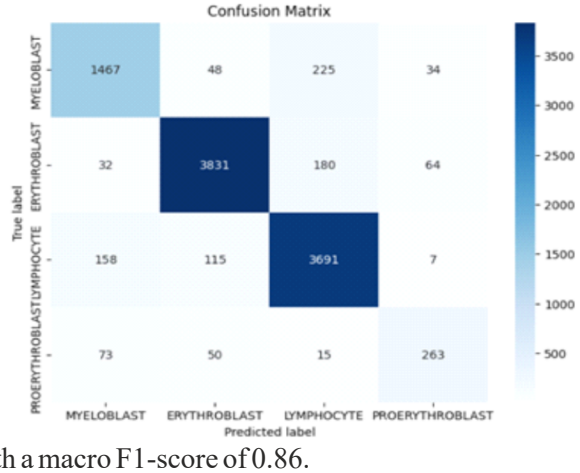
The MobileNet V2 model performed slightly better, with a test accuracy of 90.83%:

Myeloblast: Precision 0.83, Recall 0.86, F1-Score 0.85

Erythroblast: Precision 0.95, Recall 0.94, F1-Score 0.95

Lymphocyte: Precision 0.92, Recall 0.91, F1-Score 0.92

Proerythroblast: Precision 0.71, Recall 0.71, F1-Score 0.71



The overall test accuracy for MobileNet V2 was 90.83%, with a macro F1-score of 0.86.

Conclusion

Both models demonstrated significant improvement in differentiating nRBCs from lymphocytes, particularly in cases of hematological malignancies and splenectomized patients. However, challenges remain when multiple cell types appear in the same image. Deep learning offers substantial potential in overcoming the limitations of manual and automated diagnostic methods for hematological disorders.

Benign Hematology-laboratory (BHL) OP-BHL-32

The Spuriously High Neutrophil Cell Counter Population Data in APML - A Case Series

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Introduction

Complete blood count with differential using automated cell counters is an essential part of routine laboratory workup to evaluate various haematological malignancies. This technology has improved accuracy of cell analysis as well as effectively reduced the turnaround time by high throughput capabilities. However, every laboratory encounters, at times, some specimens that yield spurious results. We observed a spuriously high neutrophil counts of cell counter values in patients with acute promyelocytic leukemia (APML) requiring the attention of laboratory professionals.

Aims & Objectives

We aimed to compare the consecutive complete blood count values obtained on SysmexXN 1000 automated cell counters with values obtained after microscopic review of consecutive peripheral blood smears.

Materials & Methods

All consecutive newly diagnosed cases of APML at our centre from January 2023 were reviewed. The cell population data generated by XN 1000 analyzer and scatter plots from these cases was collected, reviewed, and analyzed. The consecutive review of peripheral smear stained using Leishman stain was done, and differential count were compared with automated cell counters data for one month.

Result

Total seven cases of APML diagnosed at our institute were included in our study. The analyzer exhibited very good correlation for CBC parameters. The differential count using automated cell counter showed abnormal promyelocytes distributed within monocytes and immature granulocytes region for all cases. In all the cases interestingly the abnormal promyelocytes were counted as neutrophils for a brief period of two to three days after a week of treatment. However, for rest of the days there was fairly a good correlation for the abnormal promyelocytes counts on peripheral smears and the immature granulocytes count obtained from cell counter.

Conclusion

APML cases have a characteristic scatter plot patter on SFL Vs. SSC which shows significant difference from other myeloid leukemia. These cells have high side scatter and high side fluorescence owing to the large size of the cells and dense granulations. In our observation spurious counting of APML cells as neutrophils in cell counter raises concern during the curial period of differentiation after treatment. Such phenomenon is not reported in the literature and maybe present owing to aberrantly differentiated leukemic cells. It is important to have knowledge about such anomalous results and review peripheral smears in APML during the differentiation of leukemic cells to avoid wrong intervention.

Benign Hematology-laboratory (BHL) OP-BHL-33

Significance of Emerging Inflammatory Haematological Ratios and Distribution Widths in Type 2 Diabetes Mellitus

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Introduction

Diabetes mellitus (DM) is a metabolic disorder characterized by chronic hyperglycaemia and insulin resistance. Emerging predictive inflammatory markers, such as Neutrophil-Lymphocyte Ratio (NLR), Monocyte-Lymphocyte Ratio (MLR), Platelet-Lymphocyte Ratio (PLR), Red cell Distribution Width (RDW) and Platelet Distribution Width (PDW) can be readily assessed during routine haematological analysis, facilitating early detection of DM and its complications.

Aims & Objectives

To determine the diagnostic utility of NLR, MLR, PLR, RDW, and PDW in Type 2 DM patients.

Materials & Methods

This case-control study was conducted over 6 months and involved 100 Type 2 DM patients and 100 healthy non-diabetic individuals. A complete blood count, fasting blood sugar (FBS), and glycated haemoglobin (HbA1c) levels were measured using automated analyzers. Statistical analysis was performed using tests like the Kruskal-Wallis and Spearman's correlation coefficient in the Statistical Package for the Social Sciences version 21.0 software.

Results

The mean age of the participants was 45.75 years. Among the diabetics, 35% of patients had complications. A statistically significant difference (p=0.01) was observed in the mean MLR and PLR among controls and diabetics with and without complications. The PLR exhibited a statistically significant negative correlation with FBS and HbA1c ($r = -0.24$, $p = 0.01$). NLR and MLR did not correlate significantly with either FBS or HbA1c. Further, receiver operating characteristic curve analysis revealed that PLR had the highest predictive value for Type 2 DM (AUC: 0.6254), while MLR is the most effective predictor of DM complications (AUC: 0.6591). No significant difference was observed in RDW across the groups, however, PDW showed a statistically significant positive correlation with HbA1c ($r = 0.63$, $p = 0.01$).

Conclusions

PLR and PDW exhibited a potential for detecting DM while MLR emerged as a marker for DM complications. This underscores the pivotal utility of using these ratios and distribution widths as key indicators alongside glycaemic indices such as FBS and HbA1c in monitoring DM progression and anticipating associated complications.

Malignant Hematology-Laboratory (MHL) OP-MHL-1

Impact of Cytogenetic Abnormalities on Clinico-Genetic Profiling for Enhanced Diagnosis and Prognosis in Multiple Myeloma

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Introduction

Multiple myeloma (MM) is the second most common heterogenous plasma cell malignancy, constituting 1% of all cancers and 2% of cancer-related deaths globally. Cytogenetic abnormalities are crucial for determining prognosis and treatment in MM. This study examines the impact of these abnormalities on clinical outcomes.

Aims & Objectives

This research aims to evaluate the prognostic significance of cytogenetic abnormalities in multiple myeloma by analyzing their frequency, distribution, and effect on patient survival and treatment response.

Materials & Methods

We analyzed 263 patients with suspected plasma cell dyscrasia using FISH and karyotyping to detect cytogenetic abnormalities. Patients were categorized into high, intermediate, and standard risk groups based on these findings. Active myeloma diagnosis and treatment response were assessed using IMWG criteria. Survival analysis employed Kaplan-Meier methods, Cox proportional model for hazard analysis, and correlation analysis.

Result

Among 263 patients, 194 (73.8%) were diagnosed with MM, and 69 (26.2%) were not. Cytogenetic analysis revealed 106 (54.6%) patients as cytogenetic positive, with FISH detecting 104 (53.6%) and karyotyping 2 (1%) whereas 88 patients were cytogenetically negative. Common abnormalities included 13q14.2 deletion in 59 (30.4%) patients and 1q21-22 gain in 48 (24.7%) patients. Genetic abnormalities were more frequent in 69 (35.6%) males compared to 7 (19.1%) females, with males aged 60-65 years and females 63-66 years. Double-hit phenotypes were seen in 10 (5.1%) patients—t(4;14) with 1q gain in 7 (3.6%) and del 17p with 1q gain in 3 (1.5%). Triple-hit cases with 1q gain, del 17p, and t(4;14) occurred in 3 (1.5%) patients. Risk categorization showed 79 (40.7%) patients as high-risk, 22 (11.3%) as intermediate risk, 5 (2.6%) as standard risk. Clinico-genetic profiling showed 166 (63.1%) patients with active myeloma and 28 (10.6%) with precursor conditions. Relapsed cases were 16 (9.6%), with 12 (6.2%) showing cytogenetic abnormalities. ASCT reduced the hazard of death or progression by 70% (HR = 0.3, 95% CI: 0.12–0.76). Cytogenetic-negative patients had a 21% lower risk of death or progression (95% CI: 0.57–1.76). Mean survival was 122±4 months for cytogenetic-negative and 94±9 months for cytogenetic-positive patients ($p = 0.421$). ASCT extended overall survival to 77 months, and first-line treatment prolonged progression-free survival to 62 months. Cytogenetic positivity correlated with worse outcomes ($rpb = 0.262$, $p < 0.001$).

Conclusion

Cytogenetic abnormalities are associated with poorer outcomes in multiple myeloma. FISH was found to be more effective than karyotyping. This study suggests integrating cytogenetic data into clinical profiling improves diagnosis, prognosis and enables personalised approach to disease management.

Malignant Hematology-Laboratory (MHL) OP-MHL-2

Distinguishing Chronic Lymphocytic Leukemia from Other Lymphomas: The Importance of CD200, CD38 and FMC7 Expression

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Introduction

Chronic lymphocytic leukemia (CLL) can be distinguished from other lymphomas by evaluating biomarkers like CD200, CD38, and FMC7. CD200 is highly expressed in CLL, aiding differentiation from other B-cell lymphomas. CD38 is linked to CLL prognosis, indicating disease aggressiveness. FMC7, generally low in CLL but higher in other lymphomas, helps in accurate diagnosis. These biomarkers, alongside clinical features, are key in distinguishing CLL from other lymphomas.

Aims & Objectives

Chronic lymphocytic leukemia (CLL) often presents diagnostic challenges, particularly in distinguishing it from other Lymphomas. This study aims to evaluate the expression levels of CD200, CD38 and FMC7 expression as potential diagnostic markers to enhance differentiation between CLL and other Lymphomas.

Materials & Methods

A total of 102 consecutive patients diagnosed with either CLL or other Lymphomas were assessed using flow cytometry to measure CD200, CD38 and FMC7 expression. Patients were selected based on clinical presentations that posed a diagnostic dilemma, ensuring a representative sample for analysis.

Result

The analysis revealed that CD200 was expressed in 100% of CLL cases and 30% in other lymphomas patients. Similarly, CD38 and FMC showed expression in 90% of CLL cases, whereas only 35% of other Lymphomas cases exhibited detectable levels. These findings suggest a significant difference in the expression of these markers between CLL and other Lymphomas.

Conclusion

The study highlights the critical role of CD200, CD38 and FMC as reliable biomarkers for differentiating CLL from other Lymphomas. Their distinct expression profiles provide valuable diagnostic information, particularly in atypical presentations where traditional markers may fall short. Incorporating these markers into the diagnostic workflow could improve clinical outcomes for patients presenting with lymphoproliferative disorders.

Malignant Hematology-Laboratory (MHL) OP-MHL-3

Beyond Blood: Flow Cytometry Application in Hematological Malignancies via Body Fluid Analysis

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Introduction

Flow cytometry (FC) has been utilized for diagnosing hematological neoplasms in blood, however it is now also being used for body fluids such as cerebrospinal fluid, pleural fluid and ascitic fluid.

Aims & Objectives

To assess the diagnostic utility of Flow cytometry of body fluids in Hematological neoplasms.

Materials & Methods

This is a retrospective study done from January 2019 to September 2024 and includes all cases where FC was done on body fluids. The panel of markers for each case was chosen based on clinical history, history of hematological malignancy and cytomorphology.

Result

FC was done in 54 cases of body fluids of which 28 showed involvement by hematological malignancies, 24 had reactive population and 2 were inadequate.

Fluids included were CSF (38), pleural (9) and ascitic fluid (7). Suspicion was based on the morphological findings on cytology smears. There was male preponderance with age ranging from 7 years to 76 years with a median age of 41 years. 15 out of the 38 CSF samples showed involvement of which the most common was B-ALL (8/38) followed by B-NHL (6/38) and T-ALL (3/38). 7 out of the 9 pleural fluid samples showed involvement of which most common was T-ALL (3/9). 4 out of 7 ascitic fluid samples, showed involvement of which most common was B-NHL (2/7).

In 5 cases (3-CSF, 2-Ascitic fluid), diagnosis of a hematological malignancy was initially made on flow cytometry which was later worked up to confirm the diagnosis.

Conclusion

FC represents a critical diagnostic modality for diagnosing hematological neoplasms involving body fluids with high sensitivity and specificity.

Integrating flow cytometry analysis of body fluids in routine diagnostic workup of a hematological neoplasm enhances the diagnostic accuracy and guides in the management.

Malignant Hematology-Laboratory (MHL) OP-MHL-4

Hematrack: Next Generation Sequencing Assay for High Sensitivity Measurable Residual Disease (MRD) Monitoring in Acute Lymphoblastic Leukemia

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Introduction

Acute Lymphoblastic Leukemia (ALL) outcomes are most accurately predicted by Measurable Residual Disease (MRD). Current MRD detection methods in ALL rely on Flow Cytometry and on occasion PCR-based assays. However, to address limitations in specificity, sensitivity and robustness of these methods, researchers have started investigating Next Generation Sequencing (NGS) as a potential alternative for MRD assessment. Despite the advantages, current NGS approaches face challenges: first, significant, if not prohibitive costs, especially in emerging economies; second, the need for multiple multiplex PCR reactions and numerous calibrators to compensate for PCR amplification biases

Aims & Objectives

To develop and validate HemaTrack ALL, an innovative NGS-based approach for MRD monitoring in ALL that overcomes existing limitations.

Materials & Methods

HemaTrack ALL leverages optimized PCR conditions that minimize primer-dimer formation and incorporates Unique Molecular Identifiers (UMI) in an unprecedented highly multiplexed format. The innovative laboratory workflow is complemented by QuaSIR, a newly developed software pipeline that can handle the massive data flow generated by the NGS methods, while mitigating artefacts and errors associated with sequence alignment and clonotyping nomenclature. This is achieved by utilizing a sequence-centric approach until the final clonotype reporting phase.

Result

In dilution studies, HemaTrackALL demonstrated remarkable linearity and precision in quantifying marker clonotypes, with a detection sensitivity of at least 10^-4 (one leukemic cell in 10,000 normal cells). Analysis of 38 archived biobank samples showed excellent concordance in marker clone identification and above 90% sensitivity in comparison to the gold standard Ig/TCR-PCR assay.

Conclusion

HemaTrack offers a cost-effective comprehensive end-to-end workflow for accurate identification and monitoring of dynamics of leukemic cells during treatment. Its potential to enhance MRD detection and monitoring in ALL patients, while reducing costs, in clinical practice will be further evaluated in an upcoming multi-center clinical study.

Malignant Hematology-Laboratory (MHL) OP-MHL-5

Cytogenetic Profile of Patients with Multiple Myeloma

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Introduction

Ten percent of all hematological cancers are multiple myeloma. Multiple myeloma is genetically variable and complicated, with cytogenetics being a significant element in the risk classification. Primary IGH translocations t(4;14), t(14;16), and t(14;20) as well as subsequent progressive aberrations such gain/amp(1q), 1p deletion, del(17p), and hypodiploidy are associated with high-risk multiple myeloma. Interphase FISH has demonstrated in several studies to be highly effective in identifying primary and secondary cryptic abnormalities in the lowest 5–10% normal plasma cell population.

Aims & Objectives

The present was undertaken to evaluate the incidence of cytogenetic abnormalities, to analyse their correlation with the demographic heterogeneity in Indian population.

Materials & Methods

This study comprised 40 cases of multiple myeloma patients who were sequentially referred from primary, secondary, and tertiary oncology centers across India. Isolated plasma cells were subjected to interphase FISH. The ISCN 2016 and 2020 were followed in the karyotype analysis. Sociodemographic and clinical factors were documented using semi-structured proforma.

Result

In the current study, there was a larger male to female ratio, with the majority of patients being in their fifth or sixth decade of life. The most prevalent cytogenetic anomaly was an increase in chromosomal 1q copies. Unlike FISH, multiple myeloma-related abnormalities may be found with conventional karyotyping in fewer cases. Renal failure and plasma cell leukemia were related with an elevated risk of mortality. Among high-risk patients receiving treatment with bortezomib, thalidomide, and dexamethasone, the overall response rate was 100%.

Conclusion

The current investigation shown that the high-risk characteristics of cytogenetics predict a poor prognosis for patients with multiple myeloma. FISH was discovered to be a unique, simple method with a high success rate that could identify any cytogenetic abnormality and provide useful data for the risk stratification of disease.

Malignant Hematology-Laboratory (MHL) OP-MHL-6

Mature B-cell Lymphoproliferative Disorders Gamut on Flow Cytometric Immunophenotyping at a Tertiary Health Care Centre in the Base of Himalayas

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Introduction

B-cell lymphomas are diagnosed through a combination of morphological assessment and immunophenotyping. Sub-classification of B-CLPD is essential for management related decision making. Flow cytometry is an excellent tool providing valuable insights & timely diagnosis. Over the past two to three decades, the significant influence of genetic and genomic investigations on lymphoma classification and subtyping has become evident.

Aims & Objectives

1. To sub classify mature B-cell lymphoproliferative disorders using immunophenotyping on flow cytometry.
2. To assess the CD5 negative and CD10 negative B cell lymphoma entities.

Materials & Methods

All cases subjected to flow cytometric immunophenotyping to assist in the clinicomorphological diagnosis of lymphoma during July 2015 to December 2024 were gathered. Navios EX flow cytometer (until March 2023) and the DxFLEX Flow Cytometer were used in the centre. CytExpert v2.6 software was used to evaluate the flow cytometric data. Immunophenotypic findings were analysed, and subclassification was performed based on the current WHO guidelines.

RESULTS (N=111)

Immunophenotype	Diagnosis	Cases
CD5 POSITIVE (n=75)	CLL	60
	MCL	15
CD5 NEGATIVE CD10 POSITIVE (n=05)	FL	01
	BL	02
	DLBCL	02
CD5 NEGATIVE CD 10 NEGATIVE (n=31)	MZL	11
	LPL	02
	HCL	06
	UNCLASSIFIED	12

Result

Out of 111 cases during July 2015 to December 2024 for a suspected lymphoma diagnosis, 75 cases were CD5 positive, 05 cases were CD5 –ve/CD 10 +ve lymphoma & 31 cases were CD5-ve/ CD10 –ve Lymphoma. There subcategorization is as follows:(Table attached). The cases remaining unclassifiable showed lack of characteristic immunophenotypic features ascertained based on WHO 5th edition guidelines.

FCIP is helpful in clinching the final diagnosis in most of the cases (94/111; 84.68%). Chronic Lymphocytic Leukemia/ Lymphoma is the most common CLPD in this region. Among CD5/CD10 dual negative lymphoma differentiation between LPL and SMZL is difficult even on FCIP. Even when various pathology, laboratory, clinical, and even genetic findings may suggest a LPL or MZL, the absence of any disease-specific FCIP expression pattern and the absence of any disease-specific genetic abnormality makes it challenging to make an unequivocal and definitive diagnosis of LPL or MZL based solely on blood and marrow studies without a lymph node or tissue biopsy.

Conclusion

FCIP is crucial and very helpful technique for timely diagnosis and sub-classification of B cell NHL. However, molecular diagnostics are essential for sub-classification of certain entities having limitations in immunophenotypic evaluation.

Malignant Hematology-Laboratory (MHL) OP-MHL-7

TRBC1 as a Surrogate marker for Clonality in TCR Alpha/Beta Positive T-Cell Neoplasm by Multicolor Flowcytometry

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Introduction

The diagnosis of T-cell Neoplasm is often challenging, due to overlapping features with reactive T-cells and limitations of currently available T-cell clonality assays. The description of an antibody specific for one of two mutually exclusive T-cell receptor β-chain constant regions (TRBC1) provide an opportunity to facilitate the detection of clonal TCRαβ T-cells based on TRBC-restriction by Multicolor Flowcytometry (MFC).

Aims & Objectives

The objective of the study was to detection of clonal TCRαβ T-cells based on TRBC1-restriction by MFC.

Materials & Methods

The MFC based TRBC1 antibody (JOVI1 clone), in conjunction with other T-cell markers was used to detect T-cell clonality in bone marrow (BM), peripheral blood (PB) and body fluids. 25 suspected cases of T cell neoplasms were analysed with a cocktail of monoclonal antibodies including CD2/ sCD3/ CD4/ CD5/ CD7/ CD8/ CD45/ CD26/ CD30/ TCRαβ /TCRγδ/ CD30/ CD16+56/ TRBC1(T-cell lymphoproliferative disorder MFC panel). The results were corelated with lymph node biopsy wherever available.

Result

The optimization and validation of TRBC1 MFC assay was performed on 12 normal peripheral blood samples from healthy individual as per ICCS TRBC1 validation-Practical guidance.

The TRBC1 for clonality assessment was further evaluated in 25 suspected cases of T cell neoplasms. Of these 25 cases, 18 had involvement of PB/BM by abnormal T Cells as diagnosed by T-CLPD MFC panel. Out of these 18 MFC involved cases, TRBC1 assay showed monotypic peak in 16 cases and polytypic pattern in 2 cases. In

rest 7 MFC uninvolved cases (6 of Lymph node diagnosed T-cell Neoplasm and 1 with proliferation of reactive T-LGL) the TRBC1 showed polytypic pattern. The sensitivity of TRBC1 to detect clonality on MFC in our study was 88.8%. The sensitivity to detect polyclonal/reactive T cell is 100%.

Conclusion

Single TRBC1 antibody detection of T-cell clonality by flow cytometry is a simple, rapid, and robust assay that could be routinely utilized in flowcytometry laboratories. Utilizing TRBC1 along with a comprehensive T-cell panel can diagnose or exclude a possibility of PB/BM involvement in T-cell Neoplasm cases.

Malignant Hematology-Laboratory (MHL) OP-MHL-8

The Biopsy Presentation of Acute Lymphoblastic Leukemia and Its Correlation with Clinical Outcomes

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Introduction

Bone marrow fibrosis (BMF) is not currently considered a factor that may influence treatment outcomes in acute lymphoblastic leukemia (ALL). While historically associated with impaired hematopoiesis and increased transfusion requirements, the relationship between higher grades of fibrosis and minimal residual disease (MRD) positivity remains controversial.

Aims & Objectives

To investigate the correlation between BM fibrosis, transfusion requirement and MRD status in ALL patients.

Materials & Methods

Our study explores the impact of bone marrow fibrosis, graded according to the WHO 2022 system, on MRD status in 14 ALL patients examined over two months at a tertiary care hospital in India.

Follow up taken upto first MRD.

Pearson's correlation was used to calculate the correlation between BM fibrosis, MRD positivity and transfusion requirements.

Result

This study evaluated the relationship between bone marrow fibrosis grades, transfusion requirements, and patient outcomes in acute lymphoblastic leukemia (ALL). Patient outcomes were classified as good (MRD negative), intermediate (MRD positive), or poor (death or severe complications).

The analysis showed that patients with Fibrosis Grade 1 predominantly had favorable outcomes, with 9 out of 10 patients achieving MRD negativity and only one patient being MRD positive.

In contrast, Fibrosis Grades 2 and 3 were associated exclusively with intermediate outcomes, as all patients with these grades were MRD positive. Additionally, 4 patients required significant transfusion support (>2 pRBC or >8 RDP), indicating a higher likelihood of treatment-related complications.

These findings suggest that higher fibrosis grades are associated with worse prognoses, a higher likelihood of MRD positivity, and greater transfusion dependency, emphasizing the potential prognostic value of bone marrow fibrosis in ALL.

Conclusion

Higher grades of bone marrow fibrosis are strongly associated with MRD positivity and increased transfusion dependency, indicating a more aggressive disease course in ALL. Bone marrow fibrosis may serve as a valuable prognostic marker, identifying patients at risk for persistent MRD and complications. This aligns with evidence that cancer-associated fibroblasts contribute to fibrosis and resistance to therapy. Incorporating fibrosis assessment into clinical practice could improve risk stratification and guide treatment decisions, enhancing outcomes in ALL patients.

Malignant Hematology-Laboratory (MHL) OP-MHL-9

Expression of CD304 in Pediatric B Cell Acute Lymphoblastic Leukaemia and Its Role in Measurable Residual Disease (MRD) Monitoring

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Introduction

The treatment approach for B-cell Acute Lymphoblastic Leukemia (B-ALL) involves risk-adapted therapy alongside supportive care, leading to patient survival rates of approximately 92%. However, relapses still occur in around 20% of cases, with Measurable Residual Disease (MRD) serving as a critical prognostic marker for predicting relapse. MRD detection requires differentiating between normal progenitor cells and leukemic counterparts. There is an ongoing need for dependable markers to enhance MRD detection, which would aid in guiding therapeutic decisions.

Aims & Objectives

The objective of this study was to assess the expression of CD304 in pediatric B-ALL patients and its potential role in MRD monitoring.

Materials & Methods

This study evaluated 40 newly diagnosed pediatric B-ALL patients, all under the age of 18, for immunophenotyping via multiparametric flow cytometry. The expression of MRD markers, including CD304, was analyzed both at the time of diagnosis and at day 35 post-induction chemotherapy. Additionally, mean and median fluorescence intensity (MFI) were assessed.

Result

At diagnosis, 65% (26/40) of cases exhibited CD304 overexpression. Among the 40 patients, 14 tested positive for MRD on day 35, with CD304 overexpression observed in 78.6% (11/14) of these cases. Comparing day 0 to day 35, CD304 expression was retained in 7/8 cases, lost in 1/8 case, and newly gained in 4 cases. The median and mean MFI of CD304 in leukemic blasts was significantly higher than in mature lymphocytes and normal precursor B-cells, both at diagnosis and after chemotherapy. Additionally, a statistical correlation was found between CD304 and other MRD markers.

Conclusion

CD304 demonstrated consistent expression in B-ALL cases at both diagnosis and post-induction chemotherapy. The median MFI of CD304 was notably higher in leukemic blasts compared to normal precursor B-cells or hematogones, suggesting its potential inclusion in MRD assessment panels for B-ALL, thereby enhancing the accuracy of MRD detection.

Malignant Hematology-Laboratory (MHL) OP-MHL-10

Immunohistochemical Expression of Mutant NPM1 in Adult Acute Myeloid Leukemia

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Introduction

Acute myeloid leukemia is a clonal hematopoietic neoplasm characterised by proliferation of myeloid blasts in the bone marrow which may harbour unique cytogenetics/ molecular abnormalities that may impact the biological behaviour and response to chemotherapy. Recent WHO classification has highlighted the prognostic impact mutant Nucleophosmin 1 (mNPM1) and FLT3 and other markers in risk stratification of acute myeloid leukemia. Recently IHC expression of mNPM1 and FLT3 has been shown to be simple and cost-effective tool for demonstration of above molecular abnormalities. However, data from Indian AML subjects is lacking.

Aims & Objectives

To study the clinico-hematological, bone marrow morphological changes in newly diagnosed adult (≥18 years) AML and correlate with mNPM1 expression by immunohistochemistry and molecular testing results.

Materials & Methods

All cases of adult AML diagnosed over last nine months (January-September 2024) at our center were retrospectively reviewed in regard to age, gender, complete blood count, peripheral smear blast morphology, presence/absence of blast with cupped nuclear outline, FAB subtypes, flowcytometric immunophenotyping. Pattern and intensity of NPM1 expression by the myeloid blasts by IHC were correlated with available molecular data.

Result

There were 35 cases of AML including 8 APMLs, 4 MPO-ve AMLs with a median age of 43 years (18 to 75). On peripheral smear examination, blasts with cupped nuclear outline (in at least 10% of cells) were identified in 12 cases (31%) (CD34 and HLA-DR negative in 6).Out of these Six cases, 4 showed mNPM1 and FLT3 gain, 1 showed only FLT3gain, and 1 is negative for both.

Conclusion

Immunohistochemical characterization of mutant NPM1 can be a cost-effective tool for risk stratification in adult Acute Myeloid Leukemia. Data on further studies to be presented.

Malignant Hematology-Laboratory (MHL) OP-MHL-11

The Genetic Characterization and Outcome Analysis of Acute Leukemia of Ambiguous Lineage – A Gray Zone Entity

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Introduction

Despite being a distinct entity for more than a decade, the management of acute leukemia of ambiguous lineage (ALAL) is still not clearly defined. The rarity of the disease plus the unavailability of information about the disease's biological characteristics are proposed to be the important contributors.

Aims & Objectives

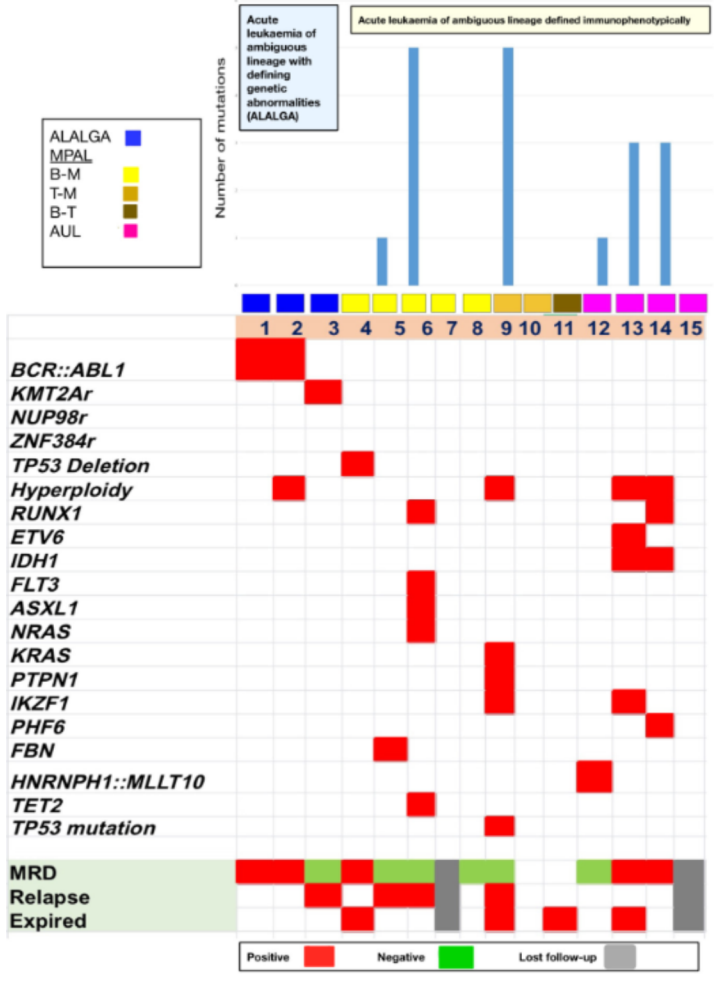
1. To evaluate the spectrum of genetic aberrations identified by a combined Karyotyping, FISH, and NGS-based DNA sequencing techniques
2. To evaluate the treatment received and patient/disease outcome

Materials & Methods

All the newly diagnosed cases of ALAL were included in this retrospective study of 56 months. The diagnosis and MRD analysis were made by 9/10 colorflow cytometric immunophenotyping as per established guidelines. Karyotyping analysis was done as per standard laboratory procedure. FISH analysis included probes for *BCR-ABL1* fusion, *KMT2A* break apart probe, *NUP98* break apart probe, *ZNF384* break apart probe, and *TP53* deletion probe. DNA-based targeted gene analysis was performed by Next Generation Sequencing (NGS). The endpoints for the outcome analysis were post-induction MRD status, relapse-free survival, and overall survival.

Result

A total of 15 cases were diagnosed during the study period (M:F=4:1; median age=32yrs, range=13-69yrs). Subtype analysis revealed - mixed phenotype acute leukemia (MPAL) associated with defined genetic abnormalities=03 cases (*BCR::ABL1* fusion=02; *KMT2A*-rearranged=01), ALAL defined immunophenotypically=12 cases (B/Myeloid=05; T/Myeloid=02; B/T=01; acute undifferentiated leukemia=04). The extramedullary disease and baseline CSF involvement were seen in 06/15 and 08/13



cases, respectively. Karyotyping showed clonal abnormality in 08/12 cases (tri-/tetraploidy=04). NGS-based sequencing results revealed the presence of at least one pathogenic variant in 06/07 cases. A total of 14 pathogenic variants were detected in 12 different genes (median=2.0/case; range=1-5 variants). ALL-based and AML-based therapy was given in 05 cases each, one patient received hyper-CVAD induction therapy. Post-induction MRD was positive in 05/11 cases; disease-relapse was noted in 04 cases; 04 patients expired during the treatment (median follow-up=14 months).

Conclusion

Though stem cell transplant is the most optimal therapy for ALAL patients, not all patients are fit enough or afford to undergo this. Understanding the clinical and biological characteristics of these patients to develop an individualized management strategy is an urgent need.

Malignant Hematology-Laboratory (MHL) OP-MHL-12

Correlation of Cytogenetic Aberrations with Clinical Characteristics and Treatment Outcome in Multiple Myeloma

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Introduction

Multiple myeloma (MM) is a clonal plasma cell disorder with significant heterogeneity. We evaluated the response to triple drug combinations, bortezomib, lenalidomide, and dexamethasone (VRd) vs VCd (bortezomib, cyclophosphamide, and dexamethasone), and their association with cytogenetic abnormalities in treatment-naive multiple myeloma patients.

Aims & Objectives

1) To determine the frequency of primary and secondary cytogenetic aberrations in MM.

2) To correlate the cytogenetic aberrations and clinicopathological characteristics with response to treatment.

Materials & Methods

We retrospectively analyzed cytogenetic data in 1677 newly diagnosed MM patients at Tata Memorial Centre, from Jan 2014 to Dec 2021 and assessed treatment response in patients wherein follow-up data was available. Overall response rate (ORR), defined as partial response (PR) and very good partial response (VGPR) was assessed in the cytogenetic subgroups identified. Statistical analyses were performed using SPSS, ver.18.

Result

Chromosomal abnormalities were detected in 1103 (65.8%) MM patients studied. Of the 1103 patients, primary abnormalities were found in 664 (60.1%) of which 197 (17.8%) patients harbored High-risk IgH-t, 194 (17.5%) had standard risk IgH-t and sole trisomies in 273 (24.7%), while secondary abnormalities were found in 292 (26.4%) of which high-risk abnormalities 1q21 amplification/1p32deletion and TP53 deletion or monosomy 17, were detected 21.4% and 6.8% cases respectively. IgH-t other than high-risk translocations along with trisomies were significantly associated with IgG isotype ($P < 0.001$). In contrast, IgH high-risk/other high-risk secondary abnormalities without trisomy and sole trisomies were significantly associated with platelet count > 150 × 10/L, LDH levels < 222 units/L, R-ISS Stage II and very good partial response (VGPR) to first-line chemotherapy. VCd was administered in 70.3% of patients, whereas 29.7% patients received VRd. After four cycles of induction treatment VGPR or better was observed in 62% of the VCd group vs. 74.4% in the VRd group ($P = 0.005$).

Conclusion

The findings highlight the importance of cytogenetic profiling is for informing treatment choices. Compared to patients treated with VCd, patients treated with VRd showed a greater ORR, especially in patients with high-risk cytogenetic profiles emphasizing the necessity for individualized treatment plans in the management of multiple myeloma.

Malignant Hematology-Laboratory (MHL) OP-MHL-13

MRD Analysis by Molecular Method (DDPCR) vs Flowcytometry in Acute Myeloid Leukemia with Recurrent Cytogenetic Abnormalities

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Introduction

Measurable residual disease (MRD) detection in acute myeloid leukemia (AML) has emerged as a powerful prognostic factor. Flow cytometry (MFC) and PCR-based methods are two most common methods for MRD analysis. The European Leukemia Net (ELN) guidelines has recommended qPCR or ddPCR for MRD analysis in cases of AML with PML::RARA, inv16, RUNX1::RNX1T1 and NPM1-mutation. However, MFC is recommended in all AML sub-groups.

Aims & Objectives

Comparison of MRD analysis between MFC and droplet digital PCR (ddPCR) in case of AML with NPM1, Inv16 and RUNX1::RNX1T1

Materials & Methods

40 bone marrow aspirate samples from 27 patients were subjected to simultaneous MRD analysis by MFC and ddPCR. An 11-color two tube MFC AML-MRD panel was performed. All samples were acquired on Beckman Coulter DxFLEX and was analyzed using Kaluza v2.2 software (Beckman Coulter Life science, California). Sample for ddPCR was performed from RNA extracted from Bone marrow sample WBC using Qiasymphony. Complementary DNA was synthesized using reverse transcriptase followed by quantification of NPM1/inv16/RUNX1::RUNX1T1 fusion transcript by ddPCR (Biorad, USA).

Result

Total 40 samples were analyzed at different time points in their treatment. Out of which maximum number of patients were showing NPM1 mutation(n=19), followed by inv16 mutation(n=13) and RUNX1::RUNX1T1(n=8). MRD positivity in MFC was 20% (n=8, range 0.02%-2.02%) where as ddPCR detected MRD in 52.5% (n=21, range-0.012-43.5%). 47.5 cases were not showing any evidence of MRD by Flowcytometry and ddPCR. When both ddPCR and flowcytometry MRD analysis were compared, concordance between both the techniques was 67.5% (n=27 cases) and discordance was 32.5% (n=13 cases). Both MFC and ddPCR were moderately correlated in our study (Spearman correlation coefficient 0.554, p value-0.0002). Compared to ddPCR, sensitivity of MRD detection by MFC is 38.1% but with a high positive predictive value of 100%.

Conclusion

MFC MRD analysis in AML has a less turn around time, however it is less sensitive compare to molecular methods. Cases where molecular targets like NPM1, inv16 and RUNX1::RUNX1T1 are available MRD analysis by ddPCR is recommended and preferred.

Malignant Hematology-Laboratory (MHL) OP-MHL-14

Mantle Cell Lymphoma - Clinicopathological Profile at a Tertiary Cancer Centre

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Introduction

Mantle cell lymphoma (MCL) is a mature B-cell neoplasm has varied clinical presentation and aggressiveness resulting in overall poor prognosis. Previously considered uncurable, the median survival rate has improved. We studied 29 cases MCL seen at a single institution over 3.75 years to determine both clinical and pathological prognostic factors.

Aims & Objectives

A retrospective study comprising a case series was conducted to describe the clinicopathological profiles of individuals diagnosed with Mantle cell lymphomas from a tertiary cancer centre.

Materials & Methods

The clinicopathological profiles of cases of Mantle cell lymphoma, were retrieved from files of Basavatarakam Indo American Cancer Hospital & Research Institute, Hyderabad from January 2021 to September 2024. The histopathological data including the immunohistochemistry markers data was analysed for aberrancies along with literature review.

Result

There were 29 cases diagnosed as mantle cell lymphoma. 79.3% (23/29) cases were male. 20.6% (6/29) were female. The age of the patient ranged from 44 to 77yrs with a median age of 59 yrs. 79.3% (23/29) on lymph nodal biopsies. 3/29 cases presented as polyps/thickenings in the GI tract. 3 cases were biopsied one each from chest wall, arm and bone marrow. Radiological investigations for staging and assessment were carried out in 21/29 cases. 14 out of the 29 cases presented as stage iv disease, 6/29 cases were stage iii, and only 1 case presented at stage ii. Splenomegaly was present in (11/18) patients evaluated. evaluated. Anemia was noted in 17/25 cases at presentation. Bone marrow was involved morphologically in 8/9 cases identified in aspirate and biopsy. IHC showed CD20 positive in 100 cases (29/29), BCL2 100% positive in 15/29 cases. Ki-67 proliferative index on 20/29 cases ranged from 15-80% with a median of 50%. CyclinD1 positive in 100 cases done(27/29). SOX11 positive in 15/17 cases perfomed. Additional markers - CD5, Tdt and MNDA were done on some cases to rule out others in suspecious cases.

Conclusion

The most common presentation was as lymph nodal swelling followed by GI tract lesions. The aggressive nature of the disease was noted as most patients presenting with stage iii & iv disease in the data presented. Spleen involvement and bone marrow involvement was noted in many cases which was in line with the literature.

Malignant Hematology-Laboratory (MHL) OP-MHL-15

Utility of KIR Markers in Establishing Clonality in Mature NK Cell Lymphomas by Flow Cytometry

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Introduction

NK cell lymphomas designate a rare group of diseases, and it is challenging to differentiate them from reactive NK cell proliferations. As clonality/marker restriction is fundamental to hematologic malignancies, it is essential in diagnosing NK-cell lymphomas,as it is challenging to diagnose based solely on morphology, clinical presentation and immunophenotypic aberrancies. Unlike other T cell neoplasms, NK cells lack unique gene rearrangements, hence clonality assessment is difficult by molecular techniques. KIR are a family of polymorphic activating and inhibitory receptors which are exclusively distributed on different NK cell subsets and expansion of particular KIR indicates clonal expansion of NK cells.

Aims & Objectives

To study utility of KIR markers in establishing NK-cell clonality by flow cytometry in NK-cell lymphomas

Materials & Methods

The study includes FNA, bone marrow, peripheral blood and body fluid samples from 12 patients. Flow cytometric immunophenotyping was performed using a 16-color antibody panel and data analyzed with Kaluza software (V2.1).

The antibody panel included NK cell markers CD4/CD38/CD7/CD56/CD8/CD314/HLADR/CD16/CD107a and KIRs(CD158a/CD158b/CD158d/CD158e/CD158i) with CD3.KIR restriction denoted a NK-cell population without any expression or restriction in any subset. Results were correlated with clinical and histopathological features.

Result

Median age of patients was 44.5 years (range 27-70 years) and M:F::3:1. Involvement by NK cell neoplasm was observed in 9/12 cases distributed as 1 FNA, 1 CSF, 1 ascitic fluid, 3 BMAs and 3 peripheral blood samples. 8 cases showed negativity for all KIR subsets. 1 case showed two populations with one being KIR negative and other only expressing CD158b. Another case showed expression of only CD158i. This was taken as indirect evidence of clonality. In 3/12 cases, FCM helped diagnose NK cell lymphoma where biopsy results were inconclusive.

Conclusion

We assessed NK cell clonality by FCM for the first time and found that KIR is a highly reliable marker for establishing NK-cell clonality and hence for the diagnosis for NK cell lymphomas.

Malignant Hematology-Laboratory (MHL) OP-MHL-16

A Comprehensive Clinical, flowcytometric & Molecular Mutational Analysis and Discussion of Variant Translocations of Acute Promyelocytic Leukemia (APL): An Experience From Tertiary Hospital

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Introduction

Data on the Acute Promyelocytic Leukemia (APL) cases from India is limited.APL with translocations t(15;17)(q22;q12) is a leukemia predominated by abnormal promyelocytes in the peripheral blood and bone marrow. It differs from other AML . The gold standard' for the diagnosis, is identification of PML-RARα´ by molecular techniques, hence, this has to be done so that appropriate therapy may be initiated.

Aims & Objectives

This present study aims to investigate the application values of immunophenotypic analysis and molecular genetics in the diagnosis of acute promyelocytic leukemia (APL) in correlation with morphological findings. To determine prognostic significance of molecular characteristics findings in APL cases were analyzed.

Materials & Methods

The relevant clinical, flowcytometry, bone marrow, molecular diagnostics and other laboratory data were retrieved from hospital and departmental records of APL patients between January 2022 and October 2024.The samples were processed by 10 color flowcytometry using Stain-Lyse-Wash method.APL cells were gated using CD45 versus side scatter plot. PML-RARA (promyelocytic leukemia /retinoic acid receptor alpha rearrangement was detected by Real time-PCR (RT-PCR) from bone marrow or peripheral blood samples, which were in EDTA anticoagulant with three transcripts studied.

Inclusion criteria: All cases were APL typically displays immunophenotypic features, including high side scatter, positivity for CD13, CD33, and CD117 and absent expression of CD34, HLA-DR, CD11b, CD11c negative and PML-RARA rearrangement detected by Real time-PCR (RT-PCR) were included.

Exclusion criteria: Other than APL or cases with insufficient data were excluded.

Result

A total of 58 patients diagnosed as APL were evaluated. Age range from16-78(mean age 44) years. M: F: 1.6:1, with male preponderance. The sensitivity and specificity of FCM were 91.9% and 98.7% respectively. Average percentage of abnormal promyelocytes in bone marrow was 84.25%. Disseminated intravascular coagulation was common at presentation (71%). Severe thrombocytopenia was seen in 73%, leukocytosis in 55% and severe anemia in 45%, pancytopenia was noted in 14 patients. PML RARA testing available in 42/58 samples with transcript of break point cluster region 1(bcr 1) in 31 /42 and bcr3 in 9 /42 samples detected. The prevalence of FLT3 -ITD , NPM 1 were detected in one case each. Post treated cases were 45 /58 cases and WBC count was significantly higher in bcr 3 comparative to bcr1 patients.

Conclusion

FCM could rapidly and effectively diagnose APL. Molecular and genetic criteria were the golden criteria for the diagnosis of APL. About 10% of immunophenotyping cases relied on molecular genetics for diagnosis. Break point cluster region 1(bcr 1) transcript is higher prevalent over bcr3

Benign Hematology - Clinical (BHC) OP-BHC-1

Performance Characteristics of % Hypochromic Red Cells in the Detection of Latent Iron Deficiency in Women with Menometrrorhagia

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Introduction

Latent iron deficiency (LID) is a precursor stage of Iron Deficiency Anemia (IDA) in which there is evidence of iron deficiency without anemia. It causes decreased work capacity, cognitive impairment and immune deficiency, which can be corrected by iron supplementation. Conventional hematologic and biochemical parameters have limitations in the diagnosis of LID. This study was done to assess the performance characteristics of percentage of hypochromic red cells (% HYPO) in the detection of LID in women with menometrorrhagia.

Aims & Objectives

To assess the sensitivity, specificity, PPV and NPV and optimum Cut Off Values of (% HYPO) in the diagnosis of LID as compared to conventional hematologic and biochemical parameters.

Materials & Methods

This study was done on 226 women attending the Gynaecology OP clinic Sree Gokulam Medical College, of which 183 had menometrorrhagia, remaining being controls. After testing for conventional hematologic indices and serum ferritin the subjects were divided into 3 groups: a LID group, an IDA group, and a control group without iron deficiency. ROC curve analysis was performed to assess % HYPO and other conventional hematological parameters in identifying LID.

Result

Most hematological indices were within normal ranges in LID population, thus limiting their utility. The AUC for % HYPO in LID population was 0.736 with an optimum cut off of 8.7 corresponding to a sensitivity and specificity of 62.3 and 76.74 respectively.

Conclusion

% HYPO is sensitive, specific, fast, cheap, and practical and thus serves as a better predictive marker than conventional biochemical and hematological parameters in the detection of LID.

Benign Hematology - Clinical (BHC) OP-BHC-2

Integrating Clinical Features and Genetic Factors with Blood Component use in Acute Leukemia

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Introduction

Acute haematological malignancies of lymphoid or myeloid origin, molecular, clinical and chemotherapy govern patient's prognosis with blood component usage in acute leukaemia a trade-off risk for maximum benefit.

Aims & Objectives

To estimate differences in blood component usage in acute lymphoblastic leukemia (ALL) and acute myeloid leukaemia (AML) during induction phase of chemotherapy based on predefined risk stratification.

To correlate baseline laboratory parameters with blood component transfusion in AML, ALL patients.

Materials & Methods

In this cross-sectional analytical study (2021 to 2024) risk classification of ALL patients based on T cell or B precursor ALL (early/mature forms); ALL with/without t (9,22)/BCR-ABL; B-Cell WBC <30,000/ µl; >30,000/ µl; ALL with/without remission and ALL in relapse into standard risk (SR), high risk (HR) and very high-risk (VHR) sub-groups.

AML stratification into favorable, Age <65y>

Transfused blood components (a factor of risk-stratification) were evaluated for significant difference by Kruskall-Wallis or One-way ANOVA and Pearson correlation coefficient (CC) of transfused components with baseline levels Hb (g/dl), Platelet counts (µl) respectively.

Result

In this study with ALL (n=45) and AML (n=32) patients. Overall baseline parameters (Table)

ALL patients of T cell, B cell origin was not significantly different (p=0.181), Median baseline Hb(g/dl), WBC (/µl) and Platelet counts (/µl) were not different across risk-groups (RG). (P>0.05). Median packed RBC (PRBC), Random donor platelets (RDP), Single donor platelets (SDP), Fresh Frozen Plasma (FFP) were not significantly different across RG. (P>0.05) Baseline Hb(g/dl) had a low CC with total PRBC transfused (P=0.54); Baseline Platelet counts (/µl) negatively correlated with RDP (P=0.12) with positive correlation with SDP. (P=0.02)

AML (n=32) mean (SD) Hb(g/dl) and median (IQR) WBC (/µl) across RG. (P=0.238), (P=0.878) with significantly different median platelets (/µl) (P=0.006). PRBC, FFP, SDP and RDP were not significantly different. (P>0.05) The CC of Hb with PRBC and Platelets (/µl) with SDP showed negative correlation. (P=0.014, 0.023) and negative correlation with RDP units (P=0.079).

Conclusion

PRBC, FFP, SDP, RDP transfusions did not differ across the RGs in ALL and AML.

SDP had significant positive correlation with baseline platelets (ALL). PRBC, SDP units showed significant negative correlation with baseline Hb, Platelet counts (AML) suggestive of evidence-based use of blood component.

Variable	Total Number	Mean	StDev	Median	IQR	CC (Hb with PRBC) Confidence interval (CI)	CC (RDP with Platelets(/µl) (CI)	CC (SDP with Platelets(/µl) (CI)
ALL								
Age	45	24	11.2472	23	15.5	0.097(-0.213,0.390)/ (n=42)	-0.255(-0.531,0.071)/ (n=38)	0.591(0.112,0.847)/(n=15)
PRBC	42	6.85714	3.80994	6	6			
FFP	3	4	1.73205	3	3			
SDP	15	4	4.0708	3	2			
RDP	38	43.2368	37.9626	32	44.75			
Hb	45	8.16222	3.61338	7.6	5.3			
WBC	45	43289.6	93266.6	8250	34280			
Platelet	45	82940	106924	50000	99500			
AML								
Age	32	35.3438	16.3463	34.5	25	-0.429(-0.676, -0.094)/ (n=32)	-0.326(-0.614,0.039)/ (n=30)	-0.408 (-0.666, -0.063)/(n=31)
PRBC	32	6.875	4.75021	6	5			
FFP	4	2	2.82843	1	5			
SDP	31	2.72581	2.86309	2	4			
RDP	30	72.6333	58.8455	63.5	74.5			
Hb	32	7.30625	2.05535	7.6	3.375			
WBC	32	38635.6	55329	17655	44130			
Platelet	32	39375	42865.7	28000	26750			

Benign Hematology - Clinical (BHC) OP-BHC-3

Targeting Intracellular Calcium: A Novel Therapeutic Strategy for Sickle Cell Disease

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Introduction

Red cell dehydration is a fundament pathological process in sickle cell disease, influencing HbS polymerization and RBC rigidity, which leads to vaso-occlusion, hemolysis, and complications such as tissue infarction, oxidative stress, and hypercoagulability. Channels such as the Gardos channel, Piezo-1, K-Cl cotransport, Na-K pump, and NMDARs receptor are involved in the dehydration process by regulating calcium ion into RBCs.

Aims & Objectives

To investigate the role of intracellular calcium ions in the pathophysiology of sickle cell disease and explore their potential as novel therapeutic targets.

Materials & Methods

50 patients with SCD (Median Age 7yrs, Female 56% and consanguinity 8%) and 50 normal healthy individuals were studied. Determination of Intracellular Free Calcium level and to detect changes in intracellular calcium in response to mechanical stimulation using Fluo-4-AM fluorescence dye. Oxidative stress markers were measured using flow cytometry. Hydroxyurea (10mg/kg/day) treatment was given to the all SCD patients. Measurement of all hematological and biochemical assay were performed before and after six months HU treatment. In addition, 4 cases of clinically non-responded to HU were also studied.

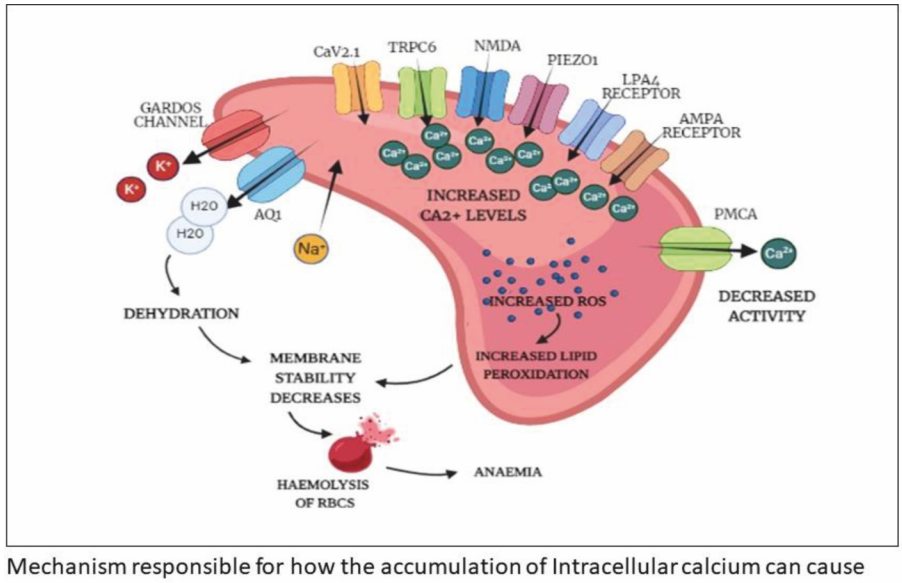
Result

The Intracellular free calcium levels (P<0.001), intracellular Ca2+ levels after spiking with distilled water (P<0.001), ROS levels (P<0.001), lipid peroxidation levels (P<0.001), Potassium ion leak/ loss (P=0.2239) all were found to have significantly increased in the SCD patient's group (Without HU) as compared to the healthy individuals.After the HU treatment for 6 months, the Intracellular Free Calcium level (P<0.001), Ca2+levels

after spiking with distilled water (P<0.001), ROS levels (P<0.001), and lipid peroxidation levels (P<0.001), were found to have significantly decreased as compared tobaseline data of SCD patients. 8 cases that showed an increase in the intracellular calcium levels (P=0.036) even after 6 months of HU treatment. The study also involved 4 knownSCD cases that were clinically non-responding to hydroxyurea and their intracellular calcium level was significantly increased (P = 0. 002) as compared to HU responders.

Conclusion

We observed elevated intracellular calcium levels were associated with several interconnected pathological processes such as dehydration oxidative stress hemolysis. These findings raise the question of whether increased intracellular calcium is a central component in the pathogenesis and severity of SCD. Targeting intracellular calcium could be a promising novel therapeutic strategy for improving the management of SCD patients.



Mechanism responsible for how the accumulation of Intracellular calcium can cause the destruction of sickle blood cells

Benign Hematology - Clinical (BHC) OP-BHC-4

Low Hemoglobin is not always Iron deficiency anemia… at least in Nilgiris, Tamil Nadu

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Introduction

Anemia is a global public health concern and accurate characterization of anemia is critical to understand the burden and epidemiology of the problem, so as to plan intervention and treatment. The tribal communities living in the Kurumbadi locality in the Nilgiris face numerous challenges and one of the prevalent health issues is anemia which affects a significant proportion of the population.

Aims & Objectives

To determine the prevalence of anemia among tribal communities of Burliyar and to improve medication adherence to iron by implementing a daily monitoring system by the community health ambassadors (CHA) and to identify any other cause of anemia in patients who do not improve with the intervention

Materials & Methods

This was a retrospective cross sectional community-based anemia screening done in the tribal hamlets in Burliyar, Nilgiris, with a total population of 230 from November 2023to May 2024.

Result

A baseline hemoglobin screening was done on 184 participants using the Accusure Hb101 system with capillary blood. The cut off to define anemia in adults was Hb < 13 gm/dl in males and < 12 gm/dl in females. Based on this criterion, we had 131 (71%) participants with anemia of which 74 (56%) were females and 57 (44%) were males. Among these, 32 (24%) participants were children < 14 years of age. There was distribution of iron supplements for 100 days along with iron rich dry ration which was monitored daily by the CHA to 110 participants. The prevalence of anemia improved from 69.8% to 61.8%. An additional 29 participants were added into the study during our monthly camps. Out of the 139 participants, 36 (26%) were suspected to have hemoglobinopathy. Of these, 30 participants underwent hemoglobin electrophoresis through which 7 of them were identified to have sickle cell trait and 1 had sickle cell disease. The remaining 22 underwent molecular testing and all were identified to have Homozygous alpha 2 gene deletion.

Conclusion

Targeted intervention and careful monitoring helps to reduce the burden of anemia in a community. Although iron deficiency anemia is the most common form of anemia, quarter of our patients have hemoglobinopathy – predominantly alpha thalassemia.

Benign Hematology - Clinical (BHC) OP-BHC-5

Study of Bone Mineral Density in Patients of Hemoglobinopathies

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Introduction

Osteoporosis is low bone mineral density that increases fracture risk. Hemoglobinopathies cause bone involvement. Dual Energy X-ray Absorptiometry (DEXA) measures bone mineral density using T-score and Z-score values. A T-score of −1.0 or higher is normal, between −1.0 and −2.5 is osteopenia, and −2.5 or lower is osteoporosis. The Z-score compares BMD to age, sex, and ethnicity norms.

Aims & Objectives

1. Primary Aim- To evaluate the Incidence of Osteoporosis in patients of Hemoglobinopathies as detected by DEXA scan.
2. Secondary Aim- To study the incidence separately in different hemoglobinopathies like Sickle Cell Disease, Sickle Cell Trait and Thalassemia Major.

Materials & Methods

A year-long study was conducted at JLN Hospital and Research Center in Bhilai to observe and measure the bone mineral density of 59 patients over the age of 18 who were undergoing treatment for Hemoglobinopathies. All eligible patients agreed to participate in the study. To provide a comparison, a control group of 59 subjects without Hemoglobinopathies was also included.

Result

- Thalassemia: 75% had osteoporosis (BMD hip), and 100% had osteoporosis (BMD spine).
- Sickle cell disease: 34.38% had osteoporosis, 40.63% had normal BMD (BMD hip); 40.63% had

osteoporosis, and 31.25% had normal BMD (BMD spine).

- Sickle cell trait: 15.79% had osteoporosis, 52.63% had normal BMD (BMD hip); 15.79% had osteoporosis, and 42.11% had normal BMD (BMD spine).
- Prevalence of osteoporosis and osteopenia: Study group: 33.9% and 27.12% respectively (BMD hip); 48.68% and 28.81% respectively (BMD spine).

Conclusion

The risk of developing osteoporosis is higher in patients with hemoglobinopathies, particularly thalassemia and sickle cell disease (SCD), and least in sickle cell trait (SCT). Individuals with low serum calcium levels are more susceptible to developing osteoporosis.

Benign Hematology - Clinical (BHC) OP-BHC-6

Efficacy of Romiplostim in Newly Diagnosed Aplastic Anaemia

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Introduction

Thrombopoietin receptor agonists like Eltrombopag have significantly improved outcomes in patients with Aplastic anemia (AA). There is emerging data that Romiplostim is also equally effective. In India, Eltrombopag is very expensive, and Romiplostim is available as a generic drug and is cost-effective. Here, we report the efficacy of romiplostim in our AA patient cohort from a single tertiary care center in India.

Aims & Objectives

To assess the safety and efficacy of Romiplostim with Cyclosporine (CSA) and Danazol with or without Anti-thymocyte Globulin (ATG) as first-line therapy in newly diagnosed AA.

Materials & Methods

OBSERVATIONAL STUDY

We treated 19 consecutive newly diagnosed AA patients with Romiplostim (10 mcg/kg), CSA, and Danazol with or without ATG. The patients who did not receive ATG were unfit to receive the same.

All patients underwent bone marrow biopsy and karyotypic analysis. Using modified Camitta criteria, the severity of the disease was graded, and British Society of Haematology guidelines for response assessment were used to assess the response

10mcg/kg of Romiplostim was used in all patients.

The primary endpoint was the overall response at 24 weeks.

The Secondary endpoints were

a) Response rates at 6 weeks, 12 weeks, and 18 weeks, including patients achieving transfusion independence.

b) Record the adverse events with the above combination.

Results

We included 19 patients (12male and 7 female). The median age was 49 years. 9 patients had PNH clone. 7 patients had no PNH clone and PNH was not assessed in 3 patients. 13 patients had severe aplastic anaemia (SAA), 4 Very severe AA, and 2 non-severe AA. 4 SAA patients received ATG the other 13 patients received CSA, Romiplostim and Danazol.

At 24 weeks, 6 patients (32%) attained complete response out of which 4 of them had received ATG and 13 patients (68%) attained partial response and all patients,19 (100%) were transfusion-independent with normalisation of at least one cell line.

Conclusion

Impressive response rates were observed with a combination of Romiplostim, CSA, and Danazol with or without ATG in our cohort

The adverse events were grade 1 CTCAE and manageable.

Romiplostim appears to offer a compelling alternative option to Eltrombopag , and these findings need to be confirmed in larger studies.

Benign Hematology - Clinical (BHC) OP-BHC-7

Reticulocyte Hemoglobin: A Novel Parameter for Detecting Iron Replete Status Among Regular Female Blood Donors

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Introduction

Regular blood donors represent healthy population. Latent Iron Deficiency (LID) is highly prevalent among females and the risk is expected to increase with regular blood donation. Current blood donor selection guidelines only screen for hemoglobin levels, potentially missing those with LID which may lead to overt Iron deficiency later. The gold standard for diagnosing LID is serum transferrin receptor level (sTfR). However, it may not be practical as a screening tool due to its high cost. Therefore, this study aims to find the utility of Reticulocyte Hemoglobin (Ret-He) in detecting LID and compare it with Serum ferritin.

Aims & Objectives

To determine the utility of Ret-He in the detection of LID among regular female blood donors.

Materials & Methods

The study subjects included 161 female regular blood donors consenting to participate in the study. Subjects were divided into two groups-LID and non-LID based on sTfR levels. Ret-He, Immature Reticulocyte Fraction (IRF), and Serum Ferritin levels were compared between the two groups. Also, the presence of LID was correlated with number of donations.

Result

Our study showed a 37.25% prevalence of LID among regular female blood donors. Donors with LID had significantly lower mean Ret-He levels(25.6±1.53pg) than non-LID donors (27.9±1.4pg). Also, Ret-He had higher sensitivity (95%) and negative predictive value (94.2%) than Serum Ferritin. However, the difference in IRF values between these two groups was insignificant. Furthermore, we found no correlation between the prevalence of LID and the number of donations.

Conclusion

LID is highly prevalent among regular female blood donors. Ret-He can be used as a screening tool for Iron status in blood donors thus preventing overt iron deficiency due to donation.

Benign Hematology - Clinical (BHC) OP-BHC-8

Clinical Profile of Inherited Platelet Disorders in Children: A Single Centre Retrospective Study

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Introduction

Inherited platelet disorders are rare conditions with diverse clinical presentations, often resulting in delayed diagnosis due to variable bleeding phenotypes and limited diagnostic facilities. Symptoms range from severe intracranial bleeds to incidental findings of abnormal platelet morphology. These disorders can occur in isolation or alongside other features, with common ones including Bernard Soulier syndrome, Glanzmann Thrombasthenia, and Platelet-type von Willebrand disorder. Diagnosis typically requires platelet function assays or genetic testing. Treatment is primarily supportive, with platelet transfusions, and bone marrow transplantation being definitive therapy. Early diagnosis and regular follow-up are critical in preventing life-threatening bleeds and guiding treatment.

Aims & Objectives

- To study the clinical profile of children with inherited platelet disorders
- To study the treatment received and outcomes of these patients

Materials & Methods

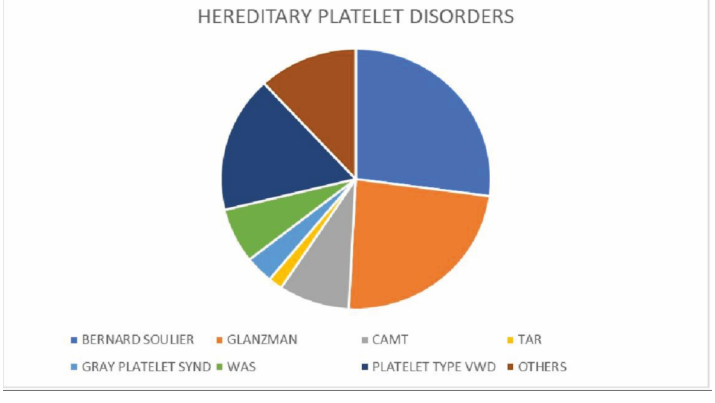
We conducted a retrospective observational study on 59 patients diagnosed with hereditary platelet disorders, who had been following up since January 2015 at BJ Wadia Hospital. Demographic data, past and family history, with clinical presentation, laboratory investigations, were recorded. Other diagnostic tests, treatment received and outcomes were entered in a pre-determined case report form.

Result

Among the 59 patients, the male-to-female ratio was 1.46:1, with a median age of diagnosis at 5 ± 4.66 years. Consanguinity was present in 51%, and 69.40% had a significant family history of bleeding disorders. Sibling death occurred in 24.5.

Conclusion

Inherited platelet disorders can present with mild to severe bleeding history, many have a family history which should prompt testing for the same. Timely diagnosis and identifying severity of bleeding phenotype can help tailoring treatment strategies, guide families on antenatal prevention in subsequent pregnancies and hematopoietic stem cell transplant in selected cases.



Benign Hematology - Clinical (BHC) OP-BHC-9

Platelet Indices and Neutrophil to Lymphocyte Ratio in Hypertensive Disorders in Pregnancy: A Case Control Study

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Introduction

Hypertensive Disorders of Pregnancy (HDP), a broad-spectrum disorder with high blood pressure and end-organ damage, including eclampsia, preeclampsia, etc. In India, prevalence of HDP was reported in 7.8

Aims & Objectives

To evaluate the variations in platelet indices & NLR in HDP versus normotensive pregnancy in reference to clinical parameters.

Materials & Methods

Inclusion criteria: Pregnant women diagnosed as HDP as case and normotensive pregnant women as control. Exclusion criteria: Twin pregnancy, IUFD, bleeding disorders, bad obstetric history, systemic disease, blood transfusion.

A detailed history was obtained, and obstetric examination was performed. Venous blood samples of the females diagnosed with HDP as per guidelines were taken. CBC was done and platelet indices were noted. NLR was calculated after obtaining the absolute values. Control samples were evaluated following same protocol.

Result

The MPV, PDW, PCT were statistically significantly different between normotensive and severe preeclamptic participants ($p < 0.001$). Statistically significant differences were not present in any of the platelet parameters between mild and severe HDP. Eclampsia was strongly associated with P-LCR (platelet-large cell ratio).When comparing HDP to normal pregnant women, there was a statistical significant increase in neutrophil to lymphocytic ratio (NLR) (mean 4.1 vs 2.5 for NLR, $p < 0.001$). In addition, women with severe pre-eclampsia had much higher NLR than those with mild pre-eclampsia. NLR was positively correlated with neutrophil counts, diastolic and systolic blood pressure, and gestational age at birth.

Conclusion

From the findings of this study, generation of platelet parameters and NLR is recommended in diagnosing HDP and determining the development of adverse feto-maternal outcome. This will help in early disease identification and timely institution of interventions to prevent progression to severe disease.

Benign Hematology - Clinical (BHC) OP-BHC-10

Outcome of Low Dose Azacitidine in Patients of Lower Risk Myelodysplastic Syndromes (Lr-Mds)

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Introduction

Myelodysplastic syndromes are clonal haematopoietic stem cell disorders characterised by dysplasia leading to cytopenias and a high probability of progression to acute myeloid leukaemia. Given the poor prognosis of a fraction of LR-MDS patients, strategies that could alter the natural history and improve overall survival are needed.

Aims & Objectives

To assess the responses of low dose Azacitidine in patients of lower risk myelodysplastic syndromes

Materials & Methods

This was a prospective observational study of 20 LR-MDS cases over a study period of 18 months. All patients received subcutaneous azacitidine at 75 mg/m2 for three days in every four weeks for six cycles and were followed up for a period of one year.

Result

The median age was 53.5 years, with Male: female ratio 1.85:1.

Six patients (30%) had MDS-SLD, 11 patients (55%) had MDS-MLD, two patients (10%) had MDS-RS-SLD, and one patient (5%) had MDS-EB1.Five patients (25%) were in the low-risk, and 15 patients (75%) were in the intermediate-risk IPSS-R category. Good cytogenetics was present in 16 patients (80%), and four patients had intermediate cytogenetics (20%).

Overall response was seen in 11 patients (55%). Four patients (20%) showed a complete remission, three patients (15%) showed partial remission, four patients (20%) showed marrow complete remission, and 11 patients (55%) showed hematological improvement.

By using the paired t test, statistically significant mean deviation rise of hemoglobin and absolute neutrophil count at 6 months was seen compared to baseline. By using an independent T test, it was observed that a better overall response was achieved among patients with a higher baseline platelet count.

At the end of one year, 62.5% of the patients had improvement in ECOG status and 55.6% were transfusion-independent. Myelosuppression and infections were observed in 35% and 25% of the patients, respectively. One-year overall survival was 95%.

Conclusion

Azacitidine can be a cost-effective treatment for transfusion-dependent LR-MDS, particularly in an emerging market and mid-income economic country like India. It is a safe drug with only minor adverse effects.

Benign Hematology - Clinical (BHC) OP-BHC-11

Large Scale Community - Based Sickle Cell Surveillance in an Aboriginal Population from Western India

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Introduction

Sickle cell disease (SCD) is an inherited blood disorder that affects millions of people worldwide. Owing to the significant burden of SCD among its aboriginal(tribal) populations, the Government of India has initiated the "Sickle Cell Elimination Mission." We designed our study in alignment with this national initiative to implement a comprehensive screening program in tribal communities of India.

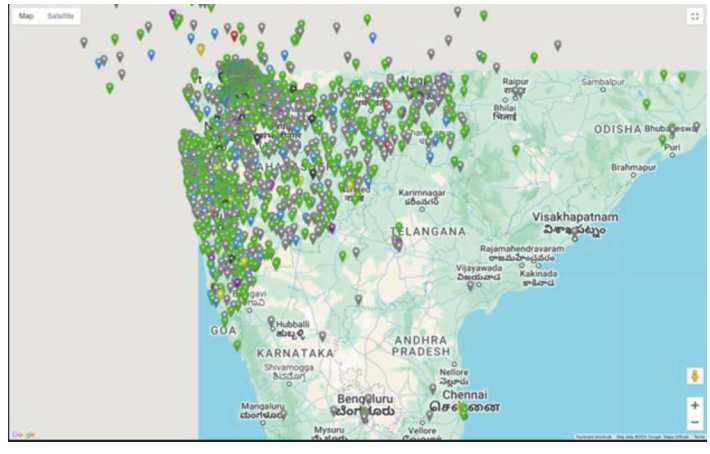
Aims & Objectives

The study aimed to determine the prevalence of SCD and sickle cell trait (SCT) among aboriginal communities in Nandurbar district in Western India. The primary objective was to develop a robust community-level screening methodology with geotagging of the affected individuals for long-term follow-up.

Materials & Methods

This observational study encompassed community-level screening of 344,374 individuals from Nov 2023 to Mar 2024, spending 208,800 man-hours. The population screened belonged to remote locales with minimal access to healthcare and had never undergone sickle screening or received care for SCD earlier. The population faced extreme disadvantages, with 69% belonging to aboriginal tribes and the majority being functionally illiterate (59.3%). Demographic details, medical history, and blood samples were collected followed by a thorough medical examination after obtaining informed consent. Hemoglobin (Hb) electrophoresis was performed at an on-site lab using capillary zone electrophoresis (CZE) (average 1390 tests/day). The data was collated using custom-built software by the primary author, available as care4sickle.in and on Google Play Store as “care4sickle” with level 4 security and is HIPAA compliant. The software is intuitive and designed for children and the functionally illiterate using pictorial representation.

Result



The prevalence of SCD was 8.68% (n-1402), and SCT was 15.23% (n-24577), with 0.16% (n-264) individuals having compound heterozygosity. Incidentally, 5.27%(n-8501) had other hemoglobinopathies. Geotagging revealed a heatmap identifying high prevalence zones among specific ethnicities and geographical locations. Mathematical modeling based on pedigree charting and positivity rates on family screening revealed a possibility of 2.84x positivity for sickle syndrome (SCT/ SCD) for every newly diagnosed SCD. The SCD individuals had transfusion requirement of 15.6/1000 patient-years, mean Hb 9.6±0.1g/dL without transfusions, mean HbF of 22.4±7.5%, low HbA2 with normal red cell indices in 32.88%, palpable splenomegaly in 58.48% with a mean size of 3.6±2.4cm, crises and pain episodes (VAS>5) of 1.92 and 112/1000 patient-years respectively.

Conclusion

We have demonstrated the feasibility of large-scale community screening for SCD in a population facing extreme socio-economic deprivation. Individuals detected to have SCD were found to have high rates of splenomegaly, High HbF/Hb, and a limited history of painful episodes or other disease complications.

Benign Hematology - Clinical (BHC) OP-BHC-12

Multicomponent Haemostatic Wound Healing Matrix

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Introduction

Excessive bleeding arising from severe injuries, accidents, or surgeries can be a life-threatening complication if left untreated. Natural and synthetic polymer based haemostatic agents in the form of patches, bandages, dressings, pads, sponges, and powders are being commercially developed to attain rapid haemostasis. However, most of them are mechanically weak, costly or do not possess robust hemostatic and wound healing property

Aims & Objectives

In this study, we aim to develop a novel and cost effective haemostatic wound healing patch from chitosan and polyvinyl alcohol loaded with thrombin and collagen peptide. Polyvinyl alcohol crosslinks chitosan molecules to improve mechanical strength, while the combination of thrombin and collagen peptide synergistically accelerates hemostasis and wound healing.

Materials & Methods

The chitosan-polyvinyl alcohol patch loaded with thrombin and collagen peptide was evaluated against a saline-soaked control and a commercial gelatin-based hemostat. The patches were lyophilized and subjected to physicochemical characterization, including FTIR analysis and swelling studies. Haemostatic efficiency was assessed via whole blood clotting assay. Haemocompatibility and cytocompatibility were evaluated following ISO10993-4 and ISO10993-5 standards. Additionally, the patch's wound healing potential was tested using scratch assay on L929 cells, by observing cell migration and proliferation

Result

The lyophilized patch was lightweight and flexible, with a slightly rough surface and revealed significant fluid absorption potential through swelling studies. Upon whole blood clotting assay, the patch exhibited 10-fold enhancement in hemostasis within 1 minute, as evidenced by blood clotting index assay. It was cytocompatible and exhibited an increased cellular viability. The patches were also found to be haemocompatibile The increased cell proliferation and migration in the scratch wound assay confirmed its efficient wound healing potential, with no observed damage to L929 cells upon direct contact.

Conclusion

The developed chitosan - polyvinyl alcohol patch loaded with thrombin and collagen peptide demonstrated strong potential as a safe and effective matrix, capable of achieving rapid haemostasis and wound healing.

Benign Hematology - Clinical (BHC) OP-BHC-13

Mechanistic Detailing of Coagulation Factor XIII Structure

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Introduction

The structure of human coagulation factor XIII (FXIII), a heterotetrameric plasma pro-transglutaminase that covalently crosslinks pre-formed fibrin polymers, remains elusive until today. The heterotetrameric complex is composed of two catalytic FXIII-A and two protective FXIII-B subunits. Structural etiology underlying FXIII deficiency has so far been derived from crystallographic structures, all of which are currently available for the FXIII-A2 homodimer only.

Aims & Objectives

Using High-resolution cryo-electron microscopy we aim to refine the structure of native coagulation Factor XIII complex to its entity (i.e. FXIII-A2B2). Furthermore, we aim to elucidate the usage of this structure to improve the understanding of the pathophysiology of rare FXIII deficiency.

Materials & Methods

Plasma derived FXIII complex was repurified by size-exclusion chromatography until a single, homogenous, monodispersed peak was obtained, which was further tested for purity by Mass spectroscopy. Purified protein corresponding to FXIII (activity and proteomic identity-wise), was then subjected to cryo-EM grid preparation. Data were collected on a Thermo Scientific Krios™G4 Cryo-TEM equipped with an E-CFEG, a Thermo Scientific Selectris™ X Energy Filter, and a Falcon 4 Detector operated in Electron-Event Representation (EER) mode. 6604 movies were recorded using EPU software (Thermo Fisher Scientific) with aberration-free image shift (AFIS). The data were collected at a nominal magnification of ×130,000 and a pixel size of 0.93 Å/pixel, with a defocus range between 0.6 and 2 µm at a total dose of 40 e-/Å2 per movie. The slit width of the energy filter was set to 10 eV. The Patient cohort included 17 samples corresponding to the index patients (13/17) and relatives of index patients (4/17) for clinical FXIII deficiency, referred to the Hematology OPD of the AIIMS in New Delhi, India. The included patients showed lab features of FXIII deficiency and were confirmed to have FXIII deficiency based on a positive Clot-solubility test. For these patients, all genetic analyses on isolated gDNA were performed on a MiSeq Next-Generation sequencing platform.

Result

The structure provides detailed information on FXIII subunit interacting interfaces as the two subunits interact strongly in plasma. The native FXIII-A2B2 complex reveals a pseudo-symmetric heterotetramer of two FXIII-B monomers intercalating with a symmetric FXIII-A2 dimer forming a "crown-like" assembly. The symmetry axes of the A2 and B2 homodimers are twisted relative to each other such that Sushi domain 1 interacts with the catalytic core of the A subunit and Sushi domain 2 with the symmetry related A' subunit and vice versa. We also report four novel mutations in the F13A1 gene encoding the FXIII-A subunit from a cohort of patients with severe FXIII deficiency. Our structure reveals the etiological basis of homozygous and heterozygous pathogenic mutations and explains the conditional dominant negative effects of heterozygous mutations. This atomistic description of complex interfaces is consistent with previous biochemical data and shows a congruence between the structural biochemistry of the FXIII complex and the clinical features of FXIII deficiency.

Conclusion

1. The native plasma FXIII complex structure reveals the intra and intermolecular arrangement between/within the FXIII-A and FXIII-B subunits.
2. The impact of disease causing, clinically relevant FXIII mutations is visualized in the assembly of the heterotetrameric coagulation complex.

Benign Hematology - Clinical (BHC) OP-BHC-14

Blood Group Distribution Patterns in Voluntary Blood Donors - An Observational Study

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Introduction

ABO and Rh blood group systems are the most important blood group systems and are genetically inherited. They play a very vital role in blood transfusions, parental and genetic testing, and addressing medical legal issues.

Aims & Objectives

This study aims to determine the blood group diversity of ABO and Rh blood groups among voluntary blood donors in Mumbai, India.

Materials & Methods

A retrospective study was conducted at Sir J.J. Blood Center over a period of four months from 1st January 2023 to 30th June 2023. ABO and Rh typing was done using the tube agglutination method with antisera against ABO and Rh, and they were further confirmed by the reverse grouping method using known pooled A and B cells.

Result

Of the 2844 donors, 462 (16.2%) were female and 2382 (83.7%) male. The majority of donors belonged to the age group 26–40 years. The commonest ABO blood group among Rhesus positive donors was B (31.5%), followed by O (30.0%), A (25.5%), and AB (8.9%), while in Rhesus negative donors it was O (1.5%), followed by A (1.1%), B (1.1%), and AB (0.4%).

Conclusion

The knowledge of distribution of blood groups is essential for effective inventory management of blood banks and transfusion services. This study throws light on the reasons for the deficiency of a particular group and to maintain a registry of each blood group so that deficient group donors may be encouraged to donate more frequently and to make available particular group donors when required.

Benign Hematology - Clinical (BHC) OP-BHC-15

Iron Overload-Related Pancytopenia in Beta Thalassemia Trait : A Rare Clinical Presentation

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Background

Beta thalassemia trait (BTT) is a common genetic disorder caused by mutations in the HBB gene, leading to reduced synthesis of beta-globin chains. BTT is usually associated with mild anemia, but complications such as iron overload are rare. Iron overload typically occurs in transfusion-dependent thalassemia major or intermedia but can also occur in non-transfusion-dependent patients due to increased intestinal iron absorption. In exceptional cases, iron overload may lead to severe complications, including pancytopenia.

Case Presentation

We report a case of a 48-year-old female with BTT who developed pancytopenia secondary to iron overload. She presented with generalized weakness, easy fatigability, and intermittent fever. She had a history of frequent blood transfusions due to worsening anemia. On admission, her laboratory results revealed hemoglobin of 3.5 g/dL, white blood cell count of 0.8×10^3/L, and platelets of 80×10^3/L, indicating pancytopenia. Serum ferritin levels were elevated (>2000 ng/mL), consistent with iron overload. Blood and urine cultures for infection were negative, and chest X-ray revealed community-acquired pneumonia.

Diagnosis

Bone marrow aspiration and biopsy showed hypocellularity and increased iron deposition, confirmed by Prussian blue staining, suggesting pancytopenia secondary to bone marrow iron overload. Nutritional deficiencies were ruled out, and further investigations confirmed osteoporosis without other organ dysfunctions due to iron overload.

Treatment

The patient was treated for febrile neutropenia with broad-spectrum antibiotics and antifungals. She was started on iron chelation therapy with deferasirox, along with vitamin B12 and folate supplementation. Supportive management, including blood transfusions and erythropoietin-stimulating agents, was provided to address anemia.

Follow-up

Over 30 days, the patient showed significant improvement in hematological parameters and a reduced need for blood transfusions. Her chest X-ray showed resolution of pneumonia, and a repeat bone marrow biopsy after two months revealed reduced iron overload.

Conclusion

This case highlights the rare occurrence of pancytopenia secondary to iron overload in BTT. Early recognition of iron overload and prompt initiation of chelation therapy is essential to prevent complications such as pancytopenia and improve patient outcomes. Further research is needed to understand the pathophysiology and management of iron overload in BTT.

Benign Hematology - Clinical (BHC) OP-BHC-16

Unmasking HLH in Tropical Infection : A Case Series from An Indian Tertiary Care Centre

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Background

Hemophagocytic lymphohistiocytosis (HLH) is a clinical syndrome characterized by excessive activation of the mononuclear phagocytic system, leading to a severe hyper-inflammatory response (1). HLH can be classified as either hereditary or acquired. Familial hemophagocytic lymphohistiocytosis (FHLH) includes immunological deficiencies such as X-linked lymphoproliferative syndrome (XLP), Griscelli syndrome (GS), and Chédiak-Higashi syndrome (CHS). The familial form often presents as HLH, while the acquired form, which can be triggered by external stimuli or infections, is less frequently associated with immunological deficits (2).In children, HLH is often linked to infections, while in adults, hematologic malignancies or other cancers are more commonly associated with the condition. If left untreated, HLH can progress rapidly and be fatal. Clinicians should maintain a high index of suspicion when patients present with symptoms such as splenomegaly, elevated liver enzymes, inflammatory markers like serum ferritin, or cytopenias (3).

Case Presentation

Case 1

A 65-year-old male from a kala azar-endemic region presented with a 6-week history of fever, weight loss, abdominal pain, and painless axillary lymphadenopathy. Examination revealed hepatosplenomegaly, ascites, and axillary lymphadenopathy. Laboratory findings included anemia, leukopenia, thrombocytopenia, transaminitis, and elevated creatinine.

Case 2

A 17-year-old male from a malaria-endemic region presented with fever, body aches, and fatigue. Examination showed hepatosplenomegaly and petechiae.

Case 3

A 26-year-old male from a dengue-endemic region presented with high-grade fever, headache, myalgia, and a petechial rash.

Diagnosis

Case 1

A positive rK39 test and bone marrow aspiration confirmed kala azar with hemophagocytosis. Elevated inflammatory markers such as ferritin, LDH, triglycerides, and soluble CD25 supported the diagnosis of secondary HLH (H score: 260).

Case 2

Blood tests revealed anemia, leukopenia, thrombocytopenia, and P. falciparum trophozoites on a peripheral blood smear. Bone marrow biopsy confirmed hemophagocytosis, consistent with secondary HLH.

Case 3

Laboratory findings showed pancytopenia, elevated ferritin, LDH, triglycerides, and soluble CD25, along with a positive dengue serology. Bone marrow aspiration confirmed hemophagocytosis, leading to a diagnosis of dengue with secondary HLH.

Treatment

Case 1

Treatment given with dexamethasone, liposomal amphotericin B, and supportive care.

Case 2

The patient was treated with intravenous Artesunate, ACT, and Primaquine for malaria and dexamethasone for HLH.

Case 3

Treatment included dexamethasone, fluids, and supportive care.

Follow-up

Case 1

Despite treatment with dexamethasone, liposomal amphotericin B, and supportive care, the patient succumbed to multi-organ failure.

Case 2

The patient showed significant improvement after 7 days and was discharged with regular follow-up.

Case 3

The patient improved after 10 days and was discharged.

Conclusion

HLH can result from various triggers, including autoimmune diseases, infections, and malignancies. It involves uncontrolled immune activation, leading to cytokine release and tissue damage (4,5). Infections like malaria, dengue, and kala azar are well-known triggers of secondary HLH, particularly in tropical regions. Our case series underscores the importance of early recognition and treatment of HLH in the context of tropical infections.HLH is a rare but life-threatening syndrome. Early diagnosis and treatment are crucial to prevent fatal outcomes. In endemic areas, clinicians should maintain a high index of suspicion when encountering patients with persistent fever, cytopenia, and hepatosplenomegaly.

Attribute	Case 1	Case 2	Case 3
Age/Gender	17-year-old male	26-year-old male	65-year-old male
Geographic Region	Malaria-endemic	Dengue-endemic	Kala azar-endemic
Presenting Symptoms	High-grade fever, chills, body aches, fatigue	High-grade fever, headache, myalgias, petechial rash	Progressive fever, weight loss, abdominal pain, lymphadenopathy
Physical Examination	Pallor, hepatosplenomegaly, petechiae	Hepatosplenomegaly, petechial rash	Hepatosplenomegaly, ascites, edema, painless lymphadenopathy
Provisional Diagnosis	Complicated malaria, severe Dengue fever, etc.	Severe Dengue fever, Leptospirosis, etc.	Kala Azar, Tuberculosis, Dengue Fever, etc.
CBC Findings	Hb: 9.2 g/dL, TLC: 3060/µL, Platelets: 80,000/µL	Hb: 8.5 g/dL, TLC: 2800/µL, Platelets: 30,000/µL	Hb: 8.5 g/dL, TLC: 2800/µL, Platelets: 60,000/µL
LFT Findings	Transaminitis (OT/PT - 92/68)	Transaminitis (AST 95 U/L, ALT 80 U/L)	Transaminitis (ALT 88 IU/L, AST 110 IU/L)
RFT Findings	WNL	Normal	Elevated creatinine (2.5 mg/dL)
Blood Culture	Sterile	Sterile	Sterile
Bone Marrow Biopsy	Hemophagocytic lymphohistiocytosis (P. falciparum)	Hemophagocytic lymphohistiocytosis (Dengue fever)	Hemophagocytic lymphohistiocytosis (Leishmania donovani)
Ferritin	1800 ng/mL	2500 ng/mL	2000 ng/mL
LDH	1127 IU/L	1050 U/L	1300 IU/L
Triglycerides	650 mg/dL	700 mg/dL	700 mg/dL
sCD25	21,475 U/mL	23,500 U/mL	25,000 U/mL
Final Diagnosis	P. falciparum malaria complicated by secondary HLH	Severe Dengue Fever complicated by secondary HLH	Kala azar complicated by secondary HLH
Treatment	Artesunate, ACT, Primaquine, supportive care, dexamethasone	Dengue-specific treatment, high-dose corticosteroids	IV dexamethasone, supportive care, liposomal amphotericin B
Outcome	Improvement with resolution of HLH and malaria symptoms	Improvement with resolution of HLH and dengue symptoms	Deterioration due to multi-organ failure and HLH
Parameters (Day 7)	Hb: 10.1 g/dL, TLC: 4250/µL, Platelets: 100,000/µL, Ferritin: 746 ng/mL, LDH: 765 IU/L	Hb: 10.2 g/dL, WBC: 3500/µL, Platelets: 60,000/µL, Ferritin: 1200 ng/mL, LDH: 800 U/L	Hb: 7.0 g/dL, TLC: 2000/µL, Platelets: 45,000/µL, Ferritin: 1500 ng/mL, LDH: 1100 IU/L
Parameters (Day 14)	Hb: 12.2 g/dL, TLC: 5326/µL, Platelets: 120,000/µL, Ferritin: 256 ng/mL, LDH: 356 IU/L	Hb: 12.0 g/dL, WBC: 4500/µL, Platelets: 90,000/µL, Ferritin: 600 ng/mL, LDH: 400 U/L	Hb: 6.5 g/dL, TLC: 1500/µL, Platelets: 35,000/µL, Ferritin: 1200 ng/mL, LDH: 800 IU/L

Benign Hematology - Clinical (BHC) OP-BHC-17

Procalcitonin is Superior to CRP in predicting Bacteraemia and Mortality in Neutropenic Fever in Patients with Haematological Malignancies.

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Introduction

Febrile neutropenia (FN) is a haematological emergency and is managed with empirical broad-spectrum antibiotics, while culture reports are awaited. However, this approach risks improper use of antibiotics and development of anti-microbial resistance. CRP and lately, procalcitonin have emerged as biomarkers of bacteraemia, but, their utility in FN is not well established.

Aims & Objectives

We aimed to assess the ability of procalcitonin and CRP at onset & 48 hours in predicting bacteraemia and in-hospital-mortality.

Materials & Methods

Ours is a prospective-observational study in adults with haematological malignancies presenting with FN. Mann-Whitney-U test was used, ROC curves were generated and $p<0.05$ was considered significant.

Result

280 FN episodes occurred in 111 patients. Median age was 50 years (range 18-77), 70% were males. Underlying diseases were AML (n=168,60%), ALL (n=31,11%), lymphomas (n=39,14%) and plasma-cell dyscrasia (n=23,8%). 80(29%) episodes occurred in patients undergoing HSCT - 52 in allogeneic and 28 in autologous HSCT. 162 episodes (58%) occurred in patients undergoing chemotherapy.

Of 66(24%) bacteraemic episodes, 44(66%) were Gram-negative bacteraemia and 22 (34%) Gram-positive bacteraemia. Of all Gram-negative cultures, 27(61%) were multi-drug resistant, 10(22%) carbapenem resistant.

Mean procalcitonin was higher in bacteraemic episodes (8.72 vs. 2.09 at onset, and 8.2 vs. 3.65 at 48-hours). At onset, at a cut-off of 2.16ng/mL, procalcitonin had a specificity of 85% for bacteraemia (PPV-47%, NPV-83%). At 48-hours, at a cut-off of 3.05ng/mL, procalcitonin had a specificity of 85% for bacteraemia (PPV-41%, NPV-81%).

Mean CRP was also higher in bacteraemia (106.8 and 86.7 at onset, and 120.9 and 91.3 at 48-hours). At onset & at 48-hours, CRP at a cut-off of 183mg/L, had a specificity of 85% for bacteraemia (PPV-27%, NPV-77%). With higher AUC, sensitivity & specificity procalcitonin predicted better.

	Bacteraemia (n=66) **Mean**	*No bacteraemia (n=214)* **Mean** *(ng/mL)*	*p*
Procalcitonin at onset (ng/mL)	8.72	2.09	**<0.001**
Procalcitonin at 48 hours (ng/mL)	8.2	3.65	**0.001**
CRP at onset (mg/L)	106.8	86.7	**0.028**
CRP at 48 hours (mg/L)	103	68	**0.002**

	Sterile (n=214) **Mean**	*Gram-negative (n=66)* **Mean**	*p*	*Gram-positive (n=22)* **Mean**	*p*
Procalcitonin at onset (ng/mL)	2.9	7.7	<0.001	5.4	**0.089**
CRP at onset (mg/L)	87.3	114	0.038	93	0.504

	Succumbed (n=31) **Mean**	*Survived (n=249)* **Mean**	*p*
Procalcitonin at onset (ng/mL)	8.63	3.04	**0.019**
Procalcitonin at 48 hours (ng/mL)	6.83	4.46	**0.005**
CRP at onset (mg/L)	119	88	0.057
CRP at 48 hours (mg/L)	75	89	0.199

Figure 1. Comparison of procalcitonin & CRP in predicting bacteraemia, Gram-negative and Gram-positive bacteraemia, and in-hospital mortality, along with their p values.

Mean procalcitonin, but not CRP, was higher in GN bacteraemia (7.7 vs. 2.9ng/mL), with 85% specificity at cut-off of 2.61ng/mL (PPV-32%, NPV-87%). Mean procalcitonin was higher in MDR bacteraemia (7.63 vs. 3.1ng/mL), with 85% specificity at 3.12ng/mL (PPV-24%, NPV-90%).

31(11%) patients died of sepsis. Mean procalcitonin levels were higher in episodes with mortality (8.63 vs 3.04 at onset, 6.83 vs. 4.46 at 48-hours). At a cut off of 3.89ng/mL, procalcitonin had with 85% specificity for in-hospital mortality in that episode (PPV-14%, NPV-90%). CRP couldn't predict mortality.

Conclusion

Procalcitonin is a better predictor of Gram-negative bacteraemia and mortality than CRP in FN.

Benign Hematology - Clinical (BHC) OP-BHC-18

A Retrospective Analysis of Hemoglobinopathy Pattern & Distribution in a New Tertiary Care Hospital of West Bengal Using CE-HPLC

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Introduction

Hemoglobinopathies, including Beta Thalassemia, Hemoglobin E disorders, and Sickle Cell Anemia, are highly prevalent in West Bengal, India. Early diagnosis through screening programs is essential to prevent severe outcomes as homozygous and double heterozygous conditions like Beta Thalassemia major, Hemoglobin E-Beta Thalassemia, and Sickle Cell-Beta Thalassemia. High-performance liquid chromatography (HPLC) is the preferred screening method, with the Arkay ADAMS HA-8180T system, based on cation-exchange chromatography is the newer instrument installed in government institutes.

Aims & Objectives

1. To evaluate the pattern and distribution of hemoglobinopathies in a newly developed tertiary care hospital of West Bengal using Arkay ADAMS HA-8180T.
2. To propose strategies for effective screening to mitigate the burden of hemoglobinopathies.

Materials & Methods

A retrospective study was conducted wherein all 1,350 blood samples received for Haemoglobin HPLC without any inclusion or exclusion criteria from December 2022 till August 2024 processed using the Arkay ADAMS HA-8180T, high-performance liquid chromatography (HPLC) system were included in this study. The study focused on determining the distribution of these hemoglobin disorders and percentage of individual hemoglobinopathy was calculated.

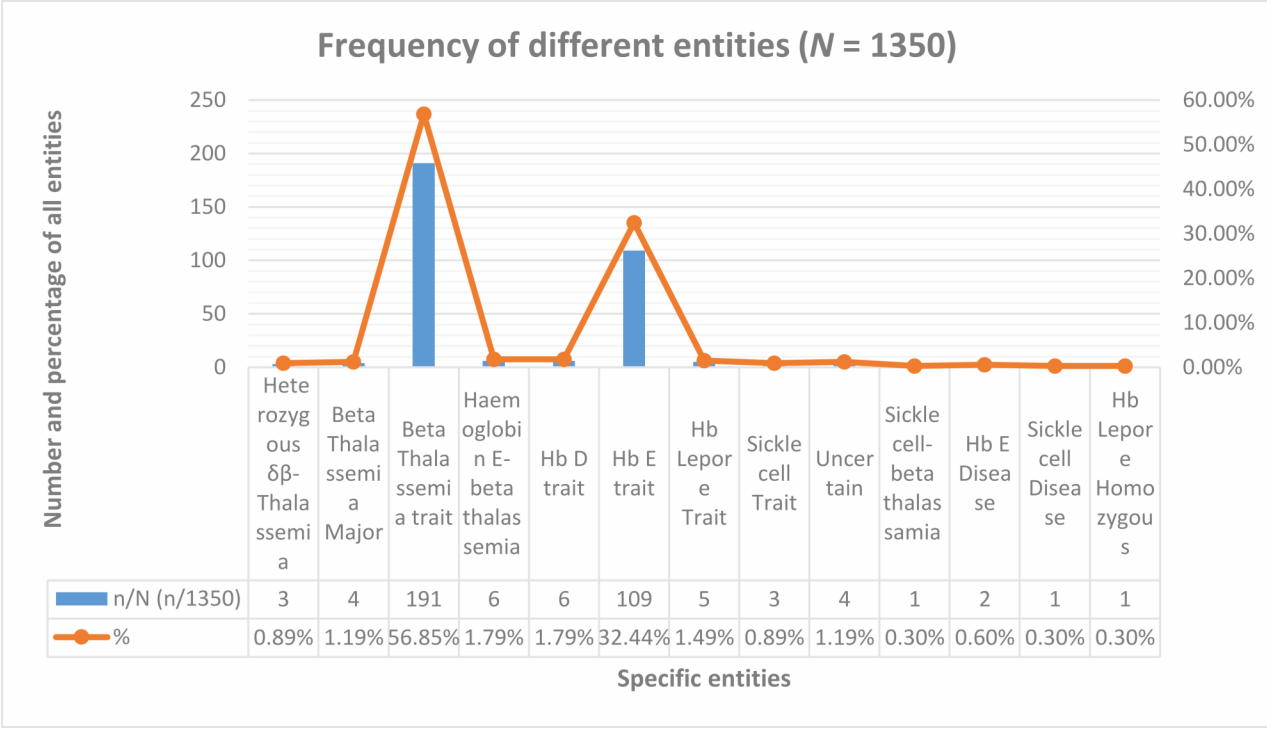
Result

Out of 1,350 blood samples analysed, 336 (24.89%) were positive for hemoglobinopathies. The most common hemoglobinopathy was beta thalassemia trait, accounting for 191 cases (14.15%), followed by Hb E trait with 109 cases (8.07%). Hb E-beta thalassemia and Hb D trait were each identified in 6 cases (0.44%), while Hb Lepore trait was found in 5 cases (0.37%). Beta thalassemia major was detected in 4 cases (0.30%), and sickle cell trait in 3 cases (0.22%). Less common hemoglobinopathies included Hb E disease (2 cases, 0.15%), sickle cell disease, sickle cell-beta thalassemia, and Hb Lepore homozygous, each with 1 case (0.07%).

Conclusion

This study reveals that beta thalassemia trait and Hb E trait are the predominant hemoglobinopathies in West Bengal. Double heterozygous conditions, although less frequent, can cause significant clinical challenges.

Early screening and diagnosis are essential for preventing the inheritance of these more severe conditions. The Arkay ADAMS HA-8180T HPLC system effectively detected hemoglobin variants, supporting its use in comprehensive screening programs. Implementing population-based screening and genetic counselling will help manage hemoglobinopathies and reduce their future burden.



Benign Hematology - Clinical (BHC) OP-BHC-19

Low Volume Therapeutic Plasma Exchange (0.5 plasma volume) in patient with Rat poisoning (Ratol 3% yellow phosphorus) with Multi-organ Involvement- A Case Report

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Background

Yellow phosphorus, the active ingredient in many rodenticides, is a potent hepatotoxin that can cause severe multisystem dysfunction, including acute liver failure (ALF), for which there is no known antidote. We present a case of a 30-year-old male who ingested Ratol®, a rodenticide containing 3% yellow phosphorus. The patient presented with gastritis, ALF, coagulopathy, acute kidney injury, and acute pancreatitis. Due to the severity of his condition, he was treated with low-volume TPE (0.5 plasma volume) using fresh frozen plasma and 0.9% normal saline with use of automated cell separator SpectraOptia (Apheresis machine) at AIIMS Nagpur.

Case Presentation

A 30-year-old male presented to the emergency department with alleged history of ingestion of rat-kill poison containing 3% yellow phosphorus. He presented with complaints of vomiting 3-4 episodes, approx. 100 ml per episode, yellow colored, no history of blood in vomitus, history of abdominal discomfort, history of nausea, no

history of bowel or bladder complaints, history of fever present. USG suggestive of gastritis, right atrophic kidney and ischemia. Patient was admitted to the local hospital and managed conservatively and then referred to AIIMS Nagpur

Diagnosis

Rat poisoning (Ratol 3% yellow phosphorus) with Multi-organ Involvement

Treatment

Patient had Underwent 5 cycles of therapeutic plasma exchange (0.5 volume) with use of 34 units of FFP over seven days. TPE was performed using a continuous-flow centrifugal apheresis system, with replacement fluid consisting of fresh frozen plasma and 0.9% normal saline.

Follow-up

Following TPE, the patient showed gradual improvement in both clinical and laboratory parameters. Liver function and renal function tests improved, coagulopathy resolved, markers of pancreatitis d

Conclusion

Therapeutic plasma exchange may be a beneficial adjunctive therapy in patients with severe yellow phosphorus poisoning, particularly in cases complicated by multisystem dysfunction. Early initiation of TPE in conjunction with supportive care measures can lead to favorable outcomes and may improve patient survival. Further studies are warranted to evaluate the efficacy and optimal timing of TPE in this patient population.

Benign Hematology - Clinical (BHC) OP-BHC-20

Significance of Mixing Study in Lupus Anticoagulant and Various Formulae used to Interpret Results

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Introduction

The antiphospholipid antibodies (APLAs) syndrome comprises of a group of heterogenous antibodies that include lupus anticoagulant (LA), anticardiolipin antibodies (aCLs) and anti-beta 2 glycoprotein antibodies (aβ2GP). APLAs specifically target phospholipid binding protein of cell membrane, prothrombin and β2GP causing prolongation of coagulation test such as the activated partial thromboplastin time (APTT). LAs are identified by using clot-based assays (Dilute Russell viper venom time (DRVVT) and activated partial thromboplastin time (APTT) test). It is challenging to arrive at diagnosis of LA due to its heterogenous nature and thus, according to the ISTH guidelines two parallel tests are required to be run simultaneously for a correct diagnosis. The integrated "three-step approach" consists of:

(1) Screening assay

(2) Mixing study test

(3) Confirmatory assay

Various formulae [Normal reference interval (NRI), Index of circulating anticoagulant (Rosner's index) and Percent correction formula (Chang's % correction method)] have been proposed for interpretation of mixing study.

Aims & Objectives

Aim: To determine the most effective formula that can be used in the interpretation of mixing study for prediction of lupus anticoagulant.

Objective: To evaluate the sensitivity of different formulae used in mixing study test for prediction of lupus anticoagulant.

Materials & Methods

A prospective analysis was performed on all the samples received in Hematology laboratory for lupus anticoagulant assay from May 2024 to July 2024. Laboratory workup including APTT and DRVVT tests were performed. Mixing study was done at 0 hr and 2 hr in all the samples. Normal reference interval (NRI), Rosner's index and Chang's % correction formulae were calculated for mixing study interpretation.

Result

The comparative analysis for mixing study using the proposed formulae, is as follows:

Rosner's index with a cut off value of ≥10% is 27.78% sensitive and 97.73% specific for inhibitor diagnosis.

Chang's % correction with a cut off value of ≤ 70% is 61.11% sensitive and 31.82% specific for inhibitor diagnosis.

The sensitivity and specificity of NRI was 16.70% and 100% respectively.

Conclusion

We recommend using both Rosner's index and Chang's % correction formulae for interpretation of mixing study to obtain highest sensitivity and specificity for lupus anticoagulant detection.

Benign Hematology - Clinical (BHC) OP-BHC-21

ONE STONE, TWO BIRDS: Therapeutic Plasma Exchange for Management of Hyperviscosity and Prevention of Rituximab related IgM Flare in Waldenstrom's Macroglobinemia

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Background

Waldenström macroglobulinemia (WM) is a lymphoplasmacytic lymphoma associated with a monoclonal immunoglobulin M (IgM) protein. Symptomatic hyperviscosity is seen in patients with an IgM concentration more than 4000 mg/dl and presentation generally includes epistaxis, gingival bleeding, and visual changes. Therapeutic Plasma Exchange (TPE) is conjunctive modality of treatment along with immunosuppressive drugs in this condition.

Case Presentation

56 years old male diagnosed case of Waldenstrom's with cryoglobinemia (IgM 2880 mg/dl) was planned for Bendamustine Rituximab therapy (BR) from 2nd cycle. He had received 1st cycle of Bendamustine 28 days back. On admission, patient complained of occasional epistaxis, blurring of vision and redness of right eye since 15 days. Ophthalmology examination showed stasis retinopathy and vitrous hemorrhage. Repeat SPEP showed IgM levels- 4270 mg/dl. Patient was planned for Therapeutic Plasma Exchange. Rationale for TPE-1. Acute symptoms of hyperviscosity (Category II Grade 2a- As per American Society for Apheresis guidelines). 2.Preventive TPE for Rituximab related IgM flare. Procedural aspects- Procedure performed under all aseptic

precautions on Spectra optia with central line access. Patient was kept warm using bed warmer, surroundings were kept warm. Packed Red Blood Cells priming was done in view of low hemoglobin. Blood warmer was also used. Patient tolerated procedure well.

Diagnosis

Waldenstrom's Macroglobinemia with cryoglobinemia

Treatment

Therapeutic Plasma Exchange

Follow-up

Patient's vision improved same day. Patient was started on BR therapy. He received 4 cycles at our institute uneventfully. IgM levels did not show any significant increase throughout that duration.

Conclusion

Patient benefitted from Therapeutic plasma exchange in two ways in this case. First, clinical improvement and reduction of hyperviscosity symptoms and secondly preventive reduction in IgM levels before rituximab to avoid IgM flare. Plasmapheresis works quickly to bring down the IgM level and can be done before or adjuvant to chemotherapy or other drugs.

Benign Hematology - Clinical (BHC) OP-BHC-22

A Tale of Two Antibodies: Mixed AIHA: A Case Report

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Background

Autoimmune hemolytic anaemia (AIHA) is characterized by progressive red cell destruction and/or diminished red cell survival caused by antibodies directed against self-antigens on red cells. These autoantibodies react at various thermal amplitudes and are classified as warm, cold, and mixed autoimmune hemolytic anaemia (AIHA). Mixed AIHA is a rare clinical condition where both warm and cold antibodies cause red cell destruction, leading to anaemia.

Case Presentation

A 44-year-old male patient was admitted with severe anaemia and generalized lymphadenopathy. His initial CBC count showed hemoglobin of 3.7g/dl . We received patient samples for two units of PRBC crossmatch . As per departmental protocol, blood grouping was done using column agglutination method. It showed blood group discrepancy: forward grouping AB positive and reverse grouping O group. We also noted that EDTA sample had multiple clumps. On further immunohematolgical(IH) workup, DCT was positive (4+), ICT - positive (2+) & auto control -positive 2+. As patient needed urgent transfusion, O Rh D positive best compatible (1+) PRBC was transfused without any adverse reaction. We suspected cold autoantibodies and hence patient sample was collected maintaining a warm chain for workup. Patient's blood group was O Rh D positive-discrepancy resolved. Polyspecific DCT–positive (2+), Monospecific DCT showed IgG, IgM, IgA and C3d positive, ICT negative. Autocontrol– positive at 4°C but negative at Room temperature and 37°C.

Diagnosis

Based on IH work up, we diagnosed that the patient as Mixed AIHA predominantly cold type. In view of lymphadenopathy,anemia and ? secondary AIHA, lymph node biopsy was done which revealed angioimmunoblastic T-cell lymphoma.

Treatment

Patient was started on CVP regimen for lymphoma.

Follow-up

He also required frequent blood transfusions which was done using blood warmer and keeping the patient warm.

Conclusion

AIHA cases are challenging both for clinicians and laboratory services.Though isolated AIHA is seen in some patients, clinical work up should be done to rule out any other primary etiology.

Benign Hematology - Clinical (BHC) OP-BHC-23

Transforming Sickle Cell Treatment : The Impact of Erthrocytapheresis on Patient Outcomes

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Background

Red cell transfusion represents one of the mainstay management of chronic as well as acute complications of Sickle Cell Disease (SCD). Erythrocytapheresis is another method of transfusion therapy in SCD. For acute complications of SCD, the goal of transfusion therapy is to reduce the posttransfusion HbS level to <30%; for chronic complications, the goal is to maintain the pretransfusion HbS level at <30%-50% while maintaining the Hb level at ?10 g/dL. This rapid lowering of HbS levels can be achieved by Erythrocytapheresis.

Case Presentation

In this case series, we have discussed three cases of Sickle Cell Disease on whom Erythrocytapheresis was performed. Case 1. 52-year-old female case of thalamic space-occupying lesion was planned for craniotomy with near total excision. She was detected with SCD with high HbS levels. Urgent erythrocytapheresis was scheduled to reduced hemoglobin S levels. HbS levels reduced from 72.6% to 14% and she could be taken for surgery. Case 2. 9 year old male known case of SCD was admitted with complaints of severe pain bilateral knee and lower back with difficulty in standing and walking since 2-3 days. He also had history of stroke with hemiparesis 1 year back. HPLC was done with haemoglobin S (HbS) concentration was 80.4 %. Post procedure HbS reduced to 16.4%. Patient's pain reduced and he was able to walk with ease. He was kept under observation for 7days and discharged on Hydroxyurea. Case 3. 19 years old female, case of SCD with vasoocclusive crisis, encephalopathy leading to quadriplegia and acute chest syndrome with respiratory failure. Erythrocytapheresis reduced HbS from 62.7% to 6.9%. However, no clinical improvement seen and patient was continued on supportive care.

Diagnosis

Sickle Cell Disease

Treatment

Erythrocytapheresis in sickle cell disease patients

Follow-up

Reduction in HbS levels was seen in all 3 patients. However, clinical improvement was seen in two out of three patients

Conclusion

Erythrocytapheresis is being used increasingly to treat acute and chronic complications of RBC disorders, particularly in patients with SCD. It is efficient in reducing HbS levels and also maintain Hb levels. However, timely initiation is essential for clinical benefit in most cases.

Benign Hematology - Clinical (BHC) OP-BHC-24

Comparative Analysis of Apheresis versus Pooled Buffy Coat Granulocytes : A Case-Based Review.

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Background

White blood cells are vital to the natural defence system against human infections. Granulocyte transfusions from allogenic donors can help in clearance of infection in patients with severe neutropenia.

Case Presentation

Case-1: 58-year-old female with sepsis and reduced absolute neutrophil count not responding to higher antibiotics. We collected two apheresis granulocyte products and two aliquots each were irradiated and transfused within 24 hours of collection, over 1–2 hours, no adverse reaction noted. Her pre and post-count is shown in Table 1. Her count maintained after transfusions and she started responding to antimicrobials. Parameter Pre 1st Post 1hr Post 24hrs Pre 2nd Post 1 hr Post 24hrs

WBC 0.05 0.82 0.66 0.19 1.6 0.89

ANC Could not be calculated 0.76 0.60 0.16 1.06 0.63

Case-2: A 61-year-old male, k/c/o aplastic anemia started on ATG. His WBC counts reduced requiring granulocyte transfusion. As donor was not timely available, we gave blood group specific, cross-matched, pooled buffy coat of 4 whole blood donors, irradiated and transfused within 24 hours. No adverse reaction. His pre and post-count is shown in Table 2. Parameter Pre Post 1hr Post 24 hr

WBC 0.52 0.75 0.68

ANC 0.31 0.47 0.45

Case-3: 32-year-old female, case of osteomyelitis with febrile neutropenia. Due to

unavailability of granulocyte donor, we gave blood group specific, cross-matched, pooled buffy coat of 4 whole blood donors, irradiated and transfused within 24 hours. no adverse reaction. Her pre and post-count is shown in Table 3. Her counts improved later.

Parameter Pre Post 1hr Post 24 hr

WBC 0.50 0.94 0.82

ANC 0.30 0.27 0.27

Diagnosis

Out of three cases , two were febrile neutropenia and one case found to be aplastic anemia under ATG.

Treatment

Two units of Apheresis derived granulocyte transfused in one of the patient and other two were transfused with pooled buffy coat.

Follow-up

All three patients showed increment in WBC count and clinical improvement.

Conclusion

A good increment in counts was seen in apheresis derived granulocytes over pooled-buffy-coat. Apheresis-derived granulocytes from a single donor are the preferred choice; however, the need for a group-specific donor, cost, and time taken for the procedure make buffy coat-derived granulocytes an alternative.

Benign Hematology - Clinical (BHC) OP-BHC-25

Application and Adherence of Deep Vein Thrombosis (DVT) Prophylaxis Risk Assessment Model in ICU Patients in a Tertiary Care Hospital

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Introduction

Venous thromboembolism (VTE) is a medical problem occurring either in isolation (unprovoked) or as a complication of other diseases or procedures (provoked). Early identification of risk factors for VTE can lead to prevention and/ or adoption of appropriate prophylactic measures. Thromboprophylaxis is the most important strategy to prevent hospital-related deaths due to VTE. Various VTE risk assessment models (RAMs) have been developed and validated for different populations who are at risk of developing VTE. In this study, we compared the two widely used RAMs – Caprini score and Padua score with our hospital-based Wells score among ICU patients.

Aims & Objectives

Aim - Application of using Risk Assessment Models for DVT prophylaxis in ICU patients and its effect on patient outcome. Objectives - Primary objective: Comparison of the three RAMs to evaluate the most relevant one in ICU patients. Secondary objective: To evaluate the impact of the RAMs on DVT prophylaxis in ICU patients and to study any adverse outcomes.

Materials & Methods

This is a prospective observational study conducted under Department of Haematology, Lilavati Hospital and Research Centre. All patients admitted in Intensive care unit from 15/03/2023 to 15/06/2023 (3 months) were included in the study based on eligibility criteria. Each patient's scores were compared and outcomes followed over a period of one month.

Result

We analyzed 96 patients over 3 months. Our findings suggest that while all three scores are correlated with each other, the relationship between Padua Score and Caprini Score appears to be the strongest ($r = 0.390$, $p < 0.0001$). Only 2 patients experienced a VTE 2/96 (2.10%). Both patients were very high risk according Caprini scores, but low risk as Padua and hospital-based Wells score. Though proportion of thrombosis was comparable, the difference was not significant.

Conclusion

Limited data is available on RAMs and also their utilization in India is limited. However, it is crucial to understand how these scoring systems relate to each other as this may help in clinical decision-making and risk assessment for relevant conditions.

Benign Hematology - Clinical (BHC) OP-BHC-26

Diagnostic Challenges in a Case of Rare Bleeding Disorder

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Background

Congenital fibrinogen disorder are rare pathologies of haemostasis comprising quantitative (afibrinogenemia, hypofibrinogenemia) and qualitative (dysfibrinogenemia and hypodysfibrinogenemia. The worldwide estimated prevalence of afibrinogenemia is approx. 1-2 per million general population (RBD). The clinical phenotype is variable being associate with bleeding, thrombosis or absence of symptoms. In addition to standard coagulation test, genetic testing is key point in confirming the clinical diagnosis. Hence diagnosing and treating these disorders is of extreme importance. We present a case of 13-year male child who presented in PHO emergency dept. with bleeding and was a known case of Hemophilia B on treatment since 2012.

Case Presentation

A case of 13-year male child who presented in PHO emergency dept. with orbital hematoma, proptosis, subgaleal bleed and Keramalacia right eye. (post traumatic).The Child was diagnosed in 2012 Hemophilia B and since then had received off and on factor therapy for joint bleed and bruises. Patient detailed clinical examination, history was taken he had a significant past history of umbilical stump bleed in neonatal period. Routine investigation CBC, PS for Platelet morphology, Coagulation profile PT, APTT was done. In CBC and PS were within normal limits. PT and APTT test done on citrated plasma (Fully automated coag. Analyzer Stago Max3) both were >120sec.Mixing studies were done and correction was noted. TT was prolonged, Fibrinogen test (Clauss Method, Clot based test) was done with normal and pathological control in (Fully automated coag. Analzer Stago tage Max3). close monitoring of fibrinogen was done.

Diagnosis

Serial samples studied showed low to absent fibrinogen levels. Hence a diagnosis of Afibrogenimia was made.

Treatment

The patient was started on fibrinogen concentrate subsequently. The median follow up was 8 months and the patient had no breakthrough bleeding after that.

Follow-up

The patient was on follow up for 8 months and had no breakthrough bleeding after that.

Conclusion

Rare bleeding disorders need a high index of suspicion for timely diagnosis to prevent mortality and morbidity.

Congenital afibrinogenimia may be delayed as much as by one decade as in our case and may present with life threating bleed (subgaleal hematoma, orbital hematoma). Incorrect diagnosis may be made due to late presentation eg. haemophilia B and such cases may be missed diagnostically.

Benign Hematology - Clinical (BHC) OP-BHC-27

One Stage FVIII Assay for Laboratory Monitoring of Extended Half-Life Factors in Hemophilia A: Challenges and Solutions.

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Introduction

Factor VIII (FVIII) replacement therapy remains central to hemophilia A management, though standard therapies have limitations, including the need for frequent infusions and an increased risk of inhibitor development, which can complicate treatment. Extended half-life (EHL) FVIII factors, developed through molecular modifications, address these limitations to varying degrees. However, EHL FVIII monitoring poses challenges, as the modified molecules show variability in activity levels across different laboratory assays, particularly between one-stage and chromogenic assays.

Aims & Objectives

This study aimed to establish a reliable one-stage FVIII assay (OSA) for patients treated with EHL FVIII, focusing on Afstyla, a single-chain EHL product.

The objectives included identifying suitable activated partial thromboplastin time (APTT) reagents, comparing standard plasma versus EHL-calibrated plasma, and validating the assay against the chromogenic assay.

Materials & Methods

Six hemophilia A patients, free of FVIII inhibitors, were included in the study. Their blood samples, collected after Afstyla infusion, were analyzed using EHL-specific OSA with serial dilutions of Afstyla and different APTT reagents.

Result

This study showed that Triniclot APTT reagent, in combination with Afstyla-specific calibrator plasma, provided accurate sensitivity for all FVIII levels on OSA. This was validated against chromogenic assay results, confirming reliable assay performance for monitoring EHL factors (Tables 1a and 1b).

Table 1a: Commercial control vs Specific EHL-rFVIII-calibrated One Stage Assay.

	APTT reagents	rFVIII-SC (Afstyla) Serial dilutions in commercial FVIII deficient plasma					
		1 IU/ml (100%)	0.5 IU/ml (50%)	0.25 IU/ml (25%)	0.125 IU/ml (12.5%)	0.0625 IU/ml (6.25%)	0.0312 IU/ml (3.12%)
APTT (Sec)	Actin FS / Ellagic acid activator	32.5	35.6	39.0	42.4	45.9	48.7
	Actin FSL / Ellagic acid activator/ Low phospholipid	23.0	26.4	32.6	37.6	42.8	52.6
	Triniclot / Silica activator	26.5	28.7	34.4	37.3	42.3	47.2
	C.K. Prest / Kaolin activator	27.6	32.3	37.5	42.6	49.1	58.5
	Actin FS / Ellagic acid activator	104 %	50 %	41.6 %	20.8 %	15.6 %	11.4 %
OSA with Commercial control plasma and APTT reagents	Actin FSL / Ellagic acid activator/ Low phospholipid	250 %	120 %	62 %	24 %	10 %	7.2 %
	Triniclot / Silica activator	114.4 %	64.4 %	37.4 %	18.7 %	7.6 %	5.2 %
	C.K. Prest / Kaolin activator	135.2 %	54 %	23.9 %	7.07 %	2.08 %	1.1 %
	Actin FS / Ellagic acid activator	72.9	36.45	28.35	12.96	10.53	7.29
OSA with EHL F8 calibrated control plasma and APTT reagents	Actin FSL / Ellagic acid activator/ Low phospholipid	81	40.5	20.25	7.77	3.321	2.18
	Triniclot / Silica activator	100	50	24.4	11.6	5.8	3.3
	C.K. Prest / Kaolin activator	97.2	38.07	17.8	5.67	1.94	0.972
	F8 Chromogenic	98.60%	53.00%	23.40%	11.80%	5.64%	3.24%

Table 1b: Evaluation of patient plasma samples for EHL- specific OSA.

		Patient 1 (R13660)	Patient 2 (R13661)	Patient 3 (R14011)	Patient 4 (R14057)	Patient 5 (R14012)	Patient 6 (R-13120)
	EHL (rFVIII-SC-Afstyla) correction % given	40%	40%	40%	40%	40	750units, 6hrs
	Expected 1 hr. factor 8 recovery (≥ 66%)	≥ 26.4%	≥ 26.4%	≥ 26.4%	≥ 26.4%	≥ 26.4%	
APTT (Sec)	Actin FS / Ellagic acid activator	38.3	40.4	43.9	42.5	40	39.2
	Actin FSL / Ellagic acid activator/ Low phospholipid	41.1	48.3	43.8	54.3	47.5	55.3
	Triniclot / Silica activator	45.6	43.8	40.8	54.1	41.1	52.4
	Synthafax	39.1	33.7	34.2	49	35.2	47.5
	C.K. Prest / Kaolin activator	44.1	45.8	41.6	50.4	43.1	51.8
OSA with Commercial control plasma and APTT reagents	Actin FS / Ellagic acid activator	18.60%	28%	46.08	24.96	31.68	12.40%
	Actin FSL / Ellagic acid activator/ Low phospholipid	26%	32.24 %	33.6	42.2	51.84	3%
	Triniclot / Silica activator	17.68%	19.76%	36.4	24	33.6	12%
	C.K. Prest / Kaolin activator	18.72 %	23.90%	31.68	24.9	32.6	5.60%
OSA with EHL F8 calibrated control plasma and APTT reagents	Actin FS / Ellagic acid activator	27%	39%	45	27	34	9%
	Actin FSL / Ellagic acid activator/ Low phospholipid	15%	18%	14.5	18	21	1.20%
	Triniclot / Silica activator	31%	34 %	40%	27%	36%	9%
	C.K. Prest / Kaolin activator	34 %	40 %	42	34	44	11%
F8 Chromogenic assay		32.40%	33.00%	41.60%	25.90%	38.00%	7.20%

Conclusion

The study highlights the importance of selecting the appropriate APTT reagent and EHL-specific calibrators for accurate monitoring of EHL therapy by OSA. The validated OSA method, supported by chromogenic assay results, ensures precise factor level assessment in patients on Afstyla. This assay model may be applied to any EHL factor monitoring. This approach facilitates better clinical decision-making in managing hemophilia A patients undergoing EHL therapy.

Benign Hematology - Clinical (BHC) OP-BHC-28

Design and Operation of a Good Manufacturing Practices (GMP) Laboratory in India

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Introduction

Cellular therapy is a rapidly evolving field worldwide. Both academic and commercial centers are planning to build their own facility to manufacture cell and gene therapy products (CGT). These centers are increasingly working to design and build clinical laboratories capable of performing cellular engineering and vector production using current good manufacturing practices (cGMPs). However, GMP facilities and CGT products are tightly controlled by regulators and numerous country specific approvals and licensure are required for it functioning. Hence, manufacturing of CGT products has become increasingly complicated and costly. It is imperative to have knowledge of current country specific regulations and design GMP appropriate for the type of manipulation

Aims & Objectives

To design a good manufacturing practices (GMP) laboratory in compliance with current guidelines and regulations

Materials & Methods

A literature search was initiated in PubMed and Google databases for International standards, Government regulations and current guidelines for setting up a GMP laboratory. Reference lists were cross-checked for relevant citations, and more searches were undertaken till the desired information was obtained. The information was discussed with all stake-holders over several meetings to develop a GMP facility design with country-specific regulatory requirements. In India, SCHEDULE M of Drugs and cosmetics Act elaborates on the Good manufacturing practices and requirements of premises, Plant and equipment for pharmaceutical products. In USA, Food and Drug Administration (FDA) provides guidance.

Result

In compliance to regulatory requirements, a GMP design and process flow was developed. It included

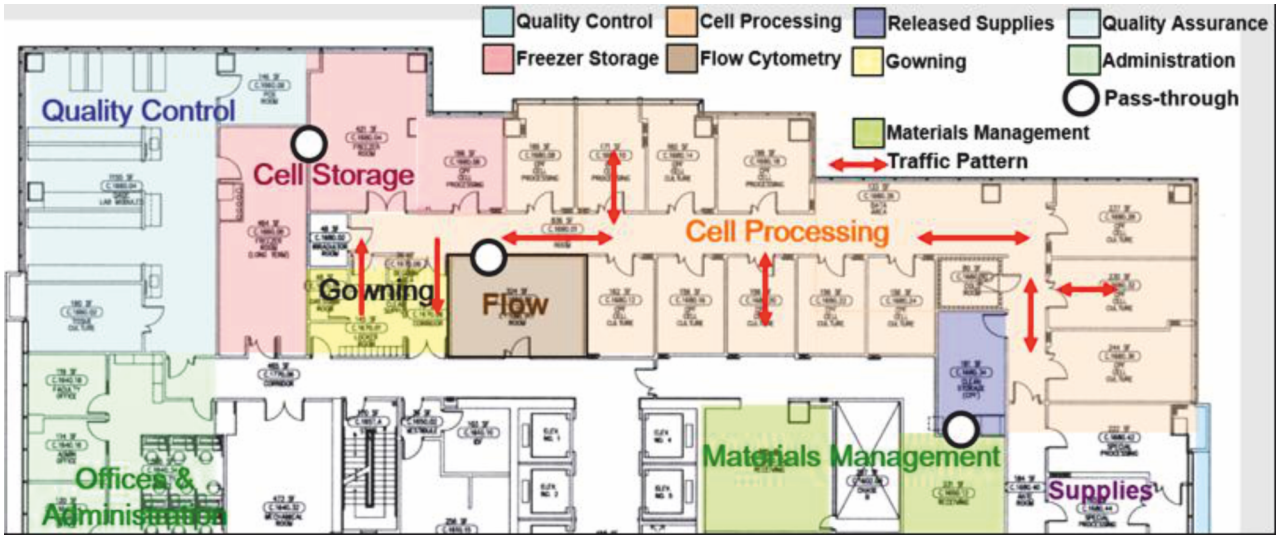
- The air handling system
- Manufacturing suites
- Process flow and Access
- Supplies
- Cell Storage Area

The different areas are colored shaded and process flow clearly depicted. Additional considerations included the gowning space that also provided storage of gowning materials. Gowning area had a changing room and a clear

division between "clean" and "dirty" sides of the room as indicated by the positioning of a bench between the two areas. The gowning room leads into the main central corridor along which are located the manufacturing suites, the clean storage room, and the cold storage facility

Conclusion

The overall design, air quality systems, and finishes meet regulatory requirements and are consistent with the need to integrate equipment and all utilities into the process of cell manufacture. A thorough thinking process, including an understanding of related regulatory requirements, working flow system and working environment, is vital to designing and constructing a GMP facility for CGT products



Benign Hematology - Clinical (BHC) OP-BHC-29

Use of Artificial Intelligence to Guide Untrained Individuals Performing Self-Ultrasound Scans of the Knee Joint

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Introduction

Recurrent joint bleeds occur frequently in persons with haemophilia, often resulting in arthropathy. The value of ultrasonography (US) in detecting bleeds has been demonstrated; however, access to proficient US operators is limited. This innovative solution proposes the integration of real-time artificial intelligence (AI) assistance, which could empower less experienced physicians and even untrained patients to perform accurate US examinations to acquire US frames of diagnostic quality.

Aims & Objectives

To investigate the performance of the AI solution in assisting untrained individuals with the scanning procedure, to acquire US frames suitable for synovial recess distension detection, indicating a joint bleed.

Materials & Methods

An AI algorithm was developed to provide real-time assessments of US frames collected during the scanning process. Two separate studies (Test I and Test II) were conducted to collect US data. We trained the algorithm with scans of 30 participants (Test I) and validated it on US scans of 6 participants (Test II); (Figure 1).

Participants were non-haemophilic and untrained in performing US. Prior to the scan, participants were provided with a video on how to perform a self-scan of the knee. During the scan, they were provided with real-time feedback from the AI algorithm (via a mobile application), to assist finding the correct location and capturing diagnostic-quality US images. To enable algorithm training and validation, images were labelled by a medical expert, based on a verified labelling protocol.

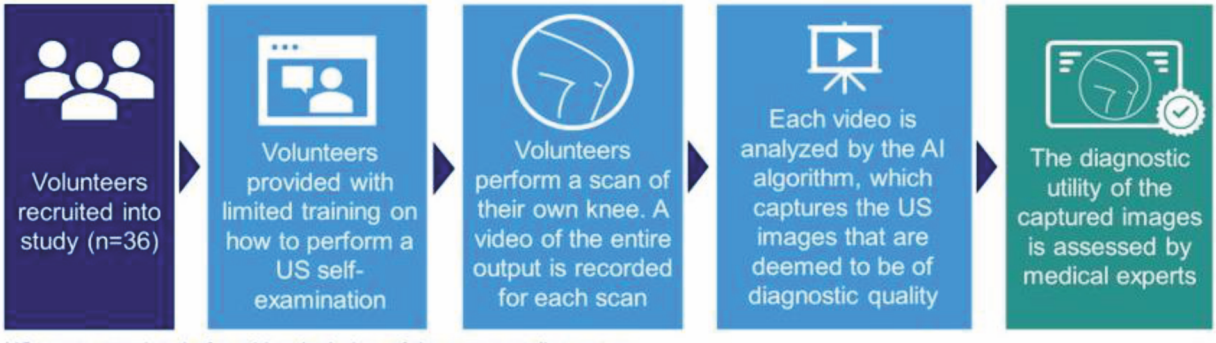
Result

A total of 27,465 (Test I) and 3,105 (Test II) images were acquired via 30 and 6 scans, respectively. Of these, 5,493 and 621 images were labelled by a medical expert. The algorithm correctly classified 449/621 images (72%) from Test II as usable/not usable, demonstrating a sensitivity of 76%, and a specificity of 71%.

Conclusion

These data support the feasibility of using real-time AI-assisted software to assist untrained patients performing US self-examinations to acquire diagnostic-quality images.

Figure 1



US scans consisted of a midsagittal view of the suprapatellar recess
The following criteria were used for expert assessment: depiction and clarity of bone landmarks, clarity of soft tissue structures (especially the synovial recess), and correct midline positioning
AI, artificial intelligence; n, number of participants; US, ultrasound

Benign Hematology - Clinical (BHC) OP-BHC-30

Prevalence of Alloimmunisation in Beta Thalassemia Major at Tertiary Care Center

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Introduction

RBC alloimmunization stands as a significant complication of chronic transfusion in beta thalassemia patient. This study aims to determine the prevalence of alloimmunization among thalassemia patients receiving regular triple saline washed red cells transfusion.

Aims & Objectives

To determine the prevalence of alloimmunization in patients with beta thalassemia major at a tertiary care center.

Objective - 1.To assess the prevalence of alloimmunization among beta thalassemia patients receiving regular blood transfusions.

2.Antibody screening and identification in transfusion dependent thalassemia

Materials & Methods

A cross-sectional study was conducted over six months in the department of transfusion medicine, involving 30 patients between 16 to 46year age group diagnosed with beta thalassemia major including thalassemia variants. Informed consent was obtained from the patients or their parents. Plasma samples were used for antibody screening and identification using the column agglutination technique. Extended red blood cell phenotyping for donor blood including C, E, c and e antigens was performed for alloimmunized patients.

Result

In a screening of 30 patients 1 individual were found to have developed alloantibodies against the Rh system (anti c antibody). The overall alloimmunization rate was found to be 3.33% in the study.

Conclusion

Employing extended antigen matched donor blood has proven effective in lowering alloimmunization rates. Washing the donor product removes plasma proteins targeted by recipient antibodies. Our study found a lower prevalence of alloantibodies compared to others, and we noted fewer transfusion reaction in this group of patients.

Benign Hematology - Clinical (BHC) OP-BHC-31

Blood Group Discrepancy in AIHA Complicated by SLE: A Diagnostic Challenge

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Background

Autoimmune hemolytic anemia (AIHA) are rare and occurs when the patient either has an antibody or complement that attaches to its own cells and results in either intravascular hemolysis such as complement activation or extravascular hemolysis in the event of an antibody attached to the red cells.

Case Presentation

A 25-year-old male with a known case of systemic lupus erythematosus (SLE) was referred to our hospital due to an incompatible cross-match issue. The patient presented with complaints of breathlessness for 15 days, high-grade fever, weakness, and hematuria for

2 days. On examination, the patient appeared pale and icteric. Laboratory investigations revealed a hemoglobin level of 3 g/dL, total bilirubin of 2.8 mg/dL (direct bilirubin 1.8 mg/dL), elevated liver enzymes, and lactate dehydrogenase (LDH) levels of 4133 U/L. Hepatosplenomegaly was noted. Further workup showed a positive ANA (1:3200) and reduced complement levels (C3/C4), consistent with SLE. Peripheral smear findings were suggestive of hemolytic anemia, and a high reticulocyte count supported ongoing hemolysis.

Diagnosis

Blood grouping performed at various temperatures revealed a Group IV blood group discrepancy. Cross-matching was conducted using three techniques, and the best-matched blood unit was identified by performing compatibility testing at 37°C. Three units of least incompatible blood were issued to the patient without any transfusion reactions.

Treatment

The patient responded well to steroid therapy. The cross-match testing revealed a reaction at the immediate spin phase and at 4°C, indicating the presence of cold-reactive IgM antibodies. The cold autoantibodies were likely triggered by the lower temperatures.

Follow-up

Patient was called for follow-up after 30 days with the latest CBC reports.

Conclusion

This case illustrates how the presence of cold autoantibodies can exacerbate autoimmune hemolytic anemia (AIHA) in a patient with SLE. Identifying the nature and thermal amplitude of the antibody was critical in resolving the blood group discrepancy and ensuring the safe transfusion of the best-matched blood.

Benign Hematology - Clinical (BHC) OP-BHC-32

Case of Chronic Cough and Interstitial Lung Disease with Neutropenia: A Diagnostic Challenge

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Background

A 59-year-old male patient presented with a chronic cough persisting for 3 months, unresponsive to symptomatic treatment with antihistamines. Despite normal chest X-ray findings, further evaluation with high-resolution computed tomography (HRCT) of the chest revealed signs suggestive of interstitial lung disease (ILD). Routine workup, including complete blood count, showed neutropenia. This case presents a diagnostic challenge involving a rare combination of interstitial lung disease, neutropenia, and a positive C-ANCA.

Case Presentation

The patient, a 59-year-old male, with no prior significant medical history, presented with a persistent, non-productive cough for 3 months. The cough was initially managed with antihistamines, but symptoms persisted, prompting further evaluation. A chest X-ray was unremarkable, but high-resolution CT revealed findings consistent with interstitial lung disease. Routine workup revealed neutropenia (absolute neutrophil count: 500/μL), which prompted an autoimmune evaluation.

Diagnosis

Autoimmune testing revealed a positive C-ANCA, with negative MPO and PR3 antibodies. Given the presence of neutropenia and C-ANCA positivity, granulocyte colony-stimulating factor (G-CSF) 300 mcg daily for 5 days was administered, but there was no improvement in the neutropenia. As a result, a bone marrow biopsy and aspiration were performed, revealing a normocellular marrow. Further molecular testing, including next-generation sequencing (NGS) and clinical axon study, showed no mutational defects.

In view of the interstitial lung disease and neutropenia with C-ANCA positivity, a positron emission tomography (PET) scan was done, which confirmed an interstitial lung disease pattern. Given the overall clinical and laboratory findings, a diagnosis of autoimmune-mediated interstitial lung disease with neutropenia was considered.

Treatment

The patient was started on a tapering dose of corticosteroids. Following steroid therapy, there was gradual improvement in neutropenia, and the patient's respiratory symptoms improved significantly.

Follow-up

The patient continues to be monitored closely with regular follow-ups with normal WBC count

Conclusion

This case highlights the importance of considering autoimmune causes, such as granulomatosis with polyangiitis (GPA), in patients presenting with interstitial lung disease and neutropenia. Despite negative MPO and PR3 antibodies, the positive C-ANCA and other clinical findings warranted steroid therapy, leading to improvement. A multidisciplinary approach is crucial in diagnosing and managing complex cases with overlapping systemic manifestations.

Benign Hematology - Clinical (BHC) OP-BHC-33

Clinical Profile of Children of Chronic Immune Thrombocytopenia (ITP): A Single Centre Retrospective Study

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Introduction

Chronic ITP is currently defined as thrombocytopenia <100 × 109/L lasting for >12 months. Although many pediatric patients with ITP have spontaneous remission or reach remission within 12 months of first-line therapy, approximately 20-25% progress to chronic ITP. According to the recent American Society of Hematology (ASH) guidelines, if there is incomplete response to treatment, further evaluation to find underlying cause should be considered.Most guidelines have conservative approach towards chronic ITP patients with minor bleeds but very low platelet counts are of great concern to both parents & physicians.Hence,we studied the clinical profile & treatment received in patients with chronic ITP.

Aims & Objectives

To study the clinical profile & treatment received by children with chronic ITP

Materials & Methods

We conducted a retrospective observational study on patients diagnosed as Chronic ITP from January 2018 to January 2023 in BJ Wadia Children Hospital, Mumbai. Demographic data, detailed history,laboratory findings along with the treatment received were recorded in the predetermined case record form.

Result

Total 36 patients were diagnosed as a case of chronic ITP from the duration of 2018 to 2023 with a male to female ratio of 1.25:1.Median age of diagnosis was 7 years(range of 2 – 16 years).The median platelet count at presentation were 4.5 × 109/L (range of 1× 109/L to 32 × 109/L). The most common clinical bleeding symptoms were mucocutaneous bleeds [n:24 (66.6%)] with few had life threatening bleeds like gastrointestinal bleeding (n:1), intracranial bleed (n:2). All patients were initially treated either by corticosteroids [n:26(72%)] or IVIG [n:10(27.7%)] according to clinical decision. Majority[n:22(61.1%)] responded to rescue therapy but response waned over time. Maintenance treatments that were used in patients were dapsone(n:24),Eltrombopag(n:18), Romiplostim (n:11), Bortezomib(n:4), rituximab (n:4),azathioprine (n:3),Mycophenolate Mofetil (n:3) & splenectomy (n:1).A partial response (platelet count 30 × 109/L to 100 × 109/L) was only observed to second line treatment.

Conclusion

In this study we reviewed the clinical course & treatment of pediatric chronic ITP.Most children clinically respond to one or the other second line drugs in terms of bleeds.All patients with chronic ITP should be evaluated for genetic disorder which might guide further treatment.Hence,pediatric chronic ITP treatment needs much more individualized approach based on the bleeding profile and underlying disease if any.

Benign Hematology - Clinical (BHC) OP-BHC-34

Clinical Profile and Treatment Outcomes of Invasive Fungal Infections in Patients with Haematological Diseases - A Tertiary Care Center Experience

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Introduction

Invasive fungal infections (IFI) pose a diagnostic and therapeutic challenge, and carry high mortality and morbidity in patients with haematological diseases. Prophylactic antifungals are routinely employed in patients with severe neutropenia.

Aims & Objectives

We, herewith, report our experience of IFI.

Materials & Methods

In this single-centre retrospective study, we studied the epidemiology, risk factors, management and treatment outcomes of IFI in patients with haematological diseases from January 2021 to June 2024.

Result

Among 561 patients with haematological diseases, 48 were diagnosed with IFI (incidence 8.6%): 9(19%) were proven, 6(13%) probable, and 33(69%) possible IFI as per EORTC/MSG criteria. Median age was 52 years(range 19-75); 56% (n=27) were male patients.

AML (n=21,44%) was the commonest underlying disease, followed by ALL (n=7,15%), severe aplastic anaemia (n=5,10%) and plasma cell dyscrasias (n=4,8%).

Among 48 patients, 28(58%) were on chemotherapy, 11 received intensive chemotherapy. Eight among 48 were undergoing HSCT (7 allogeneic and 1 autologous): among allogeneic HSCT patients, five were on GvHD prophylaxis, and two were on treatment for GvHD.

Forty-two patients (86%) were neutropenic; 30(71%) had severe neutropenia, with a median duration of neutropenia of 14 days.

Commonest organ involved was lung (58%), followed by PNS, orbit and brain (21%).

Nine cases had microbiologically documented fungus: seven (3 Aspergillus, 2 Mucor and 2 Candida) by KOH mount, 1 case of Rhizopus by tissue culture and 1 case of Candida by blood culture. Serology for Aspergillus galactomannan was positive in 6 cases; one had beta-D-glucan positivity as well.

Patients with AML, SAA and patients undergoing HSCT were on posaconazole or echinocandin prophylaxis; the rest of the patients with neutropenia were on fluconazole prophylaxis.

Liposomal amphotericin-B was the initial drug in 28(58%) patients, voriconazole in 17(35%) and posaconazole in 3(6%). Amphotericin was followed by voriconazole in 27 patients, and isavuconazole in one. Among 48 patients, 31% (n=15) succumbed. Severity and duration of neutropenia, and positive serology were significant risk factors for mortality by univariate analysis. Use of mold-active antifungal prophylaxis was associated with lower rates of mortality.

Risk factors for mortality

Factor	'p' value
Age	0.686
Sex	0.724
Aetiology	0.243
Antifungal prophylaxis	**0.035**
Yeast-active	0.161
Mold-active	**0.012**
Type of therapy (chemotherapy, SCT)	0.399
GvHD	0.559
Concurrent CMV infection	0.103
Steroid therapy	0.509
Organ involved	0.131
Positive serology	**0.027**
Morphologically documented infection	0.081
ANC < 1000/cu.mm	**0.017**
Duration of neutropenia > 14 days	**<0.001**

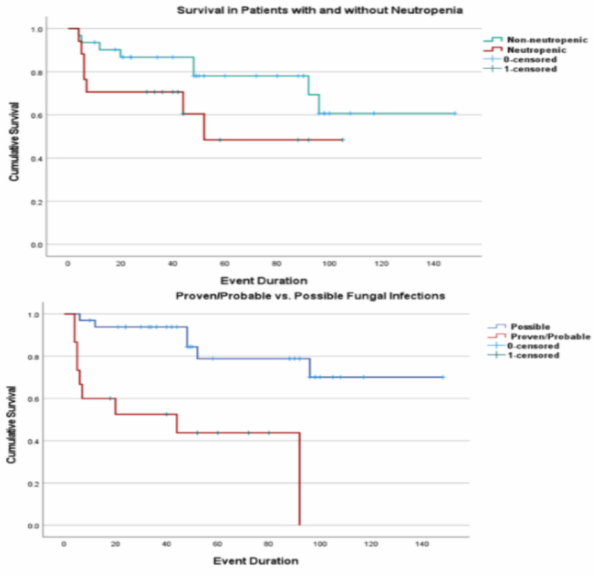

Figure 1 showing risk factors for mortality in IFI, and survival patterns in IFI in patients with neutropenia and proven or probable IFI

Conclusion

IFI carries a high mortality rate in patients with haematological diseases. Positive galactomannan was a surrogate marker, and severity and duration of neutropenia were risk factors for mortality. Timely recognition of risk factors, and use of mold-active anti-fungal prophylaxis reduces mortality rates.

Benign Hematology - Clinical (BHC) OP-BHC-35

Management of Breakthrough Bleeding Episodes in the Phase 3 Concizumab Studies

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Introduction

Concizumab is an anti-tissue factor pathway inhibitor (TFPI) monoclonal antibody in development as a once-daily subcutaneous prophylaxis for hemophilia A/B with inhibitors (HAwI/HBwI; explorer7 [NCT04083781]) and without inhibitors (HA/HB; explorer8 [NCT04082429]). Spontaneous or traumatic breakthrough bleeding (BTB) can occur in patients with hemophilia who are treated prophylactically; guidance for the management of these events should be considered.

Aims & Objectives

To investigate BTB management from the phase 3 explorer7 and explorer8 56-week data.

Materials & Methods

In the phase 3 concizumab studies, bleeding episodes were reported along with the hemostatic treatment used to manage the bleed. Guidance for managing mild/moderate BTBs was included in these studies, generally using the lowest dose of the required treatment, according to local labeling. Classification of BTB severity was the responsibility of the investigator.

Result

At the 56-week cut-off, BTBs that occurred in patients receiving concizumab were most frequently in joints, occurred spontaneously, and were reported as mild/moderate in severity (Table 1). Most BTBs of mild/moderate severity were treated with one injection of the respective BTB treatment (Table 2). In people with HAwI/HBwI, bleeds were most often managed with recombinant activated factor VII (median consumption per injection: mild/moderate bleeds in HAwI 90.0 µg/kg and HBwI 90.0 µg/kg; severe bleeds in HAwI 82.0 µg/kg and HBwI 68.0 µg/kg). In people with HA, bleeds were managed with factor VIII (median consumption per injection: mild/moderate bleeds 20.0 IU/kg; severe bleeds 20.9 IU/kg) and in people with HB with factor IX (mild/moderate bleeds 30.0 IU/kg; severe bleeds 28.9 IU/kg).

Table 1: Summary of breakthrough bleeds in the phase 3 studies (explorer7 and explorer8) in patients on concizumab prophylaxis (56-week cut-off).

	explorer7								explorer8							
	HAwI				HBwI				HA				HB			
Number of patients, N	76				51				80				64			
Number of patients with treated bleeding episodes, N (%)	43 (56.6)				29 (56.9)				56 (70.0)				48 (75.0)			
Total number of treated bleeding episodes, N	190				218				355				307			
	N	(%)	E	[%]	N	(%)	E	[%]	N	(%)	E	[%]	N	(%)	E	[%]
Cause of bleed*																
Spontaneous	32	(42.1)	119	[62.6]	26	(51.0)	150	[68.8]	47	(58.8)	190	[53.5]	39	(60.9)	196	[63.8]
Traumatic	31	(40.8)	68	[35.8]	15	(29.4)	65	[29.8]	41	(51.3)	159	[44.8]	29	(45.3)	106	[34.5]
Severity of bleed†																
Mild/moderate	41	(53.9)	163	[85.8]	27	(52.9)	204	[93.6]	56	(70.0)	344	[96.9]	46	(71.9)	294	[95.8]
Severe	13	(17.1)	27	[14.2]	10	(19.6)	14	[6.4]	3	(3.8)	11	[3.1]	8	(12.5)	13	[4.2]
Location of bleed‡																
Joint	35	(46.1)	151	[74.8]	27	(52.9)	160	[70.2]	53	(66.3)	259	[68.5]	43	(67.2)	247	[74.6]
Muscular	15	(19.7)	32	[15.8]	8	(15.7)	39	[17.1]	21	(26.3)	47	[12.4]	12	(18.8)	44	[13.3]
Skin	6	(7.9)	8	[4.0]	4	(7.8)	11	[4.8]	11	(13.8)	27	[7.1]	7	(10.9)	14	[4.2]

*Bleeds with causes other than 'spontaneous' or 'traumatic' are not presented in the table. †The investigator determined the classification of bleed severity; mild/moderate: uncomplicated musculoskeletal, mucosal or subcutaneous bleeds; severe: bleeds that required hospitalization or were life-threatening. ‡A bleeding episode that occurred in multiple locations was counted in all of these locations; only the three most frequent sites of bleeds are included. For bleeds, the location of bleeds, E, represents the number of bleeds and [%] is the percentage of bleeds.
(%), percentage of patients; [%], percentage of bleeding episodes; E, number of bleeding episodes; HA/HAwI, hemophilia A/hemophilia A with inhibitors; HB/HBwI, hemophilia B/hemophilia B with inhibitors; N, number of patients

Table 2: Summary of breakthrough bleed management in the phase 3 studies (explorer7 and explorer8) in patients on concizumab prophylaxis (56-week cut-off).

	explorer7				explorer8			
	HAwI		HBwI		HA		HB	
	Mild/ moderate	Severe	Mild/ moderate	Severe	Mild/ moderate	Severe	Mild/ moderate	Severe
FVIII								
Number of treated bleeds, n (%)	11 (100.0)	2 (100.0)	-		335 (100.0)	11 (100.0)	-	
One injection	6 (54.5)	1 (50.0)	-		242 (72.2)	0	-	
Two injections	2 (18.2)	1 (50.0)	-		54 (16.1)	0	-	
Three or more injections	3 (27.3)	0	-		39 (11.6)	11 (100.0)	-	
Median consumption per injection, IU/kg	20.0	60.0	-		20.0	20.9	-	
FIX								
Number of treated bleeds, n (%)	-		-	1 (100.0)	-		289 (100.0)	13 (100.0)
One injection	-		-	0	-		213 (73.7)	9 (69.2)
Two injections	-		-	0	-		43 (14.9)	0
Three or more injections	-		-	1 (100.0)	-		33 (11.4)	4 (30.8)
Median consumption per injection, IU/kg	-		-	134.4	-		30.0	28.9
rFVIIa								
Number of treated bleeds	114 (100.0)	25 (100.0)	203 (100.0)	14 (100.0)	-		-	
One injection	70 (61.4)	16 (64.0)	93 (45.8)	7 (50.0)	-		-	
Two injections	24 (21.1)	4 (16.0)	38 (18.7)	2 (14.3)	-		-	
Three or more injections	20 (17.5)	5 (20.0)	72 (35.5)	5 (35.7)	-		-	
Median consumption per injection, µg/kg	90.0	82.0	90.0	68.0	-		-	
aPCC								
Number of treated bleeds, n (%)	43 (100.0)	2 (100.0)	1 (100.0)	-	-		-	
One injection	7 (16.3)	1 (50.0)	1 (100.0)	-	-		-	
Two injections	5 (11.6)	1 (50.0)	0	-	-		-	
Three or more injections	31 (72.1)	0	0	-	-		-	
Median consumption per injection, IU/kg	50.0	80.0	50.0	-	-		-	

The investigator determined the classification of bleed severity; mild/moderate: uncomplicated musculoskeletal, mucosal or subcutaneous bleeds; severe: bleeds that required hospitalization or were life-threatening. For some bleeding episodes, the dosing information for the associated treatment was missing; and in some cases, a bleeding episode was treated with more than one product. One patient with HBwI had one severe bleed treated with ≥3 injections of FVIIa+FX (Byclot®) with a median consumption per injection of 40.0 µg/kg. aPCC, activated prothrombin

Conclusion

BTBs that occurred in patients receiving concizumab prophylaxis were mostly of mild/moderate severity and could be effectively treated in alignment with the trial protocol guidance provided. Most mild/moderate bleeds were resolved with a single injection of factor or bypassing agent.

Benign Hematology - Clinical (BHC) OP-BHC-36

Plasma Emicizumab Levels, Clotting Time by Rotational Thromboelastometry and Clinical Bleeds in Haemophilia Patients on Standard and Low Dose Emicizumab Prophylaxis

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Introduction

Emicizumab with the recommended dose, gives 0 treated bleeds; results in resolution of target joint bleeds in hemophilia A patients with and without inhibitors, but is very costly. Thus, a study to assess the safety and efficacy of low-dose Emicizumab was done. Low-dose emicizumab (3mg/kg every 4 weeks (no loading dose)) which is even less than half the standard-dose (loading dose: 3 mg/kg once a week for 4 weeks followed by maintenance dose of 6mg/kg every 4 weeks) clinically is almost equivalent to standard-dose with zero-spontaneous bleeds and 100% resolution of target-joints. Emicizumab prophylaxis does not require laboratory monitoring, but it is a must when we are lowering the dose, for acute bleeds and during surgery.

Aims & Objectives

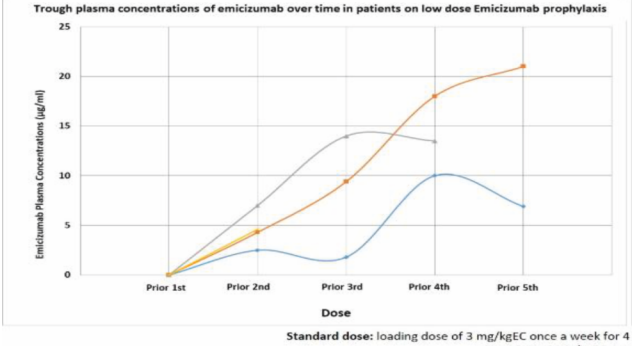
To correlate plasma emicizumab levels, clotting profile by rotational thromboelastometry and clinical bleeds in patients on standard-dose and low-dose emicizumab prophylaxis.

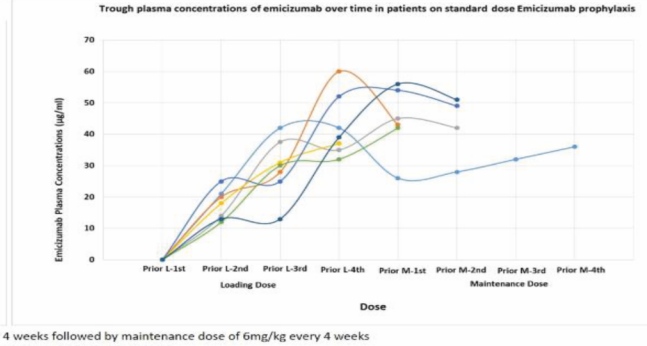
Materials & Methods

Plasma Emicizumab levels by modified one stage assay and Non-activated Thromboelastometry was performed in total 70 samples of 5 haemophilia patients on low-dose and 7 patients on standard-dose Emicizumab from prior to maximum of 5th maintenance dose. Number of bleeds was also captured.

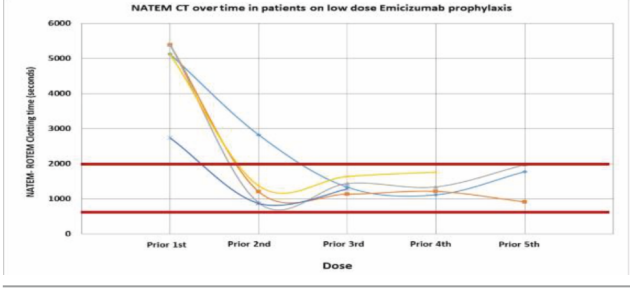
Result

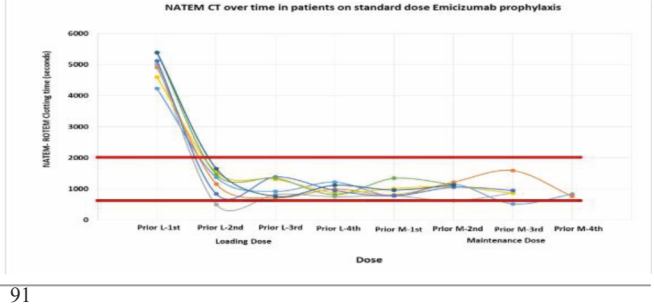
For both the groups, as number of doses increases, the plasma Emicizumab levels increases; with a statistical correlation. After 4 months, the mean plasma Emicizumab levels in standard-dose is 50µg/ml and in low-dose is 23µg/ml.





Standard dose: loading dose of 3 mg/kgEC once a week for 4 weeks followed by maintenance dose of 6mg/kg every 4 weeks
Low dose: 3 mg/kgEC every 4 weeks (no loading dose)





The clotting time by NATEM-ROTEM, shorten with the number of doses given. However though it takes more time to achieve in patients on low-dose Emicizumab, after 4 months, the clotting time(CT) in both the groups reach the range obtained in mild haemophilia patients; increase in dose after a certain point shows no further shortening of CT. Interestingly, both the groups clinically also show same results i.e. zero spontaneous bleed.

Conclusion

A strong correlation is seen between the dose, no. of doses given to the patient and plasma Emicizumab levels. However, interestingly the clotting time by NATEM-ROTEM as well as number of bleeds observed after 4-5 months in low or standard-dose Emicizumab groups are the same. Is this a detection limit of the assay or maybe after a certain concentration of Emicizumab, there is no further improvement in clotting time which explains why both the doses clinically are also working at par?

Benign Hematology - Clinical (BHC) OP-BHC-37

Utilizing Screening Assay Results to Predict Bethesda Inhibitor Titres in Patients with Hemophilia A: A Cost - Effective Strategy

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Introduction

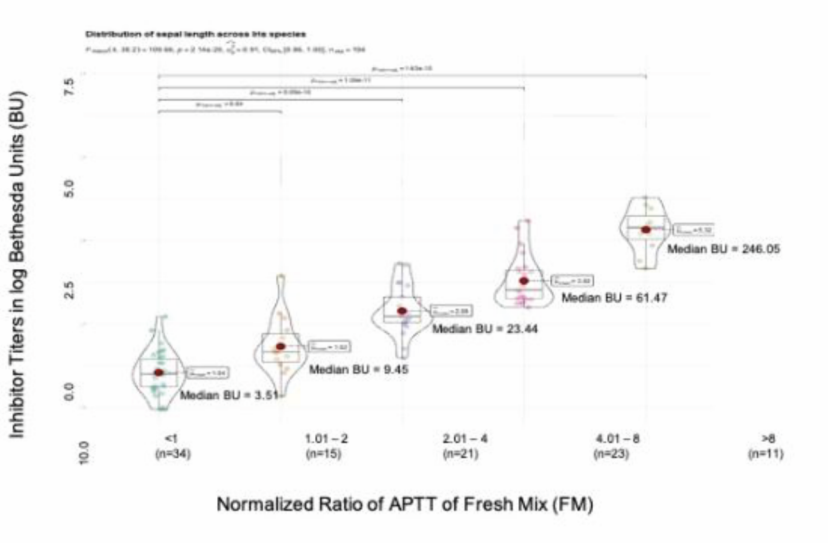
The classic or the Nijmegen-modified Bethesda assay for inhibitor assay for factor VIII requires testing for residual factor VIII levels in multiple serial dilutions, exponentially raising the cost of the assay. Consequently, in resource-constrained settings, these assays become prohibitively expensive, limiting the availability of the test in a few diagnostic laboratories.

Aims & Objectives

We aimed to develop a cost-effective strategy to predict inhibitor titers (BU) in patients with Hemophilia A from inhibitor screening assay and ascertain the likely dilutions where the residual FVIII activity will be assessed.

Materials & Methods

Laboratory data of patients of haemophilia A with inhibitors were analyzed, where inhibitor screening and Bethesda assay (BA) were performed. The data was analyzed to develop a predictive model for inhibitor titer estimation based on the normalized ratio of APTT values of fresh mix (FM) or incubated mix (IM). Based on the results of the inhibitor screening [fresh mix (FM) or incubated mix (IM)] and BA, a predictive model was developed. The model was prospectively validated on a new set of HA with inhibitor samples (n=27).



Result

104 samples from 83 patients with haemophilia A with inhibitors were analyzed. A linear regression

analysis was performed and R-squared suggested that the normalized ratio of FM (R2=0.815) proved to be highly explanatory of the log Bethesda unit compared to IM (R2=0.536). A predictive model was designed based on the normalized ratio of FM values and validated on 27 new inhibitor-positive samples. The R-squared (R2=0.843) between observed and predicted log Bethesda units are highly correlated; consequently, suggesting that FM is a good predictor of BU.

Conclusion

The findings of the inhibitor screening assay (values of FM, IM and the difference between IM and FM) serve as potential indicators of the expected inhibitor titers (BU). This information can be used to limit the number of dilutions in which the residual FVIII assay has to be performed to estimate the Bethesda titer, effectively reducing the assay's cost in resource-constrained settings.

Benign Hematology - Clinical (BHC) OP-BHC-38

Is Bone Marrow Examination Needed for Diagnosis of Immune Thrombocytopenia

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Introduction

Immune thrombocytopenia (ITP) is an autoimmune disorder characterized by the destruction of platelets, leading to thrombocytopenia and bleeding manifestations. ITP is often diagnosed by exclusion, as there are no specific tests with high sensitivity or specificity. While bone marrow examinations (BME) are routinely used to rule out haematological malignancies, their necessity in diagnosing ITP remains controversial. This study aimed to evaluate the role of BME in the diagnostic workup of ITP at a tertiary health care center in western Rajasthan.

Aims & Objectives

The objective of this study was to review the current practice of performing bone marrow examinations in patients with suspected ITP and to assess whether BME is necessary for the primary diagnosis and treatment of ITP.

Materials & Methods

A retrospective study was conducted on 139 patients with suspected ITP between June 2016 and September 2024 at a tertiary healthcare center. Clinical and laboratory data, including hemogram and bone marrow findings, were analyzed. Cases with known causes of thrombocytopenia (e.g., viral infections, chemotherapy) were excluded. The patients were categorized by age, sex, clinical presentation, and duration of illness. The study focused on the necessity and findings of BME in suspected ITP cases.

Result

Of the 139 patients, 79 (56%) were females, and 60 (44%) were males. The median age was 27 years. Mucosal bleeding was observed in 109 cases (78.4%). Bone marrow examination revealed normal hematopoietic elements in all cases, with 79.8% showing prominent megakaryocytes. No significant findings of haematological malignancy were noted. Majority of the patients responded well to first-line steroid therapy.

Conclusion

Routine bone marrow examination may not be essential in cases of isolated thrombocytopenia suspected of being ITP, as it does not significantly alter the diagnosis or management. A careful clinical evaluation and basic laboratory tests can suffice for diagnosis. However, BME remains valuable in cases with atypical features, such as other cytopenias or organomegaly.

Benign Hematology - Clinical (BHC) OP-BHC-39

Harnessing Monocyte Distribution Width : A Game-Changer in Early Sepsis Identification in Adult Intensive Care

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Introduction

Sepsis is a life-threatening organ dysfunction caused by a dysregulated host response to infection. The average mortality due to sepsis is about 30-40%. Early recognition and diagnosis of sepsis is an essential part of sepsis management. Monocyte distribution width (MDW) is a measure of variability in peripheral blood monocyte morphologic characteristics that has shown promise for infectious disease screening and diagnosis. It is measured in advanced hematology analyzers within a few minutes and without the need for additional sample or cost.

Aims & Objectives

To identify the role of monocyte distribution width (MDW) as an early indicator of sepsis.

Materials & Methods

This prospective observational study was conducted for a period of one year in which 74 patient's venous blood samples were collected in K2EDTA vacutainers form the suspected cases of sepsis. Systemic Inflammatory Response Syndrome (SIRS) criteria were used to identify the cases of sepsis. SIRS criteria includes- Leukocytosis where W.B.C count >12,000/cumm, or leucopenia <4,000/cumm, pulse rate- tachycardia >90 beats per minute, respiratory rate >20 breaths and temperature < 96.80 or >100.40 F fever. Patients who met at least 2 of these criteria of SIRS were included in the study. Patients who received blood transfusion were excluded from this study. The value of MDW was measured using DxH800/900 hematology Analyzer (Beckman coulter Inc, Miami, FL). Other sepsis biomarkers like Total leucocyte count (TLC), procalcitonin (PCT), C-reactive protein (CRP) were also evaluated.

Result

Out of 74 patients meeting criteria for sepsis; 23 were with septic shock and 51 patients were without septic shock. MDW was highest for patients with septic shock as compared to sepsis without shock (P-value = 0.018). We have noted that with increase in TLC, CRP and procalcitonin level there is increase in the MDW. Mean value of MDW was found to be increased as the SIRS score increases.

Conclusion

MDW is a new hematological parameter that is simultaneously calculated during complete blood cell counting by newer hematology analyzers. MDW is expected to serve as a useful indicator for early screening of sepsis in conjunction with other sepsis biomarkers. However, as MDW is a newer parameter, more in depth studies are required to confirm its robustness as a sepsis biomarker.

Benign Hematology - Clinical (BHC) OP-BHC-40

Efficacy and Safety of Mim8 Prophylaxis in Adults and Adolescents with Hemophilia A With or Without Inhibitors: Phase 3, Open Label, Randomized, Controlled Frontier2 Study

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Introduction

Mim8 (denecimig) is a factor VIIIa mimetic bispecific antibody in clinical development for subcutaneous prophylaxis in hemophilia A (HA).

Aims & Objectives

Evaluate the efficacy and safety of Mim8 in males and females (aged ≥12 years) with HA with or without inhibitors.

Materials & Methods

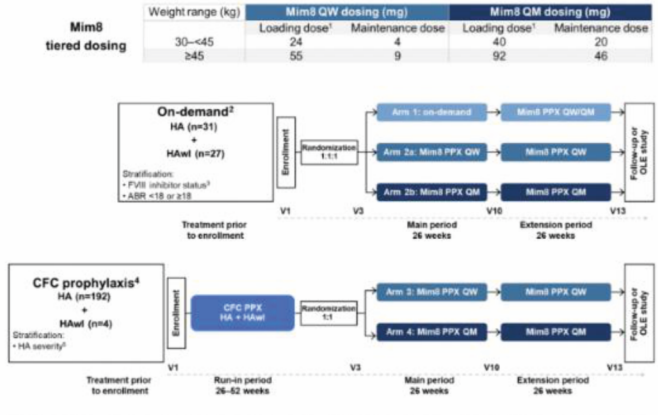
FRONTIER2 (NCT05053139) is a phase 3, open label, randomized, controlled study. Mim8 was administered using tiered dosing (Figure 1). Primary objectives: demonstrate the hemostatic effect of Mim8 once-every-week (QW) and once-every-month (QM) at week 26 versus either on demand treatment, or versus previous clotting factor concentrate (CFC) prophylaxis during the run in period. Annualized bleeding rate (ABR) was estimated using a negative binomial regression model. Safety and immunogenicity were evaluated. Study was conducted following informed consent and ethical approval.

Result

Overall, 254 patients were randomized (Table 1). In patients previously treated on-demand, estimated mean ABR [95% CI] for treated bleeds was 0.45 [0.18;1.14] for QW and 0.20 [0.06;0.72] for QM Mim8 prophylaxis, versus 15.75 [10.7;23.2] for continued on-demand treatment (Table 1). Mim8 prophylaxis was superior to on-demand treatment, with ABR reduction of 97.1% (QW) and 98.7% (QM).In patients on pre-study CFC prophylaxis, estimated mean ABR for treated bleeds was 2.51 [1.42;4.42] for QW and 1.78 [1.17;2.71] for QM Mim8 prophylaxis, versus 4.83 [3.59;6.51] and 3.10 [2.23;4.29], during run-in CFC prophylaxis, respectively (Table 1). Mim8 prophylaxis was superior to run-in CFC prophylaxis, with ABR reduction of 48.0% (QW) and 42.6% (QM). Zero bleeds were observed in 65.3–95.0% of patients treated with Mim8 (Table 1). Injection-site reactions occurred in 5.0–12.2% of patients. There were no safety concerns and no clinical evidence of neutralizing anti-Mim8 antibodies.

Figures/Tables

Figure 1: Study design of the phase 3, open-label, randomized, controlled FRONTIER2 study (NCT05053139)



(1) An initial loading dose was administered once in order to rapidly achieve steady-state levels of Mim8, followed by maintenance dose in the next scheduled dosing visit; (2) Patients treated with on-demand/no prophylaxis prior to enrollment were required to have had ≥5 bleeds in the 26 weeks before screening, for which FVIII concentrates or a bypassing agent had been prescribed; (3) The patient's FVIII inhibitor status was defined by use or prescription of bypassing agents in the past 6 months; (4) Patients with FVIII activity ≥1% who were receiving prophylactic treatment were required to have had ≥1 bleed in the 26 weeks before screening, for which FVIII concentrates or a bypassing agent had been prescribed; (5) Severity of hemophilia defined by severe (endogenous FVIII activity <1%) or non-severe (endogenous FVIII ≥1%) at diagnosis.

ABR, annualized bleeding rate; CFC, clotting factor concentrate; FVIII, factor VIII; HA, patients with hemophilia A without inhibitors; HAwI, patients with hemophilia A with inhibitors; n, number of exposed patients; OLE, Open-Label Extension study FRONTIER4; PPX, prophylaxis; QW, once-every-week; QM, once-every-month; V, visit.

Conclusion

FRONTIER2 demonstrated superiority of Mim8 prophylaxis once-every-week and once-every-month in reducing ABR for treated bleeds compared with either on-demand treatment or clotting factor concentrate prophylaxis. Mim8 was well tolerated, and no safety concerns were observed.

Table 1: Baseline demographics and selected efficacy endpoints

	Patient group: Pre-study on-demand treatment			Patient group: Pre-study CFC prophylaxis			
	Arm 1 (On-demand) n=17	Arm 2a (Mim8 QW) n=21	Arm 2b (Mim8 QM) n=20	Arm 3 (Mim8 QW) n=98		Arm 4 (Mim8 QM) n=98	
				Run-in period	Main period (Weeks 0–26)	Run-in period	Main period (Weeks 0–26)
Demographics and baseline characteristics							
Males, n (%) **Females, n (%)**	16 (94.1) 1 (5.9)	21 (100.0) 0	18 (90.0) 2 (10.0)	98 (100.0) 0		97 (99.0) 1 (1.0)	
Severe HA, n (%)	13 (76.5)	14 (66.7)	18 (90.0)	84 (85.7)		83 (84.7)	
Positive FVIII inhibitor status at baseline, n (%)	8 (47.1)	10 (47.6)	9 (45.0)	2 (2.0)		2 (2.0)	
Body weight ranges, n (%) 30–<45 kg ≥45 kg	1 (5.9) 16 (94.1)	2 (9.5) 19 (90.5)	4 (20.0) 16 (80.0)	5 (5.1) 93 (94.9)		- 98 (100.0)	
Mean (SD) age, years	31 (13)	32 (16)	34 (16)	33 (16)		32 (16)	
Efficacy outcomes[1]							
Treated bleeds Estimated mean ABR [95% CI]	15.75 [10.7;23.2]	0.45 [0.18;1.14]	0.20 [0.06;0.72]	4.83 [3.59;6.51]	2.51 [1.42;4.42]	3.10 [2.23;4.29]	1.78 [1.17;2.71]
Median ABR	12.24	0.00	0.00	2.11	0.00	1.46	0.00
Patients with zero treated bleeds during the main period of study, n (%)	0	18 (85.7)	19 (95.0)	-	65 (66.3)	-	64 (65.3)
Estimated mean ABR ratio [95% CI] p-value	-	**0.029** *vs Arm 1* [0.011;0.078] p<0.0001	**0.013** *vs Arm 1* [0.003;0.046] p<0.0001	-	**0.520** *vs run-in* [0.278;0.973] p=0.0406	-	**0.574** *vs run-in* [0.385;0.857] p=0.0066
Spontaneous bleeds Estimated mean ABR [95% CI]	11.78 [7.48;18.54]	0.09 [0.01;0.69]	0.24 [0.07;0.85]	2.73 [1.94;3.86]	1.49 [0.65;3.42]	1.83 [1.10;3.04]	0.74 [0.42;1.32]
Treated joint bleeds Estimated mean ABR [95% CI]	10.60 [6.28;17.89]	0.48 [0.18;1.29]	0 -	3.60 [2.62;4.95]	1.80 [0.91;3.55]	2.06 [1.43;2.97]	1.09 [0.60;1.99]

(1) For efficacy outcomes (except for proportion of patients with zero treated bleeds), the data presented pertain to the main period (26 weeks) for Arms 1, 2a, 2b, and to the run-in period (weeks 26–52) and main period (26 weeks) for Arms 3 and 4.

ABR, annualized bleeding rate; CFC, clotting factor concentrate; CI, confidence interval; FVIII, factor VIII; HA, hemophilia A; QW, once-every-week; QM, once-every-month; SD, standard deviation.

Benign Hematology - Clinical (BHC) OP-BHC-41

Platelet Parameters and Red Cell Transfusions in Patients of Postpartum Hemorrhage

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Introduction

Postpartum hemorrhage (PPH) is a leading cause of maternal morbidity and mortality worldwide. Timely red blood cell (RBC) transfusions are essential for managing PPH, but access to blood supplies in low- and middle-income countries is often limited. Studies have shown that women with thrombocytopenia are at a higher risk for severe PPH, which requires blood transfusion. Additionally, platelet indices such as mean platelet volume (MPV) and platelet distribution width (PDW) may help predict bleeding risk.

Aims & Objectives

1. To correlate near term platelet count and indices (mean platelet volume (MPV) , plateletcrit (PCT) , platelet distribution width (PDW)) in women who develop primary PPH with red cell transfusion requirements.
2. To compare the near-term platelet count and indices in women who develop primary PPH with women who do not develop PPH.

Materials & Methods

3 ml of venous blood was collected in EDTA anticoagulant vial within 72 hours before delivery from all near-term women undergoing delivery. These patients were followed up, and those who developed PPH were taken

as cases, and those who did not, were taken as controls. The number of red cell transfusions given to cases, were recorded. Sample was tested by Mindray BC-6800 5 component hematology analyzer for platelet count and indices.

Result

Cases were divided into two groups (A) Transfusions: Yes (B) Transfusions: No. Among groups A and B, 63% and 40% had platelet count of less than 1 lakh respectively. Significant difference between the two groups in terms of PCT (%) was observed, with the median PCT being highest in the group requiring no transfusions (0.21% vs. 0.26%, p = 0.026). There was no significant difference between the groups in terms of mean MPV(Group A=12.15, Group B=12.05, p=0.971) and mean PDW(Group A=16.55, Group B=16.46, p=0.838).

There was no significant difference between cases and controls in terms of age, blood group, platelet count, MPV, PDW, PCT, mode of delivery and number of previous births.

Conclusion

Thrombocytopenia and low plateletcrit are associated with increased risk of requirement for blood transfusions.

Benign Hematology - Clinical (BHC) OP-BHC-42

Hemoglobin E Hemoglobinopathy, The Silent Epidemic: An Institutional Experience from Kalyani

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Introduction

Hemoglobin E (HbE) is a common structural β-hemoglobin variant that has the phenotype of a mild form of β thalassemia, whose interactions with other thalassemias produce syndromes of varying severity. HbE occurs at an extremely high frequency in many states in India and because there is also a high frequency of different β-thalassemia alleles in these populations, the coinheritance of HbE and β thalassemia leading to HbE-β thalassemia, occurs very frequently leading to a transfusion dependent anemia. Knowing the frequency and heterogeneity of a particular haemoglobinopathy in a target population is an important prerequisite in planning an adequate screening strategy for carrier identification.

Aims & Objectives

1. To study the spectrum of HbE Thalassemia found on High-Performance Liquid Chromatography (HPLC) at a tertiary care centre in Kalyani.
2. To find out the distribution of different red blood cell (RBC) indices in HbE hemoglobinopathies and to determine their significance as screening tests in identifying cases with HbE trait.

Materials & Methods

This is a retrospective study of all cases sent for HPLC and Complete Blood Count (CBC)to the Haematology laboratory from December 2022 till September 2024.

Result

Out of 1523 cases received for HPLC 370(24.3%) cases were positive for hemoglobinopathies. Of these cases 111 were HbE heterozygous (30% of positive cases), 6 were HbE homozygous (1.62% of positive cases) and 9 (2.43% of positive cases) were double heterozygous for HbE beta thalassemia. Mean hemoglobin is the highest

for HbE trait and the minimum for HbE-beta. A value of MCV at 73.8 (fl) or more and MCH 21.9pg or more gives the highest sensitivity and specificity for the diagnosis for HbE-trait. However, a good number of cases showed MCV >80 but still turned out to have Hb E trait.

Conclusion

West Bengal has a high prevalence of HbE trait. Unlike the other thalassemia traits, HbE trait show mild to no changes in a screening CBC, almost no symptoms and can hence be often missed. Mass screening programmes including premarital, preconception and antenatal are absolutely essential to prevent and reduce the burden of transfusion dependant double heterozygous states.

Benign Hematology - Clinical (BHC) OP-BHC-43

Shrouded in Mystery: The Lincoln Log Vertebra's Silent Signal in Sickle Cell Disease

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Background

Sickle cell anaemia is type of hemoglobinopathy characterized by presence of HbS . Its a autosomal recessive disease. Disease is characterised by sickle cell RBCs which when subjected to some triggers like inflammation, hypoxia causes polymerization leading to varied complications Diagnosing the correct cause of musculoskeletal pain in such patients can be a challenge sometimes

Case Presentation

The study consists of findings from 2 patients of different age group one 50 yrs male and another 27 yr female with sickle cell presented to Hospital with comorbidity of sickle cell disease. When evaluated for the backache got similar set of findings on radiological investigations. Radiological findings so found have a result of microvascular pathology of the sickle cell disease.

Diagnosis

Lincoln Log vertebrae

Treatment

Analgesic application and postural re-education made a significant reduction in the symptoms

Follow-up

Patient were followed up at a regular intervals and the change in intensity of the symptoms were noted. Some radiological investigations were repeated at the follow up.

Conclusion

The outcomes of the case study is that sickle cell disease may present with varied bony manifestations Lincoln Log vertebrae being one of the same. Severity of the pain were significantly related to pathological modifications. Understanding the pathology behind the change in bone will help in improving the outcomes. High index of suspicion is the key for reaching the diagnosis and management,which ultimately helps in halting the progression of vertebrae destruction

Benign Hematology - Clinical (BHC) OP-BHC-44

Acute Pain Management Strategies in Sickle Cell Anaemia : A Two-Year Comparative Study of Adult and Paediatric Emergency Visits

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Introduction

Sickle cell anemia (SCA) is a hereditary condition marked by chronic hemolysis and recurrent vaso-occlusive crises (VOC), frequently resulting in emergency department (ED) visits for pain relief. Effective pain management is essential for improving both immediate outcomes and overall quality of life in SCA patients. However, approaches to acute pain management can differ significantly between adult and pediatric populations. This study aims to compare the pain management strategies employed for adult and pediatric patients presenting with VOC to the ED over a two-year period.

Aims & Objectives

Aims:

To compare acute pain management strategies between adult and pediatric sickle cell anemia patients during vaso-occlusive crises in emergency visits.

Objectives:

Analyze opioid use in adult SCA patients.

Assess multimodal pain management in pediatric patients.

Compare complex analgesic regimens between adults and children.

Materials & Methods

A retrospective analysis of ED visits at KIMS Hospital was conducted over two years, examining 62 paediatric patients (122 visits) and 77 adult patients (100 visits) presenting with VOC. Data were collected on the types of analgesics used, including opioid and non-opioid therapies, and comparisons were made between the treatment strategies for adult and paediatric patients. Descriptive statistics were used to assess analgesic use patterns, and comparative analyses were conducted to identify key differences in pain management approaches.

Result

Adult patients predominantly received opioid-based regimens, with Tramadol administered in 56 visits, either alone or in combination. More complex regimens, such as Tramadol + Ketorolac (18 visits) and Tramadol + Ketorolac + Morphine (6 visits), were used for more severe cases. Additionally, opioid patches were prescribed in 12 visits, reflecting the need for sustained pain control. Non-opioid analgesics were used in 8 visits. In contrast, pediatric patients were more often treated with a combination of Paracetamol + Tramadol, accounting for 72 visits. Opioid monotherapy was used in 14 visits, while Ketamine was administered in 12 visits as an alternative pain control method. These data suggest a more cautious approach to opioid use in pediatric cases, favoring multimodal therapies over stronger opioid-based regimens.

Conclusion

This study reveals significant differences in pain management strategies between adult and paediatric patients with SCA. Adults were more likely to receive stronger opioid-based regimens, while paediatric patients were managed with a multimodal approach that minimized opioid use. These findings underscore the need for tailored pain management protocols that address the distinct needs of adult and paediatric SCA patients. Further research is warranted to explore the long-term outcomes of these treatment strategies in both populations.

Benign Hematology - Clinical (BHC) OP-BHC-45

Comparison of D-Dimer to Fibrinogen Ratio (DFR) With Doppler Ultrasonography in Evaluation of Suspected Deep Venous Thrombosis

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Introduction

Deep vein thrombosis (DVT) is characterized by blood clot formation in deep veins, leading to potentially fatal pulmonary embolism if untreated. While colour Doppler ultrasonography is the gold standard for DVT diagnosis, it faces challenges such as operator dependence, false negatives, and limited accessibility in remote areas.

Aims & Objectives

This study aims to compare and analyse the predictive performance of D-Dimer, Fibrinogen, and DFR against Doppler ultrasound findings in the assessment of DVT.

Materials & Methods

Conducted prospectively from April 1, 2023, to June 30, 2024, this study involved 95 patients suspected of DVT, selected using modified Well's criteria. Exclusion criteria included previous DVT, pregnancy, anticoagulant use, liver disease, and thrombocytopenia. Detailed clinical histories were recorded, followed by venous blood sample collection for D-Dimer and Fibrinogen analysis and DFR calculation. Results were statistically analyzed and correlated with Doppler ultrasonography.

Result

The average patient age was 43.07 years, with a male predominance (57.89%). Elevated D-Dimer levels (≥250 ng/dL) were observed in 92.63% of patients. Those with positive Doppler results exhibited significantly higher D-Dimer (mean 2167.16 ng/dL), Fibrinogen (87.10% >400 mg/dL), and DFR (mean 4.07). D-Dimer demonstrated the highest Area Under the Curve (AUC) of 0.964 (95% CI: 0.901–1.000, $p < 0.0001$), followed by Fibrinogen (AUC 0.927) and DFR (AUC 0.814). Cut-off values were >996 ng/dL for D-Dimer, >320 mg/dL for Fibrinogen, and >3.4419 for DFR. Sensitivity was highest for Fibrinogen (96.77%) and D-Dimer (93.55%), while D-Dimer also exhibited the highest specificity (98.44%). The overall diagnostic accuracy was 96.84% for D-Dimer, 90.53% for Fibrinogen, and 84.21% for DFR.

Conclusion

D-Dimer proved to be the most effective predictor for positive Doppler findings, followed by Fibrinogen, which exhibited high sensitivity and negative predictive value. DFR was less reliable as a stand-alone predictor but remains useful as a supplementary marker. These findings underscore the importance of D-Dimer in DVT evaluation, with Fibrinogen and DFR also providing additional diagnostic support.

Benign Hematology - Clinical (BHC) OP-BHC-46

A journey of Hb E Beta thalassemia with thalidomide over time: Therapeutic Benefits, Safety and Tolerability

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Introduction

Hb E-β-thalassemia is a significant concern in Southeast Asia and in India eastern and north eastern states are mostly affected, owing to the high prevalence of both genetic mutations. Blood transfusions & chelation therapy remain the standard of care for transfusion dependent thalassemia patients. Thalidomide is an immunomodulator with antiangiogenic effects, recently been demonstrated to induce γ-globin gene expression to increase the proliferation of erythroid cells.

Aims & Objectives

The primary objective of this study is to assess potential therapeutic benefits, safety and tolerability of thalidomide in E- βeta thalassemia patients in reducing transfusion frequencies and its consequences who failed a reasonable trial with hydroxyurea (6 months)

Materials & Methods

- This is a retrospective study (2018 to 2024).
- Total 150 patients were enrolled in the study,Transfusion-dependent thalassemia (TDT was 130 , non-transfusion-dependent thalassemia (NTDT) was 20 ,Male-84♀36 .
- TDT was considered as patients receiving PRBC transfusion >1 Unit/2 month or >6 Units annually and NTDT as those receiving lesser units of transfusion.
- Patients received thalidomide 50 mg folic acid along with Aspirin.
- Response assessment was categorized as three groups (Major responder > 2gm / dl, Responder >1gm/dl - <2>
- Increments of haemoglobin, ferritin & transfusion requirement were assessed after 3 & 6 months with strict monitoring of adverse events
- Women of childbearing age who do not want to use contraceptive measures, pregnant, lactating women, age <2>65yearsage were excluded.

Result

In our study after 3 months, major responder was -33.3%, minor responder was-47.6%, Overall responder-80.9%, Non-responder was-19.1%.

After 6months, major responder was -49.5%, minor responder was-40.4%, Overall responder-89.9%. Non-responder was-10.1%.

After 15 months, major responder was -78.5%, minor responder was 13.7%, Overall responder-92.2%. Non-responder was-7.8%

Side effects-headache 41%, Sedation 36%, constipation 14%, rash 5%, deep vein thrombosis (DVT) 2%, menstrual irregularities 4.5 %

Conclusion

In our scenario, Thalidomide is a safe, effective strategy at reducing transfusion requirement in patients with E-βeta thalassemia and response increases over time.

Benign Hematology - Clinical (BHC) OP-BHC-47

Behind the Pale and Beyond the Red - A Case Series on Pure Red Cell Aplasia

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Introduction

Pure red cell aplasia (PRCA) is a rare condition where the bone marrow fails to produce red blood cells. Its incidence is low, often linked to autoimmune disorders, malignancies and certain medications. Early diagnosis is crucial to address the underlying cause and prevent severe anemia, which can significantly impact overall health and quality of life.

Aims & Objectives

To assess the prevalence of pure red cell aplasia in Pediatric and adult population and the various causation factors and coexisting conditions.

Materials & Methods

All patients diagnosed with Pure red cell aplasia in Pediatric and adult population with histologically documented pure red cell aplasia were collected from the HIS records for 8 years from 2017 to 2023. Various causes and conditions coexisting with pure red cell aplasia were studied.

Result

Total 30 patients were diagnosed as Pure red cell aplasia in Pediatric and adult population in 8 years.The age group ranges from 3 months to 68 years old. Male to female ratio is 1:1. Varous conditions seen associated with pure red cell aplasia. One patient associated with T - Large granular lymphocytic leukemia, one with Downs phenotype and thalassemia, one with autoimmune hemolytic anemia and one with Thymoma. One patient was diagnosed during staging marrow for neuroblastoma and other during staging marrow for burkitt lymphoma.

Conclusion

Bone marrow plays a crucial role in diagnosing pure red cell aplasia. Identifying the condition early helps in addressing its root causes such as viral infections, autoimmune disorders, malignancies and reduces the risk of severe anemia and related complications, ultimately enhancing patient outcomes and well-being.

Benign Hematology - Clinical (BHC) OP-BHC-48

Identification of Parvovirus B19 Infection in Paediatric Acute Lymphoblastic Leukaemia Patients Undergoing Chemotherapy.

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Introduction

Parvovirus B19 is known to cause aplastic crises, particularly in immunocompromised populations such as paediatric patients undergoing chemotherapy for acute lymphoblastic leukaemia (ALL). This study aims to investigate the incidence and implications of early detection of Parvovirus B19 infection in this vulnerable cohort.

Aims & Objectives

To identify and document clinical prodrome and laboratory findings of Parvovirus B19 in paediatric patients with ALL on chemotherapy.

Materials & Methods

A retrospective data analysis was conducted over fifteen months for paediatric ALL patients. Total eighty-three bone marrows were screened for ALL patients during this period. Sixteen were newly diagnosed cases and sixty-seven were the follow up cases at various phases of chemotherapy. Complete blood count and Bone marrow aspirate and biopsy findings were reviewed. Clinical details, laboratory results including PCR and serological testing for Parvovirus B19, and treatment responses were analysed. Descriptive statistics was utilized to summarize findings.

Result

Four cases of Parvovirus B19 infection were identified among the sixty-seven paediatric patients receiving chemotherapy for ALL. Clinical manifestations included fatigue, anaemia, and fever, with laboratory findings confirming Parvovirus B19 infection. The laboratory findings showed reduced Haemoglobin concentration, reticulocytopenia, marked erythroid suppression in the marrow with occasional large proerythroblasts. Further testing for Parvovirus PCR or serological testing for IgM was positive for these cases. The management strategies employed for these patients included supportive care with blood transfusion, intravenous immunoglobulins and adjustments to chemotherapy protocols.

Conclusion

Erythroid suppression in the marrow aspirate may get overlooked as an effect of chemotherapy. The identification of Parvovirus B19 in bone marrow in paediatric patients with acute lymphoblastic leukaemia on chemotherapy underscores the need for heightened awareness and monitoring for viral infections in this population. These findings underlines the significance of a detailed clinical evaluation, and laboratory profile associated with Parvovirus B19 infection. It also highlights the importance of high degree of suspicion for an early detection of these cases in patients on chemotherapy. It is necessary to do further studies to explore preventive measures and treatment adaptations to optimize patient outcomes.

Benign Hematology - Clinical (BHC) OP-BHC-49

The Clinical Utility of Neut-X And Neut-Y in the Diagnosis and Identification of Sepsis

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Introduction

Sepsis is a critical, life-threatening response to infection, resulting in over 11 million deaths annually, highlighting the urgent need for timely and accurate diagnosis. Conventional diagnostic methods, such as blood cultures and biomarkers like procalcitonin (PCT) and C-reactive protein (CRP), are often constrained by lengthy processing times and low specificity. Recent advances in hematology have identified two promising automated neutrophil parameters, Neut-X and Neut-Y, which represent cellular complexity and nucleic acid content of neutrophils rspectively

Aims & Objectives

This study the diagnostic value of Neut-X and Neut-Y in diagnosing sepsis, evaluate their sensitivity, specificity and diagnostic accuracy and to compares their performance to traditional biomarkers like procalcitonin, lactate, and C-reactive protein.

Materials & Methods

80 participants were included in the study, 40 adults with suspected sepsis based on Sepsis-3 criteria, following the Surviving Sepsis Guidelines and 40 healthy controls. Blood samples were collected to identify Neut-X and Neut-Y parameters. Biomarkers such as procalcitonin, lactate, and C-reactive protein, were also measured. Sensitivity, specificity, and diagnostic accuracy of Neut-X and Neut-Y were statistically analyzed in comparison to traditional biomarkers.

Result

For Neut-X, the median value was 334 and it demonstrated a P-value of <0.0001 and an Area Under the ROC Curve (AUC) of 0.902, with a sensitivity of 92.5% and specificity of 77.5% at a cut-off of >325. Neut-X achieved a diagnostic accuracy of 85%. Neut-Y , with a median value of 707, exhibited an AUC of 0.984, 95% sensitivity, and 92.5% specificity at a cut-off of >689, resulting in a diagnostic accuracy of 93.75%.

Conclusion

Neut-X and Neut-Y exhibited strong diagnostic potential for sepsis, with Neut-Y showing superior accuracy. These biomarkers can effectively complement traditional markers,to provide a robust ancillary diagnostic tool in the armamentarium of sepsis diagnosis.

Benign Hematology - Clinical (BHC) OP-BHC-50

Outcome Assessment of Phenotype Matched Packed Red Blood Cell (PRBC) Transfusion in Thalassemia Patients, in Relation to Alloantibody, Autoantibody Formation and Transfusion Requirement

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Introduction

Thalassemia (βeta / E-βeta) affects 2-3% of Eastern-Indian population. This huge health burden is managed by transfusion due to paucity of curative treatment. Rate of alloantibody (4-50%) & autoantibody (10-30%) formation in thalassemia patients following usually matched RBC transfusion is documented and its consequences are of great concern.

Aims & Objectives

- To estimate the presence of allo & autoantibody in previously diagnosed patients receiving usually matched RBC transfusion and in newly diagnosed receiving phenotypically-matched RBC transfusion.
- To assess transfusion requirement & iron-overload in previously diagnosed patients.

Materials & Methods

Total 81cases enrolled into 2 groups. Group-1: 41 previously diagnosed patients on usually matched RBC transfusion, Group-2: 40 newly diagnosed patients on phenotypically-matched RBC transfusion.

Post-enrolment both groups received phenotypically-matched RBC transfusion for 6 months.

Baseline Hb, direct Coomb's test for autoantibody detection, indirect Coomb's test for alloantibody screening, specific antibody identification by 11 cell panel kit. Extended RBC phenotype detected by commercially available kit.

Result

Group 1 - alloantibody screening positive-17%, DCT positive at baseline-9.8%. Alloantibody positive patients developed significant erythrocyte alloantibodies particularly against anti-C (40%), anti-c (20%), anti- E (20 %), anti-e (20%), anti-jkb (20%)

- After 6 months of enrolment 2.4 % were allo and autoantibody positive.
- Mean transfusion requirement 6 months before & after enrolment 8.93±5.84 and 6.47±4.13 respectively (p<0>
- Mean Hb 6 months before & after enrolment 6.77±1.18 and 7.43±1.07 respectively (p<0>
- Mean ferritin 6 months before & after enrolment 1465.58±872 & 1164.95±625.52 (p=0.004).

Group 2-

- Alloantibody screening positive-5.4% and no DCT positive cases at baseline. Alloantibody positive patients developed significant erythrocyte alloantibodies (50%) particularly against anti -c and e.
- After 6 months of enrolment, no alloantibody & autoantibody detected.
- Mean Hb at baseline and 6 months after enrolment 6.4± 1.02 & 7.77±1.19 respectively (p=.016).

Conclusion

Phenotype matched RBC transfusion & pretransfusion screening is cost effective, feasible approach needs to be ensured when transfusion strategy is planned for all thalassemia patients irrespective of their antibody status.

Benign Hematology - Clinical (BHC) OP-BHC-51

Unlocking Hope : Utility of Emicizumab in Acquired Hemophilia

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Introduction

Acquired haemophilia-A (AHA) is a rare, life-threatening bleeding disorder caused by autoantibodies against factor VIII. Standard treatments include bypassing agents, recombinant-FactorVII, and immunosuppressants, but access to these agents can be difficult. Emicizumab, a bispecific antibody that mimics FVIII, offers a promising alternative.

Aims & Objectives

To describe the clinical presentation, therapeutic responses, and clinical outcomes in patients with AHA with Emicizumab.

Materials & Methods

We conducted a retrospective analysis of adults with AHA (2022-2024), documenting clinical presentations, coagulation profiles, FVIII and inhibitor levels, treatments administered, and evaluations for secondary causes.

Result

Five patients were identified with a median age of 50 years (range: 43–76) with male preponderance (Males-4; Females-1). Four presented with spontaneous intramuscular hematomas and generalised ecchymosis; one had recurrent hemarthrosis (Pt#3). During the initial evaluation, prolonged aPTT led to FVIII and inhibitor testing. Baseline FVIII levels were <1>Four received upfront Emicizumab at 3 mg/kg; one received 1.5 mg/kg(Pt #5).

Another patient, facing financial constraints with no clinicalresolution, received 1.5mg/kg in week two (Pt #4). Additional doses were needed for only one patient after two weeks (Pt#2). All received Prednisolone (1mg/kg) and Rituximab (375mg/m² weekly for four doses), except one who succumbed (Pt #5-one dose) and another who received two doses (Pt#4). Three patients required PRBC transfusions. PET-CTscans ruled out malignancy, except for one with a pylorus growth who succumbed(Pt #5).

Primary-AHA was considered in three patients(Pt#1, Pt#2, Pt#3) while secondary-AHA was identified in two(IgA-nephropathy-(Pt #4) and Rheumatoid-Arthritis(Pt #5).Improvement in Factor VIII levels to safe level was achieved within one week(except-Pt #4), with no recurrent bleeding during median 60-day follow-up, although one patient died(Pt #5). Factor-VIII levels recovered to 10% two weeks post-treatment and normalised at one month.

Conclusion

Our experience indicates that Emicizumab can be considered as an alternative to achieve hemostasis in AHA patients where access to bypassing agents is difficult.Further studies are warranted with larger cohorts to refine treatment protocol further.

Table 1: Patient Details, Treatment Outline, Factor VIII, and Inhibitor Levels

Sl No	Baseline FVIII clot based assay (IU/DL)	Baseline Inhibitor titre (BU/DL)	Treatment	Week 1 FVIII Level	Week 2 FVIII Level	Week 3 FVIII Level	Week 4 FVIII Level	Week 5 FVIII Level	Week 6 FVIII Level
	Clot-based assay			Chromogenic assay					
Pt #1	<1	35.21	*1, *2,*3	4.7	8.6	28	246	64	379
Pt #2	<1	460	*4, *2,*3	18.6	38	-	-	-	51
Pt #3	<1	4096	*1, *3,*5	-	-	-	108	-	-
Pt #4	1.3	108	*1, *2,*3	-	97	-	-	-	81
Pt #5	<1	435	*1, *2,*3	12.7	-	-	-	-	-

*1 Emicizumab - 3 mg/kg (Week 1)
*2 Rituximab - 4 doses(Weekly once) (Except Pt #5 - 1 dose - Succumbed)
*3 Prednisolone - 1mg / kg (Except Pt #3 - 0.5mg/kg)
*4 Emicizumab - 3 mg/kg +Repeat dose- 1mg/kg 2 weeks later
*5 Rituximab - 2 doses

Pt - Patient

Benign Hematology - Clinical (BHC) OP-BHC-52

High-Dose Dexamethasone with Romiplostim as Frontline Therapy in Acutely Presenting ITP: A Step Forward in Enhancing Response Rates and Quality of Life

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Introduction

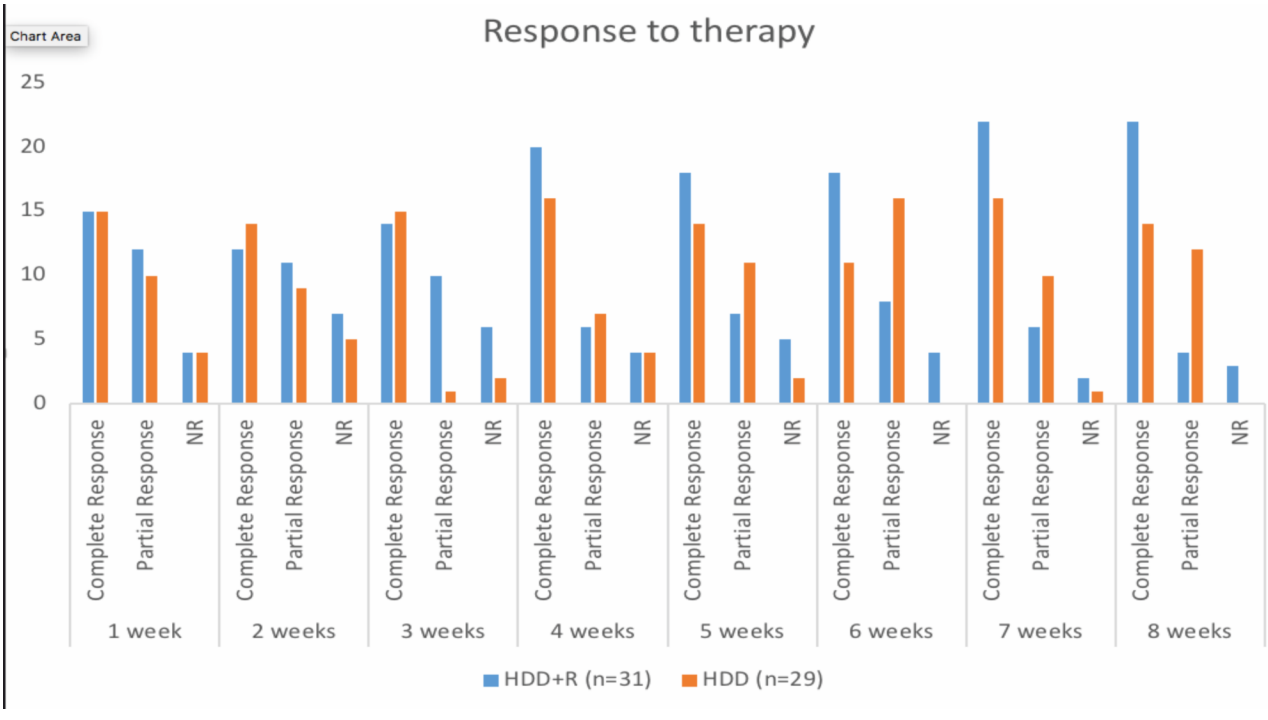
Immune thrombocytopenia (ITP) is an autoimmune disorder characterized by reduced platelet counts due to increased platelet destruction and impaired production. High-dose dexamethasone (HDD) and thrombopoietin receptor agonists (TPO-RA) like romiplostim are established treatments for ITP. However, limited studies have evaluated their efficacy as first-line therapies in combination versus monotherapy. This study aims to compare the efficacy of HDD plus romiplostim against HDD alone in the management of acute ITP, focusing on response rates, steroid-sparing benefits, and impact on patient quality of life.

Aims & Objectives

To assess the therapeutic outcomes, response rates, side effect profiles, and Health-Related Quality of Life (HRQoL) of HDD with and without romiplostim. Additionally, the study evaluates the impact of these treatment modalities on steroid use and the quality of life (QoL) of ITP patients.

Materials & Methods

A prospective observational study was conducted at IMS and SUM Hospital, Bhubaneswar, Odisha, involving 60 patients with acutely presenting ITP. Participants were categorized into two groups: those receiving HDD with romiplostim and those receiving HDD alone. Primary endpoints included initial response rates, complete response (CR), partial response (PR), and sustained response (SR). Response rates were evaluated at weeks 6 and 8, with a focus on reducing steroid use and HRQoL assessment. Secondary endpoints involved the correlation of laboratory parameters with clinical outcomes and treatment impact on QoL



Result

The HDD + romiplostim group demonstrated significantly higher response rates at both week 6 (p=0.035) and week 8 (p=0.028) compared to the HDD alone group. Patients treated with the combination therapy required lower cumulative steroid doses, achieving faster and more sustained CR with reduced steroid-related adverse events. Importantly, the addition of romiplostim significantly improved HRQoL scores compared to HDD monotherapy, highlighting the dual benefit of better disease control and enhanced patient well-being. No significant differences were observed in overall side effect profiles between the groups, although the frequency of adverse events was lower in the combination therapy group.

Conclusion

The combination of high-dose dexamethasone and romiplostim resulted in superior response rates at weeks 6 and 8 with statistically significant improvements compared to dexamethasone monotherapy. This combination not only reduced the need for steroids but also led to significantly better Health-Related Quality of Life outcomes, improving patient experiences by achieving better response rates with fewer adverse effects. These findings support the use of HDD plus romiplostim as a frontline approach in acute ITP to optimize both treatment efficacy and quality of life.

Benign Hematology - Clinical (BHC) OP-BHC-53

Clinical Profile and Laboratory Parameters of Paroxysmal Nocturnal Hemoglobinuria

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Introduction

Paroxysmal Nocturnal Haemoglobinuria (PNH) is a chronic, progressive, life-threatening, rare, multi-systemic disease, developing because of somatic mutation of hematopoietic stem cell, characterized by clonal, complement-mediated intravascular hemolysis.

The diagnosis of PNH can be delayed due to varied clinical manifestations which increases the risk of mortality and morbidity. Therefore, early diagnosis is crucial for preventing morbidity and reducing mortality risk.

Aims & Objectives

Primary: To study the clinical and hematological profile of paroxysmal nocturnal hemoglobinuria.

Secondary: To study the association between clone size and its presentation and prognosis.

Materials & Methods

This study is a retrospective and prospective analysis of the clinical characteristics and laboratory parameters of patients identified with PNH positive clones using FLAER-based flow cytometry (Three laser eight color BD FACS CANTO instrument) conducted in Haemato-Oncology department of Mazumdar Shaw Hospital from January 2019 to April 2024.

Result

The study includes 40 patients, majority of them were males 31(77.5%) with male to female ratio was 3.4:1. The most common subtypes were subclinical PNH (55%) followed by PNH with bone marrow failure (25%), and Classical PNH (20%). Out of 40 cases, 19 (47.5%) had a larger PNH clone, 14 (35%) had a medium clone, and 7 (17.5%) had a small clone.

Anemia and fatigue were the most common presentations. Two patients (5%) had a history of thrombosis at baseline. At the end of 6 months, 7(17.5%) had expired, 10(25%) were lost to follow-up, 12(30%) became transfusion-independent and 11(27.5%) were transfusion dependent.

Out of the remaining 23 patients, 10 patients had PNH-related complications.

Conclusion

The presence of a large clone size in this study aligns with the findings from other studies. Detecting PNH clone size is significant in identifying complications at the earliest.

Benign Hematology - Clinical (BHC) OP-BHC-54

Rare But Real; Insights into a Case Series on Shwachman Diamond Syndrome

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Background

Shwachman-Diamond syndrome is a rare inherited disorder with predominantly autosomal recessive inheritance pattern. It typically presents with pancreatic exocrine insufficiency, bone marrow dysfunctions and skeletal abnormalities. We report 3 cases of Shwachman- Diamond syndrome having varying presentations.

Case Presentation

1. 11-month-old with bicytopenia i.e. anemia and persistent neutropenia.
2. 6-year-old boy with short stature diagnosed with central hypothyroidism with growth hormone deficiency at 1 year of age. Child was referred due to neutropenia
3. 11-year-old with history of failure to thrive and loose stools since 1-year of age and had gradually progressive liver cirrhosis. He also had history of repeated hospital admission for multiple infections since 4-years of age. His serial CBCs showed anemia evolving to neutropenia followed by pancytopenia at current presentation.

Diagnosis

In the first case, the bone marrow aspirate was normocellular and negative for parvovirus. The skeletogram displayed dense metaphyseal bands at the distal femur. Stool examination showed fat globules. These symptoms suggested Shwachman-Diamond Syndrome (SDS), which genetic workup confirmed.

In the second patient, the bone marrow examination showed a leftward shift in the myeloid series with a scarcity of mature neutrophils. Genetic testing eventually identified a heterozygous SBDS gene mutation consistent with an autosomal recessive inheritance pattern.

In the third patient, MDCT of the abdomen revealed a cirrhotic liver, dilated portal and spleen veins, and pancreatic lipomatosis. Genetic analysis uncovered a compound heterozygous SBDS gene mutation and TP53 AD inheritance. MDS cytogenetics indicated deletions on chromosome 5q and 13q.

Treatment

In the first two cases, the administration of granulocyte-stimulating factor was recommended to address the neutropenia, and pancreatic enzyme replacement therapy was initiated with thorough monitoring. A bone marrow transplant was proposed as a curative approach.

For the third case, a multidisciplinary team convened in the presence of both parents, and it was determined that pursuing palliative care was the most suitable approach under the circumstances.

Follow-up

Close monitoring is necessary to detect the progression to myelodysplastic syndromes. Hematopoietic stem cell transplantation may be considered with the intention of curing the condition.

Conclusion

Shwachman-Diamond syndrome is a rare, multisystemic disorder with gradual symptom evolution. Our case series highlights the heterogenous nature of the disorder and the diagnostic challenges it poses. Genetic testing with clinical correlation confirms the diagnosis in most cases.

In conclusion, a high index of suspicion followed by timely referrals and multidisciplinary approach is key to improving outcomes in children. Given the progressive nature of hematological abnormalities, regular CBCs and bone marrow examination are crucial for long term management.

Benign Hematology - Clinical (BHC) OP-BHC-55

Experience of low dose first line and second line ITI in Severe Hemophilia A patients with Inhibitors from a single centre in India

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Introduction

In developing nations the care for Hemophilia A patients, particularly the severe phenotype is often distraught with severe roadblocks, like timely universal availability of Factor VIII concentrates, compliance, difficult venous accesss, particularly in pediatric population.

However, one aspect, that is the development on neutralizing antibodies to exogenous Factor VIII concentrates, leading to loss of efficacy, is a particular unique problem, which adds to the economic burden, both to the patients and the healthcare system.

Aims & Objectives

In this study 15 patients diagnosed with Severe hemophilia A and inhibitor, were analysed for outcome of Immune Tolerance Induction with 1st line ITI (low dose FVIII at 50U/kg twice weekly) followed by 2nd line ITI using Rituximab at 375mg/m2 iv once weekly for 4 weeks.

The Inhibitor titre was measured using Bethesda assay.

Materials & Methods

Prospective observational study

15 patients suffering from Severe Hemophilia A with Inhibitor, who were undergoing Immune Tolerance Induction with low dose FVIII (50 U/kg), twice a week , were analyzed for Inhibitor status at the end of 12 months , using Bethesda Assay.

Those who had persistence of Inhibitor , were further treated with 2nd line ITI , Rituximab at 375mg/m2 iv once a week for 4 weeks. Inhibitor status was measured at the end of 6 weeks and every 2 weeks thereafter for 4 such events.

Result

Out of n=15 patients, n=3 (20%) patients became FVIII Inhibitor negative after 1st line ITI. n=2(13.3%) patients were still on their 1st line ITI. 2nd line ITI was administered to n=4 (26.6%) patients , of which n=1 patient became Inhibitor negative after 1 year 3 months. Rest n=3 patients on 2nd line ITI had persisting positive Inhibitor titres at the end of 6 weeks. n=6 (40%) patients did not follow up for 2nd line ITI.

Median age of diagnosis of Severe Hemophilia A was 12 months; (range 04 months to 37 years). Median interval between the diagnosis and start of prophylaxis with rFVIII was 36 months; range(0-120 months). Median duration between starting prophylaxis and detection of inhibitor was 2.5 months;(range 02-132 months). Average number of exposures to rFVIII concentrates was 24; (range 16-224). Median interval between detection of inhibitor and starting 1st line ITI was 05 months; (range 01-50 months).

Conclusion

Despite the issue regarding compliance of patients, Severe Hemophilia A with Inhibitor, can be successfully managed using low dose FVIII ITI for a minimum of 12 months followed by 2nd line ITI (Rituximab), if 1st line therapy fails.

Benign Hematology - Clinical (BHC) OP-BHC-56

Comparisons of Reticulocyte Parameters between Neonates of Gestational Diabetic Mothers and Healthy Neonates born to Mothers with Uncomplicated Pregnancy

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Introduction

Reticulocyte Parameters are an early indicator of iron deficiency anemia. The presence of iron deficiency can create a diagnostic dilemma in neonates for anemia evaluation. Here we analyzed the effect of reticulocyte parameter in neonates of gestational diabetic mother for its early diagnosis

Aims & Objectives

Comparision of reticulocyte parameters between neonates of gestational diabetic mothers and healthy neonates born to mothers with uncomplicated pregnancy.

Materials & Methods

This is a prospective case control study conducted for a period from March 2023 to August 2024. 30 Cases of neonates of gestational diabetic mothers were taken as cases and 58 cases of neonates of uncomplicated pregnancy were taken as controls. All the hematological parameters taken from extended CBC, reticulocyte parameters were analyzed. Statistical analysis was done.

Result

Age ranges from 1 day to 28 days with the mean of 2.8 ± 1.2 days.Hb ranges from 7.7g/dl to 21.5g/dl with a mean of 17±3.4g/dl.Retic% 5.33±1.57, absolute retic count of 0.34 ±0.27, immature reticulocyte fraction 36.3±11.2 of cases showed a significant correlation with controlled cases, having P value 0.00,0.02 and 0.03 respectively. However, there is no significant correlation between Hb values and ret-Hb having p value of 0.3 and 0.71respectively.

Conclusion

Hemoglobin level is significantly low in neonates of gestational diabetic mothers. Reticulocyte is a useful parameter to suspect early anemias in neonates of gdm, as a result early treatment can be provided precisely in due time. Retic %, ARC, IRF could be used as screening test for neonates for iron deficiency.

Benign Hematology - Clinical (BHC) OP-BHC-57

Hematological Profiles in Gilbert Syndrome : Increased Hemoglobin and Cardiometabolic Insights

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Introduction

Gilbert syndrome (GS) is a prevalent inherited condition characterized by lifelong mild unconjugated hyperbilirubinemia without hepatocellular dysfunction or hemolysis. It results from a polymorphic (TA) dinucleotide insertion in the UGT1A1 gene promoter, leading to a homozygous A(TA)7TAA state. Compared to the wild-type A(TA)6TAA allele, this variant reduces uridine diphosphate-glucuronosyltransferase (UGT) enzyme activity to approximately 30% of its normal level. GS is associated with a reduced risk of metabolic syndrome, non-alcoholic fatty liver disease (NAFLD), endometrial cancer, Hodgkin lymphoma, and cancer-related mortality.

Aims & Objectives

Aim: To study the hemogram parameters across individuals with and without Gilbert's syndrome and assess its implications in anemia and cardiometabolic health.

Objectives:

1. To assess the hemogram parameters of individuals with GS in comparison to healthy controls
2. To examine the relationship between the hematological profile in GS and its potential protective effects

Materials & Methods

We analyzed hemogram data from 300 individuals with GS (262 males, 38 females), confirmed via direct DNA sequencing of the UGT1A1 gene promoter. Participants aged <14 years were excluded, as well as those with reticulocytosis ≥3.0%, β-thalassemia trait, symptomatic hemoglobinopathies, or significantly abnormal leukocyte or platelet counts (TLC <2.0 or >20.0, platelets <80 or >500 x10^9/L). A separate cohort of 163 healthy non-GS controls (105 males, 58 females), confirmed through DNA sequencing, was also evaluated.

Result

Males with GS showed significantly higher levels of hemoglobin, hematocrit, red blood cell (RBC) count, mean corpuscular volume, mean corpuscular hemoglobin, and red cell distribution width, along with lower reticulocyte, total leukocyte and platelet counts, compared to non-GS males (Table 1). Females with GS exhibited higher Hb and RDW, with lower reticulocyte and platelet counts. Anemia, based on W.H.O. cut-offs, was present in 13.0% of GS males and 44.7% of GS females, compared to 47.6% of non-GS males and 46.6% of non-GS females (p <.0001 for males, p = .8615 for females).

Table 1: Hemogram values in individuals with and without Gilbert syndrome. All values except for the frequency of anemia are expressed in mean±SD (range).

Parameter	GS Males *(n=262)*	Control Males *(n=105)*	p-value (males)*	GS Females *(n=38)*	Control Females *(n=58)*	p-value (females)*
Age (years)	29.3±12.2 (14-80)	33.9±8 (23-58)	***<.0001***	33.9±12.1 (17-68)	35.4±9.9 (23-59)	.524
Hb (gm/dL)	14.3±1.2 (10.8-18.1)	13.2±1.1 (11.4-16.1)	***<.0001***	12.5±1.1 (11.1-15)	12.1±0.7 (10.7-14.7)	***.031***
Hematocrit (%)	45.1±3.6 (39.6-58.7)	42.3±3.3 (36.1-50)	***<.0001***	39.8±3.1 (34.9-46.8)	39.0±2.2 (34.7-43.9)	.192
RBC count (x10^12/L)	4.9±0.6 (3.11-6.77)	4.7±0.4 (3.84-5.54)	***<.0001***	4.4±0.4 (3.58-5.38)	4.3±0.3 (3.76-5.13)	.203
Anemic% (WHO cut-off's)	13.0% (34/262)	47.6% (50/105)	***<.0001***	44.7% (17/38)	46.6% (27/58)	0.8615
MCV (fL)	93.2±8.2 (68.5-120.8)	90.9±3.9 (83.4-102.7)	***.007***	91.9±5.9 (76.7-111.8)	91.5±4 (82.5-103.1)	.727
MCH (pg)	29.7±2.9 (18.1-39.8)	28.3±1.4 (26.1-31.4)	***<.0001***	29.0±2.3 (24.7-36.5)	28.5±1.3 (26.2-31)	.166
MCHC (gm/dL)	31.8±1.6 (19.2-34.5)	31.1±1.14 (28.5-33.6)	.202	31.5±1.1 (29.4-33.7)	31.1±1.1 (28.6-33.5)	.092
RDW-CV (%)	15.3±2.6 (12.1-40.9)	14±1.1 (28.5-33.6)	***.002***	15.5±1.7 (13-19.7)	14.2±1 (12.1-17.1)	***<.0001***
Reticulocyte count (%)	1.2±0.5 (0.2-3)	1.5±0.4 (0.83-2.37)	***<.0001***	1.2±0.5 (0.33-2.41)	1.6±.5 (0.86-2.39)	***<.0001***
TLC (x10^9/L)	6.8±1.9 (2.5-16.7)	7.4±1.7 (4.5-11.1)	***.006***	7.5±2.3 (2.4-12.2)	7.8±1.9 (4.5-10.9)	.618
Platelet count (x10^9/L)	187.8±63.9 (82-366)	243.8±61.5 (136-431)	***<.0001***	201.3±53.6 (102-316)	244.8-67.6 (138-396)	***.001***

**p-values from unpaired T-test (2-tailed) for all parameters, except anemic% by $\chi 2$ test. Significant p-values in bold italics.*

Conclusion

This is the second and largest study to date demonstrating increased hemoglobin levels in individuals with GS. The inheritance of GS appears to confer protection against anemia in males. The elevated red cell mass in GS may contribute to the observed unconjugated hyperbilirubinemia, while lower leukocyte and platelet counts might offer insights into the protective effects of GS against cardiovascular and metabolic diseases.

Benign Hematology - Clinical (BHC) OP-BHC-58

Optimizing Large Language Models for Clinical Decision Support in Hematology : A Comparative Study of Customization Approaches

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Introduction

Various customization and optimization strategies have been employed to improve the output quality of Large Language Models (LLMs) in clinical settings, as Artificial Intelligence (AI) and Machine Learning (ML) hold significant promise for enhancing clinical decision-making in healthcare. A major limitation of these technologies is the potential for generating unreliable or inaccurate information, often referred to as "hallucinations. This study focuses on evaluating different approaches to customizing LLMs, specifically, a Retrieval-Augmented Generation (RAG) based model and other custom-built models to enhance their performance in real-time clinical decision support systems within hematology.

Aims & Objectives

To compare and assess 4 LLMs using different customization and optimization approaches applied for generating accurate and reliable responses in clinical decision support systems, with a focus on improving outcomes in hematology.

Materials & Methods

A RAG-based model, termed Haematology Clinical Decision Support System (CDSS) was built which integrated a meticulously annotated knowledge base with comprehensive guidelines and illustrative examples embedded into the prompt architecture. Other evaluated models included ChatGPT o1 (with Reasoning)Model, ChatGPT 4 Turbo, and a custom-built Google Gemini Advanced model. A questionnaire was devised, encompassing a range of clinical hematology scenarios with varying complexities. Each model was presented with this questionnaire, and their responses were anonymized. A panel of subject matter experts evaluated the responses across multiple categories, including accuracy, personalization, patient safety, and ethical considerations.

Result

Individual scores for each model were recorded, and comprehensive statistical analyses were conducted to compare the performance of the different models along with evaluation using a Likert scale through a scoring tool for LLMs (developed by bainxai). The analysis revealed that the Hematology CDSS, enhanced with Graph RAG methodology, achieved the highest overall scores across all evaluated parameters. . The ChatGPT with Reasoning Preview Model also demonstrated superior performance compared to the other LLMs, showcasing enhanced reasoning capabilities that contributed to more accurate and personalized responses. Statistical analysis indicated that the Hematology CDSS achieved the highest mean score of 8.20(out of 10) with 95% CI and a standard deviation of 0.33. One-Way ANOVA revealed significant differences in mean scores between models across all evaluated categories ($p < 0.001$).

Conclusion

These findings suggest that models augmented with domain-specific knowledge and enhanced reasoning abilities are more effective for aiding clinical decision making in hematology.

Benign Hematology - Clinical (BHC) OP-BHC-59

A Study of Endocrinological Dysfunction in Transfusion - Dependent Thalassemia Patients with Iron Overload

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Introduction

Transfusion-dependent thalassemia (TDT) is associated with a wide range of complications, primarily arising out of a huge transfusion load, which varies from cardiomyopathy to endocrinopathies and hepatic dysfunction. Common endocrinological abnormalities associated with TDT include short stature, hypogonadism, hypothyroidism, delayed puberty, diabetes, and hypoparathyroidism. The data on this subject are scarce and heterogeneous in our country.

Aims & Objectives

The primary objective of this study was to describe endocrinological dysfunction in TDT patients with a cumulative transfusion load of more than 50 ml/kg body weight. The secondary objectives were to study the correlation of endocrinological dysfunctions (if any) with cumulative transfusion load, serum ferritin levels, and duration of Iron chelation.

Materials & Methods

A cross-sectional observational-analytical study was conducted in a tertiary health care center in Western Maharashtra. The study was conducted from Oct 2022 to June 2024. Patients diagnosed with Transfusion-dependent females and males with thalassemia (of any genotype) with a history of at least five years of chronic transfusion (defined as cumulative transfusion load of more than 50 ml/kg body weight) were included in the study. Pregnant females or lactating women were excluded from the study. The endocrine evaluation was done in an approved lab. The assessed parameters were analyzed using JMP ver 17.0.0.

Result

Ninety patients were selected for the observational study, of which 62% were male and 38% were female. The participant's mean age was 19.4y, ranging from 12 to 35. Assessment of endocrinological dysfunctions in TDT patients revealed that 50% of participants were short for age (with the mean height of all the participants being 151.75 cm), 36% had GH deficiency, 55.5% had clinical hypogonadism, 20% of male and 12% of females participants had biochemical evidence of hypogonadism, 13% had subclinical hypothyroidism, 6% had hypothyroidism, 2% had hyperthyroidism, 11% of patients had biochemical evidence of hypocortisolism, 22% of participants were Pre-diabetic, 7% were diabetic, and rest were euglycemic.There was a statistically significant correlation between serum ferritin levels and HbA1C levels ($p<0$)

Conclusion

Transfusion-dependent thalassemia is associated with debilitating morbidity and mortality secondary to significant endocrinological dysfunction despite chelating agents for iron overload.

Benign Hematology - Clinical (BHC) OP-BHC-60

Impact of Hemoglobin Content on Post - Transfusion Outcomes in Adult Hemato - Oncological Patients

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Introduction

Transfusion medicine is critical in managing hemato-oncological patients, with 30% to 100% experiencing anemia necessitating packed red blood cell (PRBC) transfusions. This study evaluated the efficacy of RBC transfusions by correlating post-transfusion hemoglobin increments with the hemoglobin content of PRBC units in adult hemato-oncological patients, aiming to standardize transfusion practices.

Aims & Objectives

The study aimed to assess the increments in hemoglobin concentration relative to the hemoglobin content of the transfused red cell unit and identify influencing factors.

Materials & Methods

A prospective observational study was conducted in a tertiary care center in Central India after obtaining ethical approval. Hemodynamically stable patients over 18 years with hemato-oncological disorders requiring RBC transfusions were enrolled. Pre-transfusion hemoglobin levels were assessed, and Coombs tests were performed to rule out alloantibodies. Hemoglobin content of cross-matched PRBC units was calculated, and post-transfusion levels were assessed within 24 hours. Data were analyzed using SPSS.

Result

A total of 219 patients were included in the study, with a mean age of 41.30 ± 16.10 years. Pre-transfusion hemoglobin levels ranged from 2.06 to 8.93 g/Dl (mean 6.27 ± 1.27 g/Dl). Post-transfusion levels significantly increased to a mean of 7.51 ± 1.30 g/Dl. The mean increment was 1.25 g/Dl, lower than the targeted 1.68 g/Dl. A strong correlation was found between hemoglobin increment and the hemoglobin content of transfused units ($p < 0.001$).

Conclusion

The study highlights the significant relationship between the hemoglobin content of the transfused PRBC units and post-transfusion increments. Adjusting transfusions based on total blood volume may improve hemoglobin outcomes, while age, gender, and diagnosis did not significantly affect increments. These findings can help optimize transfusion practices in hemato-oncological care

Benign Hematology - Clinical (BHC) OP-BHC-61

Challenges in managing hematological malignancies with tuberculosis : A single - center study

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Background

Patients with hematologic malignancies (HMs) are thought to have a relative risk of tubercular infections that is two to forty times higher than the general population. Patients with HMs are present with different Clinical features in contrast to individuals without any other underlying diseases, making the diagnosis of tuberculosis challenging. Treatment of TB is complicated for these patients because of the many drug interactions between antitubercular drugs, hematological and immunosuppressive therapy.

Aims & Objectives

To determine the atypical clinical features, diagnosis and treatment of TB in HMs.

Materials and Methods

This is an observational study conducted at a tertiary care centre in IMS and SUM Hospital in eastern India from January-2023 and December-2023.

Results

We detected 30 cases of TB over the past year in all types of HMs. Out of 30 patients, 18 (60%) were male and 12 (40%) were female. Most common malignancies associated with TB were acute AML 15(50%) patients, followed by MDS 5 (16.67%); CML 4 (13.33%); ALL 3 (10%); DLBCL 2 (6.67%); and APML 1 (3.33%) cases. A CT-scan of the thorax detected cavitary lesion in 4(13.33%) cases, which was further diagnosed as a PTB. Pleural effusion evaluation was done and suggestive of pleural TB in 3(10%)cases. TB lymphadenitis was detected in 9(30%) cases. MRI-brain detected tuberculoma in 1 (3.33%) case. Disseminated TB was also diagnosed in 2 (6.66%) patients. Azacitidine and Venetoclax combination were given in 15(50%) cases of AML, and Azacitidine alone in 5 (16.67%) cases of MDS. R-CHOP was given in 2(6.67%) cases of DLBCL. Imatinib was given in 3 (10%) cases of CML-CP, and Ponatinib was given in 1(3.33%) case of CML-lymphoid blast crises. All patients received anti-tubercular treatment(ATT). A standard ATT was given to18 patient and 12 patient received a modified regimen due to drug-drug interactions, and adverse effects related to ATT.

Conclusion

We would like to emphasize valuable insights into the clinical characteristics and management strategies for tuberculosis in patients with HMs, especially drug-drug interactions that occur between rifampicin and chemotherapeutic agents used to manage hematopoietic disorders. These insights can reform clinical practice and guide future research.

Benign Hematology - Clinical (BHC) OP-BHC-62

A Diagnostic Predictive Model for Macrothrombocytopenia

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Introduction

Asymptomatic macrothrombocytopenia is an underdiagnosed condition characterized by large platelets and thrombocytopenia, often mistaken for ITP. Misdiagnosis can lead to unnecessary treatments and invasive procedures, so it is crucial to distinguish this entity from other causes of thrombocytopenia.

Aim

This study aims to develop a predictive model to differentiate asymptomatic macrothrombocytopenia from true thrombocytopenia.

Methods

An observational analytical study was conducted on 200 patients, 100 with asymptomatic thrombocytopenia and 100 cases of ITP. Key predictive variables, including MPV, presence of large and giant platelets, differences between automated and manual platelet counts, family history, and retaining repeat value after four weeks were analyzed. Dataset was randomly divided into a training (70%) and a validation sets (30%). Training set was used to train multiple machine learning algorithms, including Support Vector Machine (SVM), Multiple Logistic Regression (MLR), Classification and Regression Trees (CART), Random Forest, and Naïve Bayes. performance of each trained model was evaluated using the validation set based on key metrics, including accuracy, sensitivity, specificity, F1 score, and Area Under the Receiver Operating Characteristic curve (AUC-ROC). Prediction scores were generated using the optimized model's weighted coefficients on the training set. Various thresholds were applied to the prediction scores, and their performance was evaluated using accuracy, sensitivity, specificity, F1 score, and AUC on the validation set.

Results

MLR model performed best among those tested with an accuracy of 88.3%, sensitivity of 93.1%, specificity of 83.9%, F1 score of 88.5%, and AUC of 0.94. Prediction scores were generated using the optimized model's weighted coefficients on the training set on MLR analysis with "Large," "Giant," "Repeat," and "Difference" were identified as statistically significant predictors ($p < 0.05$), and assigned scores of 5, 3, 4, and 3 respectively (Cumulative score 15). Various thresholds were tested on the validation set. At threshold score of 7 accuracy was 83.3 %, sensitivity 93.1%, specificity 83.9%, precision 84.3% and F1 score remained 88.5 %. At this threshold model achieved an Akaike information criterion (AIC) of 58.3 suggestive best fit.

Conclusion

MLR model using simple laboratory and clinical parameters effectively differentiates asymptomatic macrothrombocytopenia from ITP, improving diagnostic accuracy.

Benign Hematology - Clinical (BHC) OP-BHC-63

Assessment of Red cell distribution width (RDW) as prognostic factor in case of Febrile neutropenia

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Introduction

The red blood cell distribution width (RDW) is a parameter, historically used to explain the degree of heterogeneity in the distribution of red cells volume and used for differentiation of types of Anemia. Being a part of the routine automated blood cell counters, RDW can be easily and inexpensively assessed. Recently it has been found that, Increased RDW levels are associated with a higher mortality, which was supposed to be linked with oxidative stress or poor nutritional status.

This study has been done to evaluate the role of RDW as prognostic factor and its correlation with severity and outcome of febrile neutropenia.

Aims & Objective

1. To study the serial variation and its correlation with outcome in Febrile Neutropenia.

2. To find out the correlation between MASCC score and RDW value.

Methodology

Study Center : This study has been done in Department of Clinical Hematology, IHTM (Institute of Hematology and Transfusion Medicine), Medical college Kolkata.

Study Design : This is a prospective, single center based, observational study, conducted between January 2024 to September 2024 (9 months).

Result

Total numbers of 154 patients were included in this study, among which 42 patients expired during study time and 112 patients completed the study. Among all study population, total numbers of male and female were 81 & 31 respectively. Age ranges of the population were between 2yrs to 56 yrs. Total numbers of events were 167. Average duration of recovery of febrile neutropenia was 11 days. Febrile neutropenia was managed with intravenous antibiotics and antifungals according to latest IDSA guideline. This study showed that, level of raised RDW value at onset of febrile neutropenia was negatively associated with outcome of febrile neutropenia.

Conclusion

Our study is the first prospective study which has sequentially monitored and assessed RDW variation with severity and outcome in Febrile neutropenia patient.

Benign Hematology - Clinical (BHC) OP-BHC-64

Insights into Diamond Blackfan Anemia Pathophysiology in Indian Patients with RPL5 and RPL35A gene Deletions

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Background

Diamond Blackfan Anemia is a congenital anemia with pure erythroid hypoplasia, skeletal anomalies, and short stature. The RP gene mutations have been identified to be inherited in Autosomal dominant manner and De novo in few cases. However, in certain cases, the presence of mutations in non-RP genes such as GATA1, EPO, ADA2, and TSR2 adds complexity, turning it into an unsolved puzzle. The pathophysiology of the disease is still unclear and genotype-phenotype correlation in DBA patients is underexplored in India.

Aims and Objectives

1. To carry out molecular characterization in suspected DBA patients and carry out genotype-phenotype correlation
2. To validate the findings by gene expression study

Materials and Methods

The study evaluated two suspected DBA patients using various methods, including clinical history, physical examination, hematological assessment, and biochemical assays. Whole Exome Sequencing was carried out and variant annotation was performed using ACMG guidelines. The gene deletions were confirmed by Multiplex Ligation-dependent Probe Amplification (MLPA) in patients and family members. RNA isolation was carried out from peripheral blood and gene expression analysis was performed via qRT-PCR.

Results

Whole exome sequencing identified RPL5 and RPL35A gene deletions in two patients by copy number variation analysis. The patient with the RPL5 deletion, managed on steroids, presents with short stature, Ostium secundum atrial septal defect (OS-ASD), cryptorchidism, low reticulocytes, low Hb, low RBC count, and raised MCV. With similar hematological features the patient with the RPL35A deletion is transfusion dependent, with mild cardiomegaly, splenomegaly. The eADA activity found to be raised in both the patients. The mutation in both the patients were De novo. Functional assays confirmed altered expression of deleted RP gene along with MDM2, TP53, and GATA1, supporting DBA pathophysiology in both cases.

Conclusion

Our study represents rare large RPL5 and RPL35A deletions in DBA, providing novel insights into the genotype-phenotype spectrum within Indian patients. The distinct clinical profiles and gene expression data, highlight the complex pathophysiology of DBA and offer potential markers for diagnosis and therapeutic intervention.

Benign Hematology - Clinical (BHC) OP-BHC-65

Efficacy of Daily Versus Alternate Day Oral Iron Therapy in Newly Diagnosed Iron Deficiency Anaemia

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Introduction

Iron deficiency anaemia (IDA) is the most prevalent form of anemia worldwide, and it significantly affects development, productivity, and quality of life. The standard therapy is daily oral iron therapy for 3 to 6 months, often guided by estimation of serum ferritin. Daily oral iron therapy is associated with significant gastrointestinal (GI) symptoms, which ultimately leads to poor adherence and failure of intervention.

Aims and Objective

To evaluate

- Efficacy of alternate-day oral iron therapy compared to daily therapy
- GI side effects of alternate-day oral iron therapy compared to daily therapy
- Therapy adherence to alternate-day oral iron therapy compared to daily therapy

Materials and methods

This prospective, longitudinal, intervention study, conducted at the Institute of Haematology and Transfusion Medicine, Kolkata, included 131 patients with newly diagnosed iron deficiency anaemia in the period of January 2023 to May 2024. Then 5 patients were excluded according to exclusion criteria (active blood loss, on anticoagulant therapy and received IV iron). One hundred and twenty-six patients were randomised in daily and alternate-day oral iron therapy (63 patients in each arm). Twenty-nine patients discontinued the treatment. Finally, 97 patients with newly diagnosed iron deficiency anaemia completed the therapy according to protocol, 54 patients on alternate days, and 43 patients on daily oral iron therapy arm. Then patients were followed up for the next 6 months for haemoglobin correction and iron store replenishment.

Result

In the alternate day therapy arm, 11.11% (9 patients) discontinued treatment due to GI side effects, while 31.74% (20 patients) discontinued in the daily therapy arm. By the end of the study, 92.50% of the alternate-day therapy group and 88.83% of the daily therapy group had responded to treatment. Complete response was noted in 62.3% of the alternate- day therapy group and 41.9% of the daily therapy group. Adequate ferritin response was noted in 40% of the alternate-day treatment group and 31.9% of the daily therapy group.

Conclusion

Alternate-day oral iron therapy is as effective as daily oral iron therapy with fewer GI side effects and a significantly lower discontinuation rate.

Malignant Hematology-Clinical (MHC) OP-MHC-1

Thyroid Profile and Molecular Response in Patients of Chronic Myeloid Leukemia (CML) on Tyrosine Kinase Inhibitor (TKI)

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Introduction

Tyrosine kinase inhibitors (TKIs) are a group of drugs that disrupt signal transduction pathways of protein kinases through various modes of inhibition. The approval of the first TKI, imatinib, in 2001 marked a significant advancement in the treatment of chronic myeloid leukemia (CML), leading to the evolution of cancer chemotherapy into the current era of targeted therapy. TKIs are now considered the standard of care for several cancers, with CML being a prominent example where TKIs are the preferred treatment regardless of the stage of the disease.

TKIs function by inhibiting tyrosine kinase enzymes, which can be classified into receptor tyrosine kinases, non-receptor tyrosine kinases, and dual specificity kinases. Currently, the United States Food and Drug Administration (FDA) has approved over 50 FDA TKIs for use. Adverse drug events of TKIs are generally dose-dependent and are associated with specific side effect profiles unique to each drug. Due to similarities in drug targets, different classes of TKIs may produce similar side effects. Common side effects shared by TKIs include cutaneous drug reactions, fatigue, fever, gastrointestinal disturbances, cardiovascular side effects (such as hypertension), and endocrine-related issues like thyroid dysfunction.

CML is a myeloproliferative neoplasm caused by the reciprocal translocation between chromosomes 9 and 22, resulting in the formation of the BCR-ABL1 fusion gene, which drives the disease process. CML represents a rare hematological malignancy with remarkable responses to targeted therapy. TKIs are presently used in the management of CML patients at any stage. There are 6 TKIs approved and in use for CML treatment, categorized into three generations:

1st generation – Imatinib

2nd generation – Dasatinib, Nilotinib, Bosutinib, and Radotinib

3rd generation – Ponatinib

These drugs vary in their pharmacological profiles. Clinical, hematological, cytogenetic, and molecular responses are used to assess the response of CML patients to these drugs and reflect the leukemic burden in these patients.

Aims & Objectives

To study the relationship between thyroid profile and molecular response in patients of chronic myeloid leukaemia on tyrosine kinase inhibitors.

Materials & Methods

Study design: a cross-sectional observation study.

Sample size: 100

Inclusion criteria: Patients of age > 18 years of any gender diagnosed as a case of chronic myeloid leukemia on tyrosine kinase inhibitors for more than 18 months with molecular response (major and deep molecular response).

Exclusion criteria: Patients with pre-existing thyroid alterations, Patients on thyroid hormone supplement therapy or anti-thyroid drugs or any other drug-altering thyroid function test (amiodarone, lithium, selective serotonin reuptake inhibitors, rifampin…. etc.), Patients with nephropathy of any cause, chronic liver illness, Patients on tyrosine kinase inhibitors not in remission.

Methodology: After applying the inclusion and exclusion criteria, eligible patients were included in the study. The recruited patients underwent a detailed history, physical examination, and investigations. Molecular response (MR) was defined according to the European Leukemia Network guidelines – Major Molecular Response (MMR) was defined as BCR-ABL1 IS transcripts less than 0.1%, and Deep Molecular Response (DMR) was defined as BCR-ABL1 IS transcripts less than 0.01%. Both MMR and DMR patients were assessed for thyroid function. The test results were interpreted and then subjected to statistical analysis. Molecular response was confirmed by subjecting the patient to RT-PCR of peripheral blood.

THYROID FUNCTION TEST was done by chemiluminescent microparticle immunoassay.

Result

In our study most of the patients were male and the mean age of the population was 50.4 years, the youngest patient was 26 years old and the eldest was 78 years old. The majority of the patients received imatinib and most of the patients were in deep molecular response. Abnormal thyroid function test was observed in 75/100 patients with hypothyroidism being the most common abnormality (Table 1). Out of 75 patients with abnormal thyroid function tests, 70 were observed to have hypothyroidism. Among these, 37 patients were clinically hypothyroid, with 27 in deep molecular response and 10 in major molecular response. 33 patients were sub-clinically hypothyroid, with 24 in deep molecular response and 9 in major molecular response. Additionally, 5 patients were hyperthyroid, all of whom were in major molecular response. Finally, 25 patients had a normal thyroid profile (Figure 1). Out of 37 patients with clinical hypothyroidism, 7 did not show symptoms, while the remaining 30 did. Among the 33 patients with sub-clinical hypothyroidism, 4 displayed symptoms, and the other 29 were asymptomatic. Additionally, 5 patients were diagnosed with hyperthyroidism, with 4 showing symptoms and 1 being asymptomatic. Notably, 2 out of the 4 hypothyroid patients displayed thyroid eye signs (Figure 2). The results showed a significant association between thyroid function tests and molecular response, specifically deep and major molecular responses. There was a notable correlation between serum TSH level ($p < 0.001$) and free T3 level ($p = 0.047$) with both deep and major molecular responses. In this study, $p < 0.05$ was considered statistically significant (Table 2). In analyzing the thyroid profile alongside the molecular response, a significant association was discovered between hyperthyroidism and both molecular responses, with a p-value of 0.008. Additionally, a significant association was observed between patients with a normal thyroid profile and both molecular responses, with a p-value of 0.013 (table 3).

Conclusion

Our study confirms and extends our knowledge of the tyrosine kinase inhibitor's effects on the thyroid, our study also concludes that thyroid function abnormality produced by TKI's has an association with molecular response attained by patients of CML

Malignant Hematology-Clinical (MHC) OP-MHC-2

Clinical Profile and Outcomes of Hairy Cell Leukemia from Two Centers in India: A Call for Collaborative Research

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Introduction

Hairy Cell Leukemia is a rare B cell hematologic malignancy with excellent survival reported in literature but little data from India.

Aims & Objectives

This study was performed to describe disease characteristics and survival outcomes of patients with hairy cell leukemia from two academic centers.

Materials & Methods

Data was collected retrospectively for patients diagnosed with hairy cell leukemia between January 2018 and June 2024. Clinical and treatment data were extracted. Baseline characteristics, treatment details, and survival outcomes were analysed.

Result

A total of 16 patients (M:F, 15:1) with a median age of 50 years (IQR, 47 to 54) were included. The most common symptoms were fever (30%) and abdominal pain (25%). The median Hb, WBC and platelet counts at diagnosis were 7.85 g/dl (IQR, 6 to 9.4), 2400/ul (1650 to 6950) and 45000/ul (33000 to 62250), respectively. Spleen was palpable in 13 patients, a median of 7 cm below LCM. Immunohistochemistry for DBA44 and Annexin were available for 5 (31%) patients and positive for all. The most common positive markers on flowcytometry were CD20 (93%), CD103 (87.5%), CD25 and CD11c (68.7% each). All patients received Cladribine as initial therapy with a median time of 15 days (IQR, 9-27) from diagnosis to start of therapy. The median time to ANC recovery above 1500/ul was 22 days (IQR, 14-31 days). Nine patients (56.25%) had febrile neutropenia with initial therapy, and possible fungal pneumonia based on imaging was present in two (12.5%) patients. Repeat BM examination was performed in 7 patients, after a median of 107 days (IQR, 96-112) from start of treatment. MRD by flowcytometry MRD was available for seven patients, with median value of 0.2% (IQR, 0.025 to 0.55). Consolidation Rituximab was received by 6 patients. All patients were alive at the end of a median 18 months (IQR 4.5 to 33.5) months of follow up.

Conclusion

Treatment of hairy cell leukemia with Cladribine indicates excellent responses with low rates of infection during treatment. Multi centre data is required to indicate the role of rituximab consolidation, immune reconstitution and long-term risk of infections post treatment.

Malignant Hematology-Clinical (MHC) OP-MHC-3

MGUS Prevalence in Special Populations: Insights from A Large - Scale Community Study from Rural India

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Introduction

Considerable variation has been observed in the prevalence of monoclonal gammopathies across the globe. Although the prevalence of monoclonal gammopathy of undetermined significance (MGUS) has been evaluated in two hospital-based studies in India, no data exist on its prevalence in community-based settings among the rural Indian population.

Aims & Objectives

To determine the prevalence of MGUS in a rural Indian population in a community-based setting.

Materials & Methods

A cross-sectional study was conducted across 66 agrarian villages/hamlets of Western India, spreading over 2299 square miles (sq-mi). Demographic details, medical history, and blood samples were collected after a thorough medical examination. Hemograms and serum protein electrophoresis (SPEP by on-site capillary zone electrophoresis) were performed in all individuals. Serum immunofixation electrophoresis (SIFE) and biochemistry were performed for those with abnormal SPEP graphs. Patients with monoclonal protein on SPEP or SIFE were further assessed for any smoldering/ multiple myeloma features. The data was analyzed using JMP ver. 17.2.0.

Result

A total of 10,024 individuals were screened, and data was analyzed for 9283 individuals. The prevalence of MGUS in the study population was 62 (0.66%) and was 1.79

Conclusion

The prevalence of MGUS in the rural population of Western India is low at 0.66%, rising to 1.79% in individuals over 55 years, predominantly affecting older males, with IgG MGUS being the most common type. The background prevalence appears to be lower compared to the Western (both USA ~3% and European~5%) population

Malignant Hematology-Clinical (MHC) OP-MHC-4

Differences in Perception of Symptom Burden and Treatment Goals Regarding Myelofibrosis in India: Inland Survey Insights

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Introduction

Patients with myelofibrosis (MF) suffer from range of symptoms affecting their quality of life (QoL).1 Discordance in patient-physician perception of disease burden impacts patient outcomes.2 Data on such differences is limited in India and better understanding could enhance patient care.3

Aims & Objectives

This study aimed to identify patient-physician disparities in perception of symptoms and MF treatment goals in India.

Materials & Methods

The INLAND survey was conducted between 7th October to 20th November 2021 in 154 MF patients under the management of 50 hematologists/medical oncologists in India. The survey assessed patient-physician perceptions of symptom severity, in-clinic communication, and MF treatment goals.

Result

HCP and patient perceptions for symptom severity, treatment goals, and satisfaction with management are reported in Table 1.

Table 1. Perception of MF among patients and HCPs (5-point rating scale responses)

	HCPs		Patients	
	Response	Percentage	Response	Percentage
Symptom severity assessment	Proactively asks for symptoms	80%	Believes they are asked proactively about symptoms	50%
	Use MPN-10 Questionnaire	54%	Knew about the MPN-10 Questionnaire	1%
Treatment goals	Better QoL	88%	Better QoL	74%
	Healthy blood count	66%	Healthy blood count	40%
	Anemia management	62%	Anemia management	37%
	Symptom improvement	12%	Symptom improvement	69%
Satisfaction with management and treatment	Involves MF patients in decisions about their treatments	84%	Involves my decisions about MF treatments	99%
	Asked MF patients about their symptoms at every appointment	76%	Were asked about their symptoms at every appointment	97%
	Kept MF patients informed about new treatment options	64%	Were informed about their new treatment options	97%
	Felt that they could listen and address MF patient's concerns	18%	Believed that HCPs listen to and address their concerns	97%
	Prioritize blood counts over symptom management	10%	Believes that HCPs prioritize blood counts over symptom management	91%
	Dissatisfied with the consultation time	6%	Dissatisfied with the consultation time	94%
	Satisfaction with symptom management practices (somewhat satisfied)	68%	Satisfaction with communication on condition and treatment (somewhat satisfied)	80%
	Satisfaction with Treatment and Management of MF (somewhat satisfied)	70%	Satisfaction with Management and treatment of MF (somewhat satisfied)	78%

Symptoms

Both HCPs and patients identified fatigue, abdominal pain, and fever, as prominent symptoms, with fatigue being most reported. Patients also reported bone pain, headaches, psychological distress, and sleeplessness, which significantly impacted their QoL but were not prioritized by HCPs.

Symptom Assessment

A disconnect was noted in symptom assessment between doctors and patients. While 80% of doctors claimed to ask about symptoms proactively, only 50% of patients agreed. Additionally, 54% of doctors reported using tools like MPN-10 questionnaire, but only 1% of patients recalled this. Patients felt that doctors wait for them to raise symptoms, suggesting need for more structured assessments.

Treatment Goals

HCPs viewed successful therapy for MF patients as achieving a good anemic profile, healthy blood counts, and reduced spleen size. In contrast, patients considered symptom improvement as a major success indicator. Regardless, HCP opinion was the key parameter for patients assessing MF treatment success.

Satisfaction with Management

Both HCPs and patients agreed on patients' involvement in treatment decisions, regular symptom check. However, discordance was noted during consultations, between HCPs and patients. Even highly satisfied patients felt follow-up consultations with HCPs weren't enough, with focus on blood counts over symptoms.

Conclusion

INLAND survey findings revealed substantial perceptual differences between physicians and patients regarding symptom burden, assessment and treatment goals. These disparities highlight the necessity for a more comprehensive approach to MF management, emphasizing improved patient-physician communication to align treatment goals and symptom assessment.

Malignant Hematology-Clinical (MHC) OP-MHC-5

Study of Quality-of-Life Assessment in Chronic Myeloid Leukemia Receiving Long Term Therapy with Tyrosine Kinase Inhibitors from A Tertiary care Hospital

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Introduction

Chronic Myeloid Leukemia (CML) is a hematologic malignancy typically managed with long-term tyrosine kinase inhibitors (TKIs).CML is the most common type of leukemia in India, accounting for 30–60% of all leukemia cases. The percentage of patients responding to tyrosine kinase inhibitors (TKIs) varies depending on the type of TKI and the time point at which response is measured .

While these therapies have significantly improved survival rates, their impact on patients' quality of life (QoL) remains a critical concern.

Aims & Objectives

This study aims to evaluate the QoL of CML patients undergoing extended TKI treatment, focusing on physical, psychological, and social aspects.

Materials & Methods

We conducted a cross-sectional study of 402 CML patients currently on TKI therapy for 4years.(JAN2020-JAN 2024) QoL was assessed using the European Organisation for Research and Treatment of Cancer (EORTC) Quality of Life Questionnaire C30 . Demographic and clinical data were collected, including Phase of disease,Type of Tyrosine kinase inhibitor, duration of TKI therapy,symptom burden requiring switching of TKIs and side effects experienced. Statistical analyses were performed to identify correlations between QoL scores and clinical variables.

Result

The study found that patients generally reported a good overall QoL, with high scores in physical and functional domains. However, significant variability was observed, with some patients experiencing reduced QoL due to treatment-related side effects such as fatigue, gastrointestinal issues, and musculoskeletal pain. Psychological distress, including anxiety and depression, was reported in 25% of patients. Social well-being was less affected, although a subset of patients reported challenges in social interactions due to health concerns.

Conclusion

Long-term TKI therapy for CML generally supports a favorable QoL, but individual experiences can vary widely. Persistent side effects and psychological distress highlight the need for comprehensive patient support beyond pharmacological management. Addressing these issues through tailored interventions could enhance overall patient well-being and adherence to therapy. Further research is needed to explore strategies to mitigate side effects and improve QoL outcomes for CML patients on extended TKI treatment.

Malignant Hematology-Clinical (MHC) OP-MHC-6

Beyond Nephrotic Syndrome: A Diagnostic Journey of Al Amyloidosis with Plasma Cell Dyscrasia

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Background

AL amyloidosis is a rare systemic disorder characterized by the deposition of amyloid fibrils derived from abnormal light chains produced by clonal plasma cells. It often leads to multi-organ dysfunction, with the kidneys and heart being common sites of involvement. The diagnosis is challenging due to non-specific symptoms, and the condition is often underreported, especially in regions with limited diagnostic capabilities.

Case Presentation

We report a case of a 54-year-old female presenting with a six-month history of worsening edema, initially in the lower limbs, extending to the face and abdomen. The patient also experienced generalized fatigue, weight loss, frothy urine, and hypercalcemia. Physical examination revealed generalized swelling and mild hepatomegaly. Laboratory investigations showed nephrotic-range proteinuria, anemia, and a monoclonal spike in serum protein electrophoresis (SPEP). Further testing confirmed elevated lambda light chains, monoclonal plasma cells in bone marrow biopsy, and amyloid deposits in the kidneys on Congo red staining.

Diagnosis

The patient was diagnosed with AL amyloidosis with plasma cell dyscrasia, confirmed by monoclonal gammopathy, light chain restriction on immunofixation electrophoresis (IFE), and >10% monoclonal plasma cells in the bone marrow. Renal biopsy revealed nodular glomerulosclerosis with amyloid deposits, confirming the diagnosis.

Treatment

The patient was initiated on a bortezomib-based chemotherapy regimen to target the underlying plasma cell dyscrasia. Supportive therapy included diuretics and ACE inhibitors for nephrotic syndrome and bisphosphonates for hypercalcemia. Anticoagulation therapy was also started to prevent thrombosis.

Follow-up

After three months of treatment, the patient showed significant improvement. Her proteinuria reduced, serum albumin levels increased, and hypercalcemia was controlled. The anemia was managed with erythropoietin-stimulating agents, contributing to overall clinical improvement.

Conclusion

This case highlights the importance of considering AL amyloidosis in patients with unexplained nephrotic-range proteinuria and systemic symptoms, especially when associated with monoclonal gammopathy. Early diagnosis is crucial, as treatment with proteasome inhibitors like bortezomib can improve prognosis. However, the overall outlook remains poor in cases with multiple myeloma and high beta-2 microglobulin levels, indicating a high tumor burden.

Malignant Hematology-Clinical (MHC) OP-MHC-7

Azacitidine and Venetoclax Combination as First Line Therapy in Acute Myeloid Leukaemia - A Tertiary Care Centre Experience

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Introduction

With a median age at diagnosis of 68 years, not all patients diagnosed with AML are eligible for induction chemotherapy. Venetoclax, combined with Azacitidine has shown improved survival as compared to Azacitidine alone in this difficult-to-treat population. However, there is paucity of published data on this combination from India.

Aims & Objectives

We report our experience of Azacitidine-Venetoclax (Aza-Ven) combination as first-line chemotherapy in AML.

Materials & Methods

We retrospectively analysed demographic, laboratory and treatment outcome data from in-patient and out-patient records in AML patients treated with Aza-Ven at our centre from November 2021 to September 2024 for response rates and survival.

Result

Thirty-one patients received Aza-Ven chemotherapy. The median age was 68 years (range 51-85); 61% were females. 23(74%) were de-novo AML; 3 had transformed from MDS and one each from CMML and severe aplastic anaemia; one was a lineage switch from ALL. One patient had therapy-related AML following autologous SCT for myeloma; one myeloid sarcoma presented with para-vertebral mass.

Table 1a & 1b. Assessment of treatment response to Azacitidine-Venetoclax combination in patients among ELN risk categories and patients with IDH gene mutations

	ELN Favourable *(n=6, 20%)*	***ELN Intermediate*** *(n=10, 32%)*	***ELN Adverse*** *(n=15, 48%)*	***p value***
ORR to first line therapy	100%	90%	67%	0.206
Median duration to response	55 days	83 days	90 days	0.412
Median overall survival	NR	12 months	11 months	0.138
Median relapse-free survival	NR	NR	11 months	0.876

	IDH mutated *(n=6, 20%)*	***IDH wild-type*** *(n=25, 80%)*
ORR to first line therapy	100%	80%
Median duration to response	48 days	90 days
Median overall survival	NR	NR
Median relapse-free survival	NR	12 months

ORR- Overall response rate

Eighteen (58%) patients had presented with infections. Median Hb, WBC and platelet counts at presentation were 7.8 g/dL, 10950/cu.mm and 44,000/cu.mm, respectively. Median BM blast counts was 65% (range 22-93%).

Karyotypes were available in 28 patients, and mutation panel by PCR and/or NGS in 30 patients. Median number of mutations per patient was 2(range 0-5). As per ELN 2022 criteria, 15(48%) patients were in adverse, 10(32%) intermediate and 6(20%) favourable risk category.

Over the 3-year study duration, the overall response rate (ORR) was 84%, and median OS was not reached. The median duration to achieve remission was 83 days. Twenty-six patients achieved remission - one patient underwent HSCT after CR1, and 19 others continue to be in remission. Six patients relapsed. Five patients were refractory.

Seven deaths occurred in the study period (23%). The survival rates at 1 year and 2 years were 68% and 62%, respectively. The OS and RFS in patients within the ELN risk categories weren't statistically different. The response was earlier, with better ORR and RFS in patients with mutated IDH than wild-type genes.

Conclusion

Aza-Ven combination has high remission rates and survival benefits in patients with AML who are not fit for intensive induction therapy, with better outcomes with mutated IDH genes.

Malignant Hematology-Clinical (MHC) OP-MHC-8

Childhood Langerhans Cell Histiocytosis (LCH) – Experience from a Tertiary Care Hospital in Eastern India

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Introduction

Langerhans cell Histiocytosis (LCH) is marked by the abnormal growth and accumulation of Langerhans cells resulting in varied clinical features. Diagnosis relies on clinical observations and histological along with immunohistochemical analysis for definite diagnosis (positive staining of the affected cells for CD1a and/or Langerin (CD207).

Aims & Objectives

To study clinico-epidemiological profile and treatment outcomes of children with LCH

Materials & Methods

This was a prospective analysis of 16 childhood (less than 18 years) LCH cases diagnosed and treated as per Histiocyte Society Evaluation and Treatment Guidelines (2009), over a study period of four years from September 2020 to August 2024

Result

The median age was 3 years, and the male: female ratio was 2.2:1.

Failure to thrive was the most common presenting complaint (68.7%). Multisystem (MS-LCH) involvement was seen in 81% patients and single system involvement was seen in 19%. Skeletal system was involved in all the cases and cutaneous involvement was seen in 50% cases. Among MS-LCH, risk organ was involved in 91.6 % cases, out of which liver involvement was the most common (63.6%) followed by spleen (45.4 %) and bone marrow (18%). Special site involvement was seen in ear and central nervous system in 25% and 12.5% cases, respectively. Lymphadenopathy was present in 37.5% patients.

Laboratory tests showed normal to elevated leukocyte counts, with two patients experiencing anemia and thrombocytopenia. Raised ALP and transaminasemia was seen in 56% and 43.7% cases, respectively.

All these patients were treated with initial 6 weeks course of vinblastine and prednisolone (VP) and further therapy was continued depending on response. At the end of initial phase, 81% patients showed improvement. Progressive disease was observed in 19% patients, to whom salvage therapy was started. One-year overall survival rate was 100%.

Conclusion

LCH is a rare, unique and highly heterogenous disease with varied clinical presentations. Early diagnosis is important for early treatment initiation, thereby preventing disease progression. VP is an effective treatment option, with improvement of both overall survival and response rate.

Malignant Hematology-Clinical (MHC) OP-MHC-9

Real-World Experience with Generic Venetoclax Plus Hypomethylating Agent Induction Therapy in Newly Diagnosed Acute Myeloid Leukemia Patients in Resource-Limited Setting : A Single-Center Study From AIIMS

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Introduction

The standard induction for acute myeloid leukemia (AML) is the intensive '3+7' regimen. Venetoclax (VEN) plus hypomethylating agents (HMA) is often used instead of '3+7' whoever are ineligible for the same.

Aims & Objectives

To study treatment outcomes with VEN+HMA induction in severely resource-constrained setting, using venetoclax in newly diagnosed AML patients who were ineligible for intensive '3+7' regimen.

Materials & Methods

Newly diagnosed AML patients considered ineligible for '3+7' induction was treated with venetoclax plus HMA (decitabine / azacitidine). Venetoclax was administered for 14 days each cycle for at least two cycles. Bone marrow morphology & flowcytometric measurable residual disease (MRD) analysis were done on day 14 of 1st cycle, and after completion of first two cycles.

Result

Total 44 patients were treated between February 2023 & June 2024. Median age was 44.5 (IQR 49) years; male: female ratio was 1:1.5. As per European LeukaemiaNet 2022 risk stratification, 20 %, 55 % and 25 % patients had favourable-, intermediate- and adverse-risk AML respectively. Most frequent genetic abnormalities were FLT3 (23 %), NPM1 (21 %), AML1: ETO (9 %) &

Number of patients	n = 44
Age	Median age 44.5 (IQR 49) years
Gender	Male: 17 (38.6 %) Female: 27 (61.4 %)
AML Risk Groups	Favourable risk: 9 (20%) Intermediate risk: 24 (55 %) Adverse risk: 11 (25 %)
Day14 response cycle 1	Less than 5 % blasts: 8 (18 %) More than 5 % blasts:8 (18 %) Not done: 28 (63.63 %)
Day14 response cycle 1	Day 14 MRD negative: 8 (18.18%) Day 14 MRD positive: 7 (15.9 %) MRD not done: 29 (65 %)
Treatment response post cycle 1 (ELN 2022)	Complete response (CR): 14 (31.8 %) CR with incomplete hematologic recovery (CRi):7 (16 %) Partial Response (PR): 8 (18 %) MLFS: 1 (2.3%) No response (NR): 6 (13.6 %) Non-evaluable for response: 8 (18 %)
Treatment response post cycle 2 (ELN 2022)	Complete response (CR): 13 (29.5%) CR with incomplete hematologic recovery (CRi):3 (6.8%) Partial Response (PR): 3 (6.8%) MLFS: 0 No response (NR): 1 (2 %) Non-evaluable for response: 24 (55%)
Flow-MRD status post cycle 1	MRD negative (< 0.1%):12 (27.27 %) MRD positive (≥ 0.1%):13(29.54 %) Not available:19 (43 %)
Flow-MRD status post cycle 2	MRD negative (< 0.1%):10 (22.72%) MRD positive (≥ 0.1%):9 (20.45%) Not available:25 (56.81 %)
Non-haematological toxicity cycle 1	Acute kidney injury: 7 (16 %) Hyperbilirubinemia: 5 (11 %) Septic shock: 5 (11 %) Neutropenic enterocolitis: 4(9 %)
Current Survival status	Alive: 23 (52.27 %) Dead:21 (47.7 %) CR:21 (44.7 %) Relapsed:4 (9 %)

DNMT3A (9 %). At day 14, 18% of evaluable patients had marrow blasts <5 % & negative flow-MRD status. Twenty-seven percent patients achieved complete remission (CR) plus MRD negative status after cycle1. Median time to hematological recovery in 1st cycle was 24 (IQR 8) days. Either CR or CR with incomplete hematologic recovery (CRi) was achieved in 45% patients after two cycles of VEN+HMA therapy. Thirteen percent patients died in 1st cycle. Twenty percent patients required intensive chemotherapy after failure of VEN+HMA. Incidence of febrile neutropenia was 100% in cycle 1 & 18% in cycle 2, 11% developed septic shock in cycle 1, & 9% had neutropenic enterocolitis in cycle 1. Commonest non-hematological toxicity in cycle 1 were acute kidney injury (16 %) & hyperbilirubinemia (11 %); 11 % required mechanical ventilation, & 5 % required haemodialysis. Results are given in table 1

Conclusion

In our single-centre experience, venetoclax plus HMA induction therapy was observed to be highly effective & relatively safe in newly diagnosed AML patients who were considered ineligible for '7+3' regimen.

Malignant Hematology-Clinical (MHC) OP-MHC-10

Characteristics and Outcomes of Patients with Multiple Myeloma Aged? 40 Years – Experience from A Tertiary Care Cancer Centre in India

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Introduction

MM primarily being disease of the elderly with a median age of diagnosis of 70 years and in India patients a decade younger, the data among young patients are limited.

Aims & Objectives

The aim of the study is to describe the presenting features, characteristics and outcomes of MM patients ≤40 years.

Materials & Methods

We analysed data of newly diagnosed Multiple Myeloma patients ≤40 years over 9 years from January 2013 to December 2021.

Result

A total of 110 patients diagnosed with MM were analysed out of the total 1980 patients screened (Incidence 5.5%). At the time of analysis 48 patients were alive, 15 patients were dead and 47 patients were lost to follow up. The median age of the cohort was 36 years with Male to female ratio of 3:1. Clinically significant anaemia, hypercalcemia, renal impairment and hypoalbumenia were seen in 42.7%, 11.9%, 17.3% and 41.8% of patients respectively. Extramedullary plasmacytoma was seen in 9% of patients. According to ISS 35.5%, 27.1% and 37.4% of patients were in stage I, II and III respectively and according to R-ISS 24%, 69.8% and 6.3% of patients were in stage I, II and III respectively. 78.3% of patients were standard risk and 21.7% of patients were high risk. LCD was diagnosed in 21.6% of patients. 38.5% of patients received VRD and 55% of patients received VCD as first line induction chemotherapy. 27% of patients received ASCT. After a median follow up of 44.2 months mPFS was 45.9 months. 1 year, 3 year and 5 year overall survival rates were 93.9%, 91.1% and 81.2% respectively. Among patients who received PI and IMiD, 3 year PFS rates were 83.9% and 78.7% respectively. 5 year PFS of patients who received ASCT were 58.5 and for those who did not receive ASCT were 27.8% (p 0.0043) .

Conclusion

Patients younger than 40 years constitute higher proportion of patients in Indian sub-continent. One fourth of patients had high risk cytogenetics. ASCT was done in approximately one fourth of patients. Anaemia, Renal failure, poor performance status, HR cytogenetics, VCD compared to VRD, poor response to therapy, no maintenance therapy and no ASCT showed poor progression free survival.

Malignant Hematology-Clinical (MHC) OP-MHC-11

Real World Outcomes with the Use of Inotuzumab Ozogamicin in Relapsed/Refractory B Cell Acute Lymphoblastic Leukemia

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Introduction

There is paucity of real-world data on the use of Inotuzumab Ozogamicin (InO) in patients with relapsed/refractory B-acute lymphoblastic leukemia (R/R B-ALL).

Aims & Objectives

To study the real-world clinical outcomes in patients with R/R B-ALL who have received InO as salvage chemotherapy.

Materials & Methods

Hospital records were used to retrieve data of patients with R/R B-ALL at our institution from January 2020 to January 2024. Data cut-off date was 1st March 2024.

Result

During the study period, 61 were diagnosed to have R/R B-ALL, of which 47 were treated. Of these, 30 patients (median age 22 years, range 6-68) received InO for refractory (n=8) or relapsed (n=22) B-ALL (3 were Ph+). Twenty-five (83.3%) were previously treated with chemotherapy following diagnosis of R/R B-ALL prior to InO while 5 had a prior allotransplant. A median of 3 doses of InO (range 1-12) were used as 1st/2nd (n=15) or 3rd/later (n=15) salvage. Three patients died before response assessment while complete remission was noted in 18 patients, of which 14 were MRD negative. Ten patients (33.3%) were bridged to HSCT (median of 42 days between last InO dose and HSCT), 3 patients (10%) received DLI (post-transplant relapse) and 2 patients underwent CAR-T cell therapy (6.6%), respectively. The 1-year overall survival was 46.6% ± 10.5% with an EFS of 38% ± 10.4%.

TABLE 1 – BASELINE PATIENT CHARACTERISTICS AND OUTCOMES

CHARACTERISTICS	NUMBER (%) OR MEDIAN (RANGE)
Total number of patients	30
Age (in years)	22 (6-68)
Male sex	23 (76.6%)
Disease type 1. Primary refractory disease 2. Very early/early relapse 3. Late relapse 4. Post-transplant relapse	 8 (26.2%) 10 (45.54%) 7 (31.8%) 5 (22.7%) (4 CR2 and 1 CR3 transplant)
Disease status prior to InO 1. Morphologic disease 2. Morphological remission with positive MRD	 28 2
Extent of disease prior to InO 1. Peripheral blood WBC count 2. Proportion of peripheral blasts on morphology 3. Proportion of marrow blasts on morphology 4. CNS disease	 5400 per cu.mm (Range: 800-66,990) 0 (0-92%) 40 (0-95%) 4 (13.3%)
Pattern of InO use 1. Single agent InO 2. Single agent InO with triple intrathecal 3. Along with chemotherapy	 26 (86.6%) 2 (6.66%) 2 (1–Mini-HYPER CVAD, 1–dasatinib) (6.66%)
Median number of doses of InO used Median number of doses of InO used among responders	3(range 1-12) 3.5(range 2-12)
Line of salvage of InO 1. First line 2. Second line 3. Third or later	 5 (16.6%) 10 (33.3%) 15 (50%)
Response to salvage InO Morphologic disease (n=28) 1. Not assessed 2. Remission 3. No response Remission with MRD positivity (n=2)	 3 (10.7%) 16 (57.1) (of which 13 were MRD negative) 9 (32.14%) (MEDIAN DOSES OF InO – 3 [2-9]) Both patients had MRD response (1 became MRD negative after 1 cycle; second had reduction of MRD from 1.4 to 0.06 after 2 cycles)
Subsequent therapies 1. Following response (n=18) 2. Following non-response (n=9)	 Allogeneic HSCT (n=10), DLI (n=3), CAR-T (n=2), Others (n=3; 1 BFM REZ Protocol; 1 – Awaiting HSCT; 1 – sepsis with encephalopathy – Palliation) Intensive chemotherapy (n=3), Palliation (n=5), DLI (n=1)
Status of last follow-up 1. Alive 2. Death due to progressive disease 3. Death while in remission	 14 (46.6%) 11 (36.6%) 5 (16.6%) (Sepsis (3), VOD (1), and intracranial bleed (1))
Median follow-up of the entire cohort from initiation of InO	7 months (Range 1-24)
Median follow-up of the surviving patients	10.5 months (Range 2-24 months)

Eighteen (60%) patients had hospital admission for febrile neutropenia. Five (16.6%) patients experienced veno-occlusive disease (VOD) of which 3 were following an allotransplant. The median follow-up after InO initiation was 7 months (range 1-22) and 14 patients were still alive at last follow up. Causes of death were disease progression (11), infection (3), VOD (1), and intracranial bleed (1).

Conclusion

InO salvage in R/R B-ALL is associated with a remission in about 60% patients enabling a subsequent transplant or cell therapy in these patients in our real-world cohort.

Malignant Hematology-Clinical (MHC) OP-MHC-12

Treatment Outcome in Adolescent and Young Adult Acute Lymphoblastic Leukemia (All) on BFM-95 Protocol: Experience of A Tertiary Care Institute from North India

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Introduction

BFM-95 protocol is among the common regimens used to treat AYA acute lymphoblastic leukemia .Five-year survival in Adolescent and young adult (AYA) patients with acute lymphoblastic leukemia (ALL) is around 40%, which is inferior when compared to children which is around 90%.

Aims & Objectives

To study treatment outcomes in AYA acute lymphoblastic leukemia patients on BFM 95 protocol.

Materials & Methods

We retrospectively analyzed the available data of 75 patients diagnosed with acute lymphoblastic leukemia in the AYA age group who received treatment as per BFM-95 protocol from 2016-2020 in the clinical hematology department of KGMU Lucknow.

Result

A total of seventy-five patient data were analyzed, out of which 56 were male and 19 were female. The age group ranges from 15- 25 years (median- 18y). High-risk patients were 15 (20%), 3 due to PPR, and 12 due to high-risk cytogenetics. Most of the patients were CNS-1 and three patients were of CNS-3. Eight (10.6%) patients did not complete induction treatment. The median duration of induction phase A was 40 days (range 35-45 days). The most common complication during induction phase A treatment was febrile neutropenia which was seen in 21 patients (28%) followed by transaminitis. The median duration of follow-up was two years (range 8 months-5 years).Five (6%) patients' bone marrow were not in remission after induction-A. Thirty three (44%) patients completed maintenance and were still on follow-up. Twenty-three (30.6%) patients relapsed and the maximum relapse was during the maintenance treatment. Six patients were lost to follow-up during maintenance. At a median follow-up of two years disease-free survival was 44%.

Conclusion

We concluded that BFM-95 is a well tolerated protocol in the management of AYA acute lymphoblastic leukemia.Outcomes are inferior when compared with the pediatric population as more high and intermediate-risk populations in the AYA group.

Malignant Hematology-Clinical (MHC) OP-MHC-13

Outcomes DLBCL Treated from 2011 To 2020: An Audit From an Eastern India Tertiary Cancer Center

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Introduction

Patterns of care and long term outcome of Diffuse Large Cell lymphoma [DLBCL] patients treated in the rituximab era in India are sparse. Treatment strategies are difficult to implement specially in the elderly because of associated co-morbidities and socio-economic dependence.

Aims & Objectives

Review disease characteristics and 5-year outcomes of patients with Diffuse large B cell lymphoma (DLBCL) treated in the rituximab era in a tertiary cancer center over a decade.

Materials & Methods

EMR records of 3319 lymphomas (>18 years) were evaluated retrospectively. First line treatment was offered to 959 patients between May 2011 to December 2020. Demography, Clinical features, staging, prognostic stratification, associated co-morbidities and first line treatment response and outcomes of DLBCL patients who started treatment at our center have been analyzed. Available paraffin blocks were subjected to immunophenotyping to subtype DLBCL into Germinal center (GCB) and Activated B cell (ABC).

Response rates, Event free survival (EFS) and OS were evaluated for patients receiving 1st line treatment, and these patients were followed till August 2024. Patients in remission were censored at last follow-up. Patients in whom there was no follow-up information available (physical/ telephonic) after progression were considered dead.

Result

The median age of presentation in our cohort is 58 years, with 292 (30%) elderly patients ≥65 years of age. Gender ratio is 1.9:1. The median duration of symptoms was 3 months.

Anthra-cycline based treatment was given to 773 (73%) patients and Rituximab based treatment to 842 (90%). Most common protocol used was CHOP- like therapy in 69% patients. The response rate (CR +PR+ SD) 87%, and the progression on treatment 10%. Patients receiving Anthra-cycline had a 5-year Event Free Survival (EFS) of 74% as compared to non-Anthracycline was 52% (<0.0001). Patients receiving Rituximab had a 5-year EFS of 72% and for not receiving Rituximab it was 58% (0.0005). No difference was seen in survival of GCB subtype and with non GCB subtype. EFS for the patients above 65 years is 60% at 5 years and for those below 65 years is 75% (<0.0001). Overall Survival (OS) and EFS is 73.53 % and 70.70 % respectively.

Conclusion

Chemo-immunotherapy with anthracycline and rituximab is the backbone of first line treatment in DLBCL. Long term results are consistent with better outcomes for patients younger than 65 years, early stage as well as favourable IPI. The cell of origin did not have an impact on long term outcome.

Malignant Hematology-Clinical (MHC) OP-MHC-14

Young Patients with DLBCL in India: Initial 1-Year Outcomes Reveal Aggressive Disease and Favorable Responses Despite High Loss to Follow-Up

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Introduction

DLBCL is seen to present at a younger age in India, but little is known about disease characteristics, treatment response and survival.

Aims & Objectives

This study evaluates their treatment responses, survival, and long-term outcomes from a single center.

Materials & Methods

Patients diagnosed with DLBCL (all subtypes) at a tertiary care center from January 2021 to June 2024 younger than 55 years at diagnosis were included.

Result

A total of 95 patients (M:F = 56:39; median age 44 years) with DLBCL had baseline data, of which 79 (81%) underwent staging, and 60 (63%) received treatment. Nineteen (20%) had comorbidities, primarily diabetes mellitus (n=9). ECOG status 0-1 was present in 56%. Clinical features included hepatomegaly (11.6%), splenomegaly (10%), and Waldeyer ring involvement (10.5%). Histology and IHC were available for 91 (95.7%) and 84 (88.4%) patients, respectively. Among DLBCL-NOS cases, MYC, BCL2, and BCL6 positivity rates were 74%, 90%, and 65%, with 13% being double expressors. The median Ki67 index was 80%. Forty-four percent had involvement of >3 lymph node regions, and the median largest disease dimension was 6.7 cm. Extra-nodal involvement occurred in 47 (49.5%) patients, including 5 with CNS involvement and 21 with primary EN lymphoma. Final stages were I, II, III, and IV in 4.2%, 18.9%, 15.8%, and 15.8%, respectively. Initial treatment was DA-EPOCH for five patients and R-CHOP for the rest (91.6%). CNS-directed IT-MTX was given to 9 patients. End-of-treatment response was available for 55% (n=33) patients, with 16 (48%) achieving CR, 8 (24%) PR, 2 (6%) SD, and 7 (21%) PD. After a median follow-up of 367 days, no patients died, and 27 were lost to follow-up. Patients not in CR, on palliation, or lost to follow-up were considered events, and median EFS was 452 days (IQR, 182-721). No association was seen between loss from follow up/discontinuation with disease stage (p=.284), CNS involvement (p=.060) or LN regions involved (p=.116).

Conclusion

Our study, one of the first on young DLBCL patients in India, reveals higher proportion of biologically aggressive and EN disease but favorable responses to therapy. Significant loss to follow-up limits long-term assessment. Longer follow up of this data will enable insights into survival and long term complications.

Malignant Hematology-Clinical (MHC) OP-MHC-15

Lymphoma Subtype Distribution, Clinical Presentation and Outcomes: Over the Last Decade from an Eastern India Cancer Center

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Introduction

The distribution of lymphoid neoplasms in an Eastern India Cancer Center was analyzed according to WHO classifications. This study aims to analyze subtype distribution of lymphomas, its clinical presentation and outcomes of common subtypes.

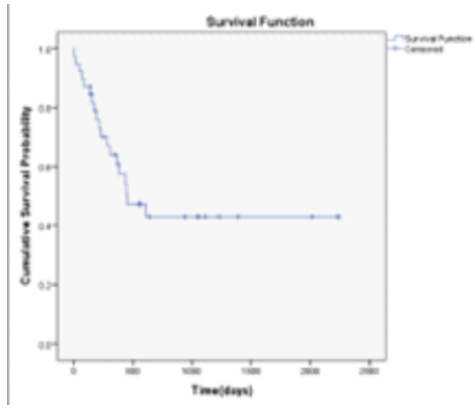
Materials & Methods

Lymphoid neoplasms diagnosed within 10 years in a single institution in Eastern India were analyzed according to the WHO classification. The patients were followed up to August 2023.

Results

From May 2011 to December 2020, a total number of 2226 patients with lymphoma were diagnosed, of which non-Hodgkin lymphoma (NHL) accounted for 82.5%, and Hodgkin lymphoma were 17.5%. Mixed cellularity (60%) was the major subtype of classical Hodgkin lymphoma. The bimodal age distribution was not observed.

The top six subtypes of B-cell NHL were: diffuse large B-cell lymphoma (51%), chronic lymphocytic leukemia/small lymphocytic lymphoma (10%) follicular lymphoma (8%), Mantle cell lymphoma (5.5%), and Marginal zone lymphoma (4%) of all NHLs. The common subtypes of T cell lymphoma were Anaplastic large cell lymphoma (ALCL), Peripheral T cell lymphoma (PTCL) and Angioimmunoblastic T cell Lymphoma (AITL).



The median age for B cell NHL at presentation was 58 years and for HLit was 40 years . The T cell NHL showed wider variation with NK T cell lymphoma presenting at a median of 38 years, ALCL at 44 years and PTCL/AITL at 58 years. Across all subtypes there was a male predominanace with the ratio being 5:1 for Nodular Lymphocytic predominant Hodgkin Lymphoma. Extranodal site involvement at presentation was seen in about half of all cases, and most frequently involved gastrointestinal tract, head and neck, and bone.

The 5-year outcome for HL, DLBCL, MCL and T-Cell lymphoma are 84%, 66%, 55%%, and 30% respectively. [for other subtypes work is in progress]

Conclusions

The lymphoid neoplasms displayed some epidemiologic features similar to those reported in literature from western and Asian countries, as well as other regions of India, whereas some subtypes showed distinct features.

Malignant Hematology-Clinical (MHC) OP-MHC-16

Outcomes in Adult Hemophagocytic Lymphohistiocytosis (HLH) with Low Dose Cyclophosphamide: A Single Centre Pilot Study

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Introduction

Adult HLH is a rare but serious entity with limited data on outcomes and most of our treatment regimens are based on pediatric data.

Aims & Objectives

To evaluate treatment outcomes in adult HLH to the combination of low-dose cyclophosphamide with steroids.

Materials & Methods

A prospective analysis of patients diagnosed with HLH using H score, at St Johns Medical Academy, Bengaluru, India, from Jan 2023 to Aug 2024 from the time of diagnosis till the end of the study, death, or last known follow-up. Patients above 18 years were included. All received cyclophosphamide at a dose of 0.3gm/m2 along with steroids because of a deranged liver profile. A non-parametric Mann-Whitney U test was used for statistical analysis.

Result

19 consecutive patients diagnosed with HLH using the H score were included .The age range was 25 -65 years. 2 were primary HLH patients (Griscelli type 2 - 1 , SH3KPB1 deletion -1).Rest 17 were secondary HLH patients of which 11 infection driven and 6 were malignancy-driven. All had deranged liver function. Patients received dexamethasone 10mg/m2 with cyclophosphamide 0.3 gm/m2 (capped at 500 mg) every 5 days in the first 2 weeks followed by a tapering dose of steroid with the addition of cyclosporine from 5th week.1 patient with T-cell lymphoma received etoposide as per CHOEP regimen. The EBV-driven HLH and the B ALL patient relapsed at a median of 38 days and they received additional anakinra 100 mg for 12 days.14 patients attained partial response at 8 weeks with this regime. By the end of the 8th week, 3 died of active disease, and 1died of mucormycosis. Additional 4 deaths were recorded by 16 weeks, of which 3 died of active disease and 1 with myocardial infarction.1-year survival in our study is 64%. 8 are in CR, and 3 are in PR at 1 year. Bilirubin (p-0.25), ALT(p-0.65), LDH (p-0.35), and Ferritin (p-0.87) were not found to be statistically significant in determining the outcome.

Conclusion

A low dose of cyclophosphamide in place of etoposide may be a better option for adult HLH. Our study has a 1-year survival rate of 64%. Etiology is a strong prognostic factor with the worst outcomes in malignancy and EBV-driven HLH in our study.

Malignant Hematology-Clinical (MHC) OP-MHC-17

Flat-Dose Nivolumab-Based Combination Regimens for Treatment of Relapse Refractory Hodgkin Lymphoma – Real-World Evidence from A Lower Middle-Income Country

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Introduction

Nivolumab, an anti-PD-1 monoclonal antibody, shows significant promise in treating relapsed/refractory Hodgkin lymphoma (HL). However, its high cost poses a limitation. Due to its linear pharmacokinetics and broad therapeutic index, flat-dosing is a viable option that could help lower treatment costs without compromising efficacy.

Aims & Objectives

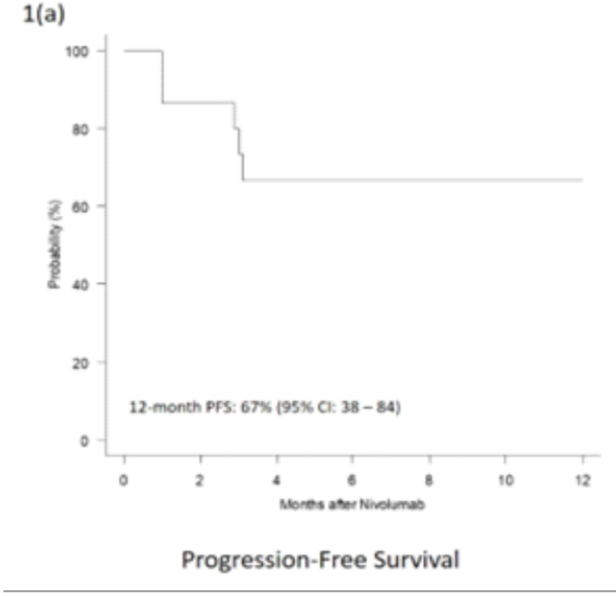
To evaluate the efficacy and safety of fixed-dose Nivolumab

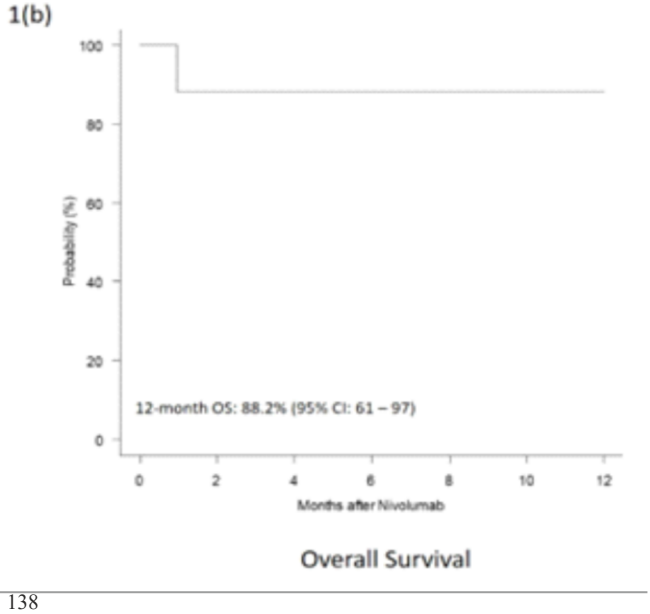
Materials & Methods

We conducted a retrospective analysis of patients receiving flat-dose nivolumab, either alone or with chemotherapy. Dosing was adjusted based on available vial strengths (100 mg and 40 mg) to approximate the recommended 3 mg/kg dose while minimizing drug wastage. The primary objective was to assess efficacy and safety. Overall survival (OS) and progression-free survival (PFS) were estimated using the Kaplan-Meier method, with statistical analyses performed using EZR (version 1.62).

Result

Fifteen patients (7 relapsed; 8 refractory) received nivolumab-based therapy. The median age of the cohort was 28 years (26-33), 12 (80%) were male. The median time to relapse was 29 months (12-33), and 20% experienced early relapse (<12 months). The median lines of treatment before nivolumab was 2 (1-3). Most patients (n=11, 73%) received nivolumab in combination with ifosfamide, carboplatin, and etoposide (N-ICE). The median dose of nivolumab was 2.3 mg/kg (2-2.5). The median follow-up after nivolumab-based treatment





was 16 months (95% CI: 15-30). The median cycles of nivolumab was 2 (2-3). The overall and complete metabolic response after 2 cycles of nivolumab-based treatment were 67% and 40%, respectively. The 12-month PFS and OS was 67% (95% CI:38 - 84) and 88.2% (95% CI: 61 - 97), respectively. Immunological adverse events occurred in 7 patients (46%) and included skin rash (n=2,13%), arthralgia (2,13 %), transaminitis (4, 26%), and autoimmune thyroiditis (1, 6%). Six patients (40%) developed febrile neutropenia which occurred exclusively in patients receiving N-ICE. Seven of ten responding patients received consolidation autologous stem cell transplantation (auto-SCT) with BEAM conditioning. The median CD34+ cell dose was 4.9 x 106/kg (4 – 5.8). The median time to neutrophil engraftment was 11 days (9-12). There was no transplant-related mortality.

Conclusion

Flat-dose nivolumab-based salvage appears highly effective in treating relapsed/refractory HL. This dosing strategy helps reduce treatment costs and holds significant potential to improve access to care in low- and middle-income countries.

Malignant Hematology-Clinical (MHC) OP-MHC-18

Feasibility of Azacitidine and Venetoclax Followed by High/Intermediate Dose Cytarabine (HIDAC/IDAC) Consolidation in Previously Untreated Acute Myeloid Leukemia Patients Unfit for Intensive Chemotherapy

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Introduction

Acute myeloid leukemia (AML) predominantly affects the elderly, posing challenges in treatment due to comorbidities and age-related factors. Azacitidine and venetoclax have shown promising results in older or unfit AML patients. However, the feasibility and efficacy of consolidative therapy with high/intermediate-dose cytarabine (HIDAC/IDAC) following azacitidine and venetoclax induction in this population remain unexplored. Cytarabine consolidation remains relevant in most of the low-middle income countries, as bone marrow transplantation is not always feasible.

Aims & Objectives

1. Primary objectives

   Overall survival (OS) and Progression free survival(PFS) for all AML patients getting azacytidine venetoclax followed by HIDAC/IDAC consolidation

2. Secondary objectives

   Remission status at the end of 2 cycles of Azacitidine + Venetoclax and at the end of consolidation(3 cycles) in both groups

   Comparison of OS and PFS with patients on continuous azacitidine and venetoclax therapy

   Barriers to HIDAC/IDAC consolidation therapy following remission after Azacitidine -Venetoclax

Materials & Methods

This ambispective non-randomized interventional study was designed to evaluate the feasibility and outcomes of azacitidine and venetoclax induction followed by HIDAC/IDAC consolidation in previously untreated, unfit AML patients. Consolidation with HIDAC/IDAC was offered to those achieving remission. Primary objectives included overall survival (OS) and progression-free survival (PFS), while secondary objectives encompassed comparison with continuous azacitidine and venetoclax therapy and barriers to administration of HIDAC/IDAC consolidation.

Result

During the study period, out of 151 AML patients admitted, 47 deemed unfit for intensive chemotherapy received azacitidine and venetoclax (AZA-VEN) induction therapy, with 75% presenting baseline infections. Twenty-two patients achieved remission, of whom 9 received HIDAC/IDAC consolidation, while 13 continued AZA-VEN therapy. With a median follow-up of 14 months, the median OS was 24 months in the Aza-Ven group and not reached in the Aza-Ven-HI/IDAC group (P=0.9840). The MRD negativity rate in the Aza-Ven-HI/IDAC group increased from 33% to 45%, while in the Aza-Ven group it rose from 15% to 31%. The relapse rate was 44% in Aza-Ven-HI/IDAC (median time=9 months) vs. 31% in Aza-Ven (11 months). The main reason for not administering HI/IDAC was higher age/multiple comorbidities.

Conclusion

Among unfit treatment naive AML patients, who achieve remission with AZA-VEN, there was no significant difference in OS and PFS between those treated with HIDAC/IDAC consolidation and those receiving continuous AZA-VEN therapy.

Malignant Hematology-Clinical (MHC) OP-MHC-19

Outcomes Of Azacitidine-Venetoclax Therapy in The Front Line Setting In Acute Myeloid Leukemia

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Introduction

The Incidence of Acute Myeloid Leukemia (AML) rises with age, predominantly affecting older individuals who often find it difficult to tolerate intensive chemotherapy (IC) regimens. The combination of azacitidine and venetoclax (Aza-Ven) presents a promising, less toxic alternative to traditional therapies, offering effective outcomes for these patients.

Aims & Objectives

To evaluate the outcomes of Aza-Ven treatment in frontline settings by assessing overall response rates (ORRs) including Complete Haematological Response (CHR), Bone Marrow Response, and Minimal residual disease (MRD) status and predictors of treatment response.

Materials & Methods

We conducted a retrospective analysis of AML patients treated with the Aza-Ven combination between June 2022 and June 2024 at our instititute, all of whom had received at least four cycles of therapy. Patients deemed unfit for IC either due to Comorbidities and age (more than 60 years) or presenting with poor performance status (PS) at diagnosis were treated with Aza-Ven. Venetoclax was administered at a dosage of 100 mg/day with posaconazole for 14 days, while azacitidine was dosed according to standard protocols.

Result

180 patients were treated for AML during this period. 48 of them were unfit for IC, 10 among them received single agent azacytidine. 38 received Aza + Ven. M:F = 1.3:1. Median age : 58y (Range : 25–77). Patients were stratified according to the European Leukemia Network 2022 - Favourable risk: 12 (31.6%); Intermediate Risk: 21,(55.3%); Adverse Risk: 5, (13.2%); CHR was noted among 22 (55%) patients, with 13 (59.7%) achieving it after Cycle 1, another 7 (31.8%) after the 2nd Cycle and the rest 9 after cycle 3 & 4. Bone Marrow responses of CR and PR together constituted a 55 %. MRD negative status among these patients was 50% (11). At a median follow up of 17 months, mPFS was 7m and the mOS was 9m. mOS was 24m among MRD negative and 17m among MRD positive patients (p:0.5). Survivals among the NPM1 mutated patients were mOS not reached vs 9m.

Conclusions

Aza-Ven offers good haematological and Bone Marrow responses, but they are not sustained for longer periods. CHRs are attained predominantly post the first and second cycles of therapy (90%), additional responses were minimal beyond the first two cycles. NPM1 mutated patients fared better among the molecularly tested patients. Patients with MRD negative status fared better but survival did not reach statistical significance.

Malignant Hematology-Clinical (MHC) OP-MHC-20

Clinical Outcomes of Ph+ ALL in Pediatric Age Group: A Retrospective Study from a Tertiary Care Center in Eastern India

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Introduction

Acute Lymphoblastic Leukemia (ALL) is a common haematological malignancy in children, characterized by the abnormal proliferation of lymphoblasts. The molecular panel plays a crucial role in determining prognosis and treatment strategies. This study aims to evaluate the clinical outcomes of pediatric Ph+ ALL.

Aim and Objectives

To analyse clinical data, treatment responses, karyotype findings and overall outcomes in pediatric patients diagnosed with Ph+ ALL over a period of 6 years.

Material & Method

This retrospective study reviewed clinical data from 14 pediatric patients diagnosed with Ph+ ALL by molecular study between 2018 and 2024 in the Pediatric Hematology and Oncology Division of AIIMS, Bhubaneswar. Chemotherapy started as per the modified EsPHALL 2009 protocol along with tyrosine kinase inhibitor (TKI). Data collected included patient demographics, baseline Total Leukocyte Count (TLC), response to prednisolone, karyotype, treatment outcome, duration of complete remission (CR) and follow-up durations.

Result

The cohort consisted of 14 children, with a gender distribution of 36 % male and 64 % female. The patients' ages ranged from 4 to 15 years (median age: 7 years). Baseline TLC values varied from 1.74 to 600 × 10^9/L (median: 73 × 10^9/L), and 86% of patients exhibited good response to prednisolone. All patients started on Imatinib, except one, who was started on Dasatinib. Out of 14 patients, 13 have opted for treatment. The majority (69%) were continuing chemotherapy, with the duration of complete remission ranging from 0 to 53 months (median: 8.5 months). At present 9 patients are on treatment and 1 patient has completed treatment. Mortality was observed in 3 patients, attributed to persistent disease and relapse, with one having very early medullary, one early medullary and one very early combined relapse with a median CR duration of 15 months. Notably, there was no evidence of CNS involvement among the patients.

Conclusion

This study underscores the diverse clinical presentations and outcomes in pediatric ALL patients, highlighting the significance of karyotype analysis and molecular study, particularly the (9:22) translocation, in prognostication. Early detection, good prednisolone response and diligent long-term follow-up are crucial for improving patient outcomes in this population.

Malignant Hematology-Clinical (MHC) OP-MHC-21

Exploring Treatment-Free Remission in CML: A Single Institute experience

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Introduction

Tyrosine kinase inhibitors (TKIs) have significantly improved the overall survival of patients with chronic myeloid leukemia (CML), bringing it close to that of the general population. While TKIs have been lifesaving, long-term use poses physical and financial challenges to the patients.

Aims & Objectives

To elucidate the success and long-term outcomes of CML patients undergoing treatment-free remission (TFR) in real-world practice.

Materials & Methods

Retrospective analysis of CML patients treated from June 2001 to June 2024 undergoing TFR.

Result

A total of 30 patients were in the study, with a median age of 35 years, 56% of whom were male. The majority (93%) of patients initiated TFR while on Imatinib, and the remaining were on second-generation TKIs. TFR was initiated for 16 patients after counseling, 5 due to pregnancy, 6 due to kidney disease, and 3 due to intolerance. Based on ELTS scores, 20% of patients were high-risk, 23% in intermediate risk, and the remainder with low risk. Two patients presented with blast crisis; TFR was later initiated in one patient due to pregnancy and in the other for renal failure. Median time to TFR is 12 years. 9 patients (30%) had a loss of MMR, prompting the resumption of TKI, with 55% of relapses occurring within the first year of TFR initiation. The median duration of Deep Molecular response (DMR) was 9.5 years, and the median time to regain DMR after resuming TKIs was 8 months. Of the high-risk patients (16%), 3 (60%) remained in remission. The median DMR duration before TKI discontinuation for pregnancy was 3 years. At the time of analysis, 24 patients (70%) are in major molecular response (MMR).

Conclusion

With 70% patients maintaining MMR after discontinuation and rest achieving MMR briefly after drug resumption,TFR offers a viable strategy for reducing the long-term physical and financial burdens with TKI therapy.

Malignant Hematology-Clinical (MHC) OP-MHC-22

Comparison of Dasatinib 70 Mg/Day Versus 100 Mg/Day in Newly Diagnosed Chronic Phase Chronic Myeloid Leukemia [CML-CP]: A Single-Center, Randomised Control Study

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Adamya Gupta,Arjun Kacchwaha, Resma Benson, Bibhant Shah, Kavya Ronanki, Prisla Dalton, Nikhil Nagpal, Shashikant Singh, Karthik Kumar, Jhasaketan Naik, Uttam Kumar Nath

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Introduction

Dasatinib 100mg/day is approved for upfront therapy in CML-CP patients but also associated with several dose-limiting adverse events. There is limited data on efficacy & safety of lower doses of dasatinib (50-70mg/day) versus 100mg/day dose. The present single-center, randomized controlled study describes early treatment results & adverse events profile of dasatinib 70mg compared to 100mg dose.

Aims & Objectives

To compare the rates of complete hematological response (CHR), early molecular response (EMR), complete cytogenetic remission (CCyR), and major molecular response (MMR) in newly diagnosed CML-CP patients treated with low-dose generic dasatinib (70 mg/day) versus standard-dose generic dasatinib (100 mg/day).

To compare the adverse events (AEs) in the two treatment groups.

Materials & Methods

The present study enrolled newly diagnosed CML-CP patients of 12-80 years of age between February-2023 & June-2024. Eligible subjects were randomised to receive dasatinib at either 70mg/day or 100mg/day dose. Response rates and adverse events were defined as per ELN 2020 recommendations & NCI-CTCAE v-5 respectively.

Result

Out of total 113 consecutive treatment-naïve CML patients screened for eligibility, 102 patients were enrolled in the study. Of these, five were non-compliant to treatment & 7 patients were lost to follow up. Data of 90 patients [dasatinib70mg (n)=45, dasatinib100mg (n)=45] who had completed at least 3 months of therapy were available for analysis. The median age of patients was 37 Years (range 17-68), with male: female ratio of 1.2:1.

Parameters	Dasatinib 70 mg/day (n=45)	Dasatinib 100mg/day (n=45)	
Median age (Years) (range)	39(18-67)	38(17-68)	
Male gender [n(%]	21(47%)	29(64%)	
Median haemoglobin (g/dl) (range)	9.4(5.6-14.4)	9.6(5.1-14.1)	
Median Total leucocuyte count (x 10^9/L) (range)	139500(19200-847600)	144600(21400-820000)	
Median Platelet Count (x 10^9/L) (range)	340000(92700-90500)	315000(96800-650000)	
complete haematological response (CHR) at 3 months [n (%)]	44(98%)	43(96%)	P value >0.05
Early Molecular response (EMR) (BCR-ABL1-at ≤10%) at 3 months [n (%)]	42(93%)	43(96%)	
Complete cytogenetic remission(CCyR) (BCR-ABL1-at ≤1%) at 3 months [n (%)]	26(58%)	27(60%)	
Major molecular response (MMR) (BCR-ABL1-at ≤0.1%) at 3 months [n (%)]	10(22%)	13(29%)	
Treatment Failure [n]	0	1	
TKI dose reduction/interruption due to toxicity [n (%)]	7 (21%)	2 (4%)	

At 3 months of treatment CHR, EMR & MMR was achieved by overall 97%, 94%, 26% respectively. In dasatinib 70mg/day group & dasatinib 100mg/day group CHR, EMR, CCyR, MMR was achieved by 98%(44/45), 93%(42/45), 58%(26/45), 22%(10/45) versus 96%(43/45), 96%(43/45), 60%(27/45), 29%(13/45) patients respectively; the differences in two groups response were not statistically significant.

Most common hematological adverse events (AEs) in dasatinib 70mg versus 100mg groups were grade 1-2 thrombocytopenia (16% vs 27%), anemia (16% vs 27%), & neutropenia (13% vs 24%); commonest non-hematological AEs in dasatinib 70mg versus 100mg groups were diarrhea (13% vs 25%), nausea (10% vs 12%), & vomiting (10% vs 12%), pleural effusion (9% vs 2%). The common grade ≥3 AEs were diarrhea (13% vs 20%) and thrombocytopenia (4% vs 13%). There was no significant difference in the incidence of AEs between the two groups.

Conclusion

Our single-center experience suggests that 70mg dose of dasatinib is non inferior & possibly better tolerated when compared to 100mg dose in CML-CP patients, while increasing compliance & reducing financial burden on patients.

Malignant Hematology-Clinical (MHC) OP-MHC-23

Treatment Outcomes of Pediatric & AYA Philadelphia-Positive Acute Lymphoblastic Leukemia Patients Using Upfront Generic Dasatinib & Augmented ALL IC-BFM 2009 Chemotherapy Protocol: A Single-Center Study

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Introduction

Philadelphia-chromosome positive(Ph+)ALL accounts for 3-5%-pediatric ALL & about 25% of adolescent & young adult(AYA)ALL patients.Herein we describe the outcomes in Ph+ALL treated with upfront generic dasatinib+ALL IC-BFM2009 chemotherapy protocol.

Aims & Objectives

To assess results of generic dasatinib+combination chemotherapy in pediatric & AYA Ph+ ALL with respect to morphological complete remission(CR),measurable residual disease(MRD) response,& leukemia relapse

Materials & Methods

The study enrolled treatment-naïve Ph+ALL patients of age 1-39 years between April-2019 & June-2024.The patients were treated as high-risk(HR) group as per ALL IC-BFM2009 protocol. All patients received generic dasatinib starting from day1 of induction chemotherapy till end of maintenance chemotherapy, with temporary dasatinib dose interruptions for toxicity as indicated.Dasatinib dose was 80mg/m2/day in children and 100-140mg/day in AYA patients. All patients received augmented early intensification & HRblocks for consolidation.Day33 bone marrow(BM) morphology & flowcytometric-MRD was performed.Complete remission was defined as BM blasts<5% without extramedullary disease, and the cutoff for flow-MRD negativity was<0.01%; molecular MRD assessment by bone marrow PCR for BCR-ABL1 could be done in selected patients due to resource constraints.

Result

Total 34 Ph+ ALL patients were treated. Median age was 16-years(range 3-39 yrs); male:female-1:1. At diagnosis, 53% had hyperleukocytosis,9% had bacterial sepsis,6% had invasive fungal infections,& 23% had CNS leukemia.Of the evaluable patients, 85%(28/33) achieved good steroid response (peripheral blood blasts<1000/µl) on day8 of induction, 81%(25/31) and 37%(11/30) achieved marrow M1 response(<5% blasts)

& flow-MRD<0.1% on day15, and 96%(26/27) and 74%(20/27) achieved morphological CR & negative flow-MRD on day33 respectively. There were 5-deaths in induction phase 1A.Out of 7-patients who had positive flow-MRD on day33, 4-patients(57%) achieved negative flow-MRD status on day78 after receiving augmented phase IB chemotherapy+dasatinib. Overall, 75% of evaluable patients achieved negative molecular MRD response(by BCR-ABL1PCR) during treatment. 2-underwent allogeneic transplantation for persistent MRD+ disease, of which 1 died of refractory CNS disease post-transplant.Two patients had relapse of leukemia on follow-up; however 1of them had defaulted treatment. None of the patients required permanent discontinuation of dasatinib due to toxicity.The causes of induction mortality were multidrug-resistant bacterial infections(n=4),& invasive fungal infections(n=1). The median duration of follow-up was 6.8(range 1-41) months. The median overall survival is 13.3 months.

Parameters	Total patients (n = 34)
Age (years)	
• Mean (SD)	16.7 (8.6)
• Median (IQR)	16 (14.5)
Male gender (%) , M:F=1:1	17 (50 %)
Total leukocyte count (x 10^9/L)	
• Mean	133
• Median (Range)	118 (1.3 - 521)
TLC subgroups (as per ALL IC-BFM 2009)	
• < 20 x 10^9/L	9 (26 %)
• 20 - 99 x 10^9/L	7 (21 %)
• ≥ 100 x 10^9/L	18 (53 %)
Hemoglobin (g/dl)	
• Mean	7.21 (2.5)
• Median (Range)	7.1 (1.2-13.2)
Platelet count (x 10^9/L)	
• Mean	57.7
• Median (Range)	40 (8 - 286)
Treatment status	
• Induction therapy completed	27 (79 %)
• Induction therapy ongoing	0(0 %)
• Induction therapy not completed	7(21 %)
- Due to death in induction	5
- Due to treatment discontinuation	2
Day 8 steroid response (n = 33)	
Good steroid response	28 (85%)
Poor steroid response	5(15%)
Day 15 BM Morphological Response (n = 31)	
• M 1 (Blasts < 5%)	25 (81 %)
• M 2 (Blasts 5% - < 25%)	2 (6 %)
• M 3 (Blasts ≥ 25 %)	4 (13%)
Day 15 BM Flow-MRD (n = 30)	
• < 0.1 %	11 (37 %)
• 0.1 - 10 %	15 (50 %)
• > 10 %	4 (13 %)
Day 33 Morphological Response (n = 27)	
• CR	26 (96%%)
• No CR	1 (4 %)
• Not available	7 out of 34
- Death before day 33	5
- Treatment discontinuation before day 33	2
Day 33 BM Flow-MRD (n = 27)	
• Negative (MRD < 0.01 %)	20 (74 %)
• Positive (MRD ≥ 0.01 %)	7 (26 %)
• Not available	7 out of 34
- Death before day 33	5
- Treatment discontinuation before day 33	2
Post induction BCRABL1 IS% RT PCR (n=16)	
• Not Detected	12 (75%)
• Detected	4 (25%)
• Not available	18
Current status of enrolled patients (n = 34)	
• Alive (and in CR)	20 (59 %)
• Dead	5 (15%)
• Treatment discontinuation / Lost to follow up	6 (17%)
• Relapsed	2 (6%)
• Refractory disease	1(3%)

Conclusion

In our single-center experience, use of generic dasatinib+intensive chemotherapy was associated with high CR & MRD negativity rates and encouraging survival outcomes in pediatric & AYA Ph+ALL patients without significant treatment-related toxicity.

Malignant Hematology-Clinical (MHC) OP-MHC-24

Transcript Profiling and its Impact on Survival in Acute Promyelocytic Leukemia (APL) patients

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Introduction

Acute Promyelocytic leukemia (APL) is a biologically and clinically distinct variant of AML resulted from translocation between chromosomes 15 and 17 t (15;17) with three distinct types of PML-RAR α hybrid transcripts viz bcr-1, bcr-2 and bcr-3.

Aims & Objectives

To investigate the Characteristics of APL patients, the distribution of PML-RARA isoforms, and Survival outcomes.

Materials & Methods

Retrospective analysis of APL patients treated at our institute from 2019 and 2023. Medical records were analysed. Kaplan-Meier analyses was used to determine the survival rates . The log rank test was applied to assess significance.

Result

63 patients were diagnosed as APL , subtyping was available for 51 patients , PML-RAR α bcr-1, bcr-2 ,bcr-3 transcripts were found in 36(70.5%),1(1.9%) and 12(23.5%)cases respectively of whom 56.8% were male, with a median age of 30 years (Range :8-74) and 20(39%) patients belonged to the High-risk group of which 13 (65%)patients had bcr1 variant and 7(35%) patients had bcr3 variant. Fever(74%) and bleeding (47%) were two most common presentation with mean Hb of 7.95 , WBC of 18020 , Platelet of 42881 . 4(7.8%) patients had additional FLT3 mutation, 3 of them associated with bcr1 and 1 with bcr3. 7(13.7%) patients had baseline infections and 14(27.4%) patients had Pneumonia during Induction . 46 (90.1 %) patients achieved complete remission and 5 (9.8%) deaths were reported during induction , 3 of them associated with bcr1 variant and 2 with bcr3 , all deaths happened in first two weeks of Induction. At a Median follow up of 3 years , 90 % of patients were alive .Median Overall Survival (OS) is not reached. No difference in survival between three transcripts (p value 0.7) and between low risk and high risk groups was identified (p value 0.9).

Conclusion

bcr1 was the most common transcript identified , risk stratified approach to treatment yielded good outcomes with similar outcomes in both risk groups and there was no impact of variants on Survival .

Malignant Hematology-Clinical (MHC) OP-MHC-25

Clinical Profile and Outcomes of Young Adults with Multiple Myeloma: A Decade Experience

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Introduction

Multiple myeloma is a disease of elderly and median age at diagnosis lies in sixth decade. Only 2% of patients with MM are less than 40 years of age. Indian data on this under represented population is scarce.

Aims & Objectives

To analyse the clinical profile, molecular characteristics and survival outcomes in young adults of age 18-40 years with multiple myeloma.

Materials & Methods

This is a single center, retrospective, observational study of young patients with multiple myeloma of age ≤ 40 years, treated at our institute from January 2014 to December 2023. Patient demographics, clinical characteristics, molecular profile, treatment details and outcomes were retrieved from case records. Kaplan-Meier method was used to estimate progression-free survival (PFS) and overall survival (OS).

Result

Out of 789 patients with multiple myeloma treated in the study period, 42(5.3%) were with age 18-40 years. The median age was 37 years (range: 20-40). Male to female ratio was 3.2:1. The most common presenting symptoms were bone pain (48%) and fatigue (16%). Anemia, renal impairment, hypercalcemia has been seen in 66.7%, 52.4%, 21.4% respectively. 31% patients had plasmacytomas at presentation. Light chain myeloma accounted for 25% of the evaluated cases. Significant proportion of patients were ISS stage III (52.4%).

Cytogenetic analysis by FISH was done in 23(55%) cases. Del 13q (30%) is the most common abnormality followed by gain 1q (17%). High risk cytogenetic abnormality was seen in 9(40%). VRd was the most used regimen 16(38%). With induction chemotherapy 26 patients (62%) had responses ≥ VGPR. Complete renal reversal at any point has been seen in 60% of cases with a median of 8 weeks. 43% patients underwent autologous HSCT. Median PFS was 35 months and Median OS was 92 months. Patient undergoing ASCT had numerically significant median PFS (35 vs 30months) and median OS (NR vs 50months).

Conclusion

Multiple myeloma younger than 40 years, constitute higher proportion of patients in India compared to the western literature. Higher stage & presence of renal impairment at presentation were more common in young myeloma patients. Light chain myeloma & plasmacytoma were more frequently seen in this age group. Despite association of more high risk features at presentation, survival seems to be comparable in young adults when compared to elderly patients.

Malignant Hematology-Clinical (MHC) OP-MHC-26

Panhypopituitarism and Osteolytic Lesions: A Rare Presentation of B-Lymphoblastic Lymphoma

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Background

B-lymphoblastic leukemia/lymphoma comprises of 2% of lymphoid neoplasms with 10% of which being B-LBL. B-LBL most commonly involves skin, soft tissue, bone and lymph nodes. When both medullary and extramedullary involvement is there, percentage of marrow blasts distinguishes B-LBL from B-ALL.

Case Presentation

A four years male child presented with complaints of abdominal distension, pain and constipation along with polyuria and polydipsia for one month. There were three episodes of unprovoked seizures for which he was getting anticonvulsants. On examination there was no palpable mass or organomegaly. His hemogram was haemoglobin-11g%, WBC-8800/mm3and platelet-3.6lakhs/mm3. Ultrasound showed mesenteric adenitis.

Diagnosis

CECT abdomen revealed multiple abdominal lymph nodes along with diffuse lytic areas noted in entire vertebral column and right iliac bone.

His serum osmolality was greater than urine osmolality suggestive of diabetes insipidus. TSH level was 0.55 mIU/L (0.7 to 4.5). Morning cortisol was 1.6 mcg/dl (2.9-19.4). He was started on desmopressin 0.1mg nasal spray and Eltroxin 25mcg once daily. Whole body FDG PET showed multiple metabolically active discrete bilateral cervical nodes, enlarged paraaortic, aortocaval, retrocaval and right external iliac lymphnodes and multiple areas of metabolic activity along bonemarrow with lytic and sclerotic lesions in sphenoid, multiple cervical and dorsolumbar vertebrae, right hemipelvis, bilateral humeri, femur and tibia.

Bilateral bonemarrow examination was done. Right side aspirate showed 18% blasts positive for Tdt, CD20,CD19,CD79a,PAX5 and negative for CD3,MPO,CD1a and S100. Left side aspirate was normal.

He also developed right sided LMN facial palsy and right ear discharge. MRI brain showed T2/FLAIR hyperintensities in right frontal lobe and bilateral dendate nucleus of cerebellum. CSF analysis showed lymphoblasts. The diagnosis of B-lymphoblastic lymphoma with CNS disease was made

Treatment

He was started on High risk BFM 2002 protocol. His postinduction marrow was MRD negative and CSF was negative for blasts. He is on Protocol M at present. He is continuing desmopressin and eltroxin.

Follow-up

Cranial irradiation is planned after phase II.

Conclusion

Diabetes insipidus, ear discharge and lytic bone lesions in this age group were all in favour of Langerhan cell histiocytosis. B-LBL presenting as bone and CNS disease is rare with only a few cases being reported. However, B-LBL should also be considered in the differential diagnosis as treatment and prognosis of it is different from that of the former condition.

Malignant Hematology-Clinical (MHC) OP-MHC-27

Response Assessment of Generic Tyrosine Kinase Inhibitors in Newly Diagnosed Chronic Myeloid Leukemia- Chronic Phase Patients- A Prospective Study in A Tertiary Care Centre in North East India

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Introduction

Chronic myeloid leukemia is characterized by the translocation t(9;22) (q34;q11), which causes the fusion of BCR and ABL1 genes into the pathogenic BCR-ABL1 oncogene. However, certain patients do not respond to therapy since additional resistance mechanisms like BCR-ABL KD mutations gets activated. With the availability of generic TKI's since 2003 and because of the marked reduction of cost of treatment, they are now the choice of frontline therapy in CML.

Aims & Objectives

To look into the response of generic tyrosine kinase inhibitors in Chronic myeloid leukemia patients and the prevalence of kinase domain mutation who are on generic tyrosine kinase inhibitors.

Materials & Methods

Relevant data of 85 newly diagnosed chronic myeloid leukemia patients in chronic phase were collected over a period of 18 months. Response assessment was done by measuring bcr-abl level at 3,6 and 12 months after starting the patients on generic tyrosine kinase inhibitors. In case of sub optimal response or failure to therapy patients were analysed for bcr-abl kd mutation analysis

Result

Out of 85 patients, based on ELTS score 51(60%) patients were stratified intod intermediate risk, 3(3.5%) into high risk and 31 patients (36.4%) into low risk. MMR was achieved at 12 months in 60 cases (70.5%). In this study, out of 25 cases who did not achieved major molecular response 11 cases (44%) were positive positive for KD mutation. The most common KD mutation was F317L in 5 (45.4%) of the cases.

Conclusion

It highlighted treatment strategies in chronic myeloid leukemia, shedding light on the advantages of using generic tyrosine kinase inhibitors in settings with limited resources and the prevalence of KD mutation in North eastern India.

Malignant Hematology-Clinical (MHC) OP-MHC-28

Unusual Presentation of Diffuse Large B Cell Lymphoma

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Introduction

Diffuse large B-cell lymphoma (DLBCL) is an aggressive, rapidly growing type of NHL constitutes approximately 30% of all NHLs. DLBCL can begin in the lymph nodes or in extranodal sites such as the CNS, GIT, liver, bone or basically any organ of the body.

Aims & Objectives

To observe varied and unusual presentation of Diffuse Large B cell Lymphoma

Materials & Methods

Patient coming to hematology OPD in Sir Sunderlal Hospital were screened. Patient with high suspicion of lymphoma on the basis of history and examination were selected and underwent through diagnostic test for the diagnosis.

Result

CASE 1

A 32/F with chief complaints Low back ache since 1 year. MRI SPINE showed multifocal areas of abnormal T2 hyperintesities at L3 and paravertebral soft tissue swelling present. Histopathology Biopsy from paravertebral mass composed of cells arranged in sheet with hyperchromatic nucleus, distinct nucleoli and scant cytoplasm. On IHC CD 20, MUM1, BCL 2 and BCL 6 was positive.

CASE 2

28/M presented with progressive Left eye swelling since 10 months. on examination Mass from left upper outer corner of eye pushing eyeball down was present. CECT orbit showed Heterogenously enhancing lobulated mass lesion in medial aspect of left orbit. Biopsy from lacrimal sac showed poorly differentiated sheets of cells with increased nucleocytoplasmic ratio. IHC showed CD 2, MUM1, BCL 2, BCL 6 positivity.

CASE 3

A 52/F presented with progressive dysphagia since 6 months. USG neck a heterogenous mass was arising from behind of tonsillar fossa. Biopsy from mass showed poorly differentiated sheets of cells. IHC showed CD 19, CD 20, MUM1,BCL 2, BCL 6 positivity.

CASE 4

A 39/M presented with swelling over chest and left shoulder for 3 months. CECT thorax showed heterogenous mass is arising from sternum destroying anterior sternal wall and similar mass arising from scapular region. Biopsy showed cells arranged in sheets and cords which are moderate to large sized with anisonucleosis, irregular membranes suggestive of undifferentiated neoplasm. On IHC CD20, BCL 2, BCL 6 was positive.

Conclusion

DLBCL remains the commonest (44%) lymphoma subtype and is curable by standard anthracycline- and rituximab-based therapies. Suspicion of lymphoma should be there even if patient is not having classical picture of lymphnode enlargement

Malignant Hematology-Clinical (MHC) OP-MHC-29

BOMBR: A Deep Learning Approach Based Dataset for Automated Reticulin Fiber Detection and Quantification in Bone Marrow Biopsies

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Introduction

Bone marrow reticulin fibrosis is associated with varied benign and malignant hematological conditions. The assessment of reticulin fibrosis is important in diagnosis, prognostication and management of such disorders. The current methods for quantification of reticulin fibrosis are time-consuming, and high high inter-observer variability and poor reproducibility. There is a scope for artificial intelligence empowered automated tools for accurate and consistent quantification of reticulin. However, lack of standardized datasets has hindered the development of such tools.

Aims & Objectives

In this study, we address the lack of annotated data sets and propose the Bone Marrow Biopsy images for Reticulin (BoMBR) dataset images for predicting fibrosis grades, showcasing the potential of our dataset in aiding clinical diagnosis and research

Materials & Methods

We present a comprehensive dataset consisting 201 semantic-segmented bone marrow biopsy images, which were meticulously annotated for semantic segmentation, with the focus on performing reticulin fiber quantification. Preliminary delineation of the reticulin fibers alongside rough annotation of other cellular components such as bony trabeculae, fat, and cells was done with the aid of Deep Learning (DL) models and image processing techniques. This was followed by annotation refinement by two experienced hematopathologists using Computer Vision Annotation Tool (CVAT). The performance of this model was then tested on a separate cohort of images.

Result

The classification report summarizes the performance metrics of our classification model across four grades of fibrosis. The Accuracy row indicates the overall accuracy of 70% for the model, demonstrating its effectiveness in classifying bone marrow biopsy images.

Conclusion

This is by far the first such publicly available resource for annotated BMT images that focuses on reticulin fibrosis both globally and in the context of the Indian subcontinent. It provides a foundation for developing robust DL models capable of accurate fibrosis grading. While acknowledging current limitations, ongoing and future research efforts will continue to refine and validate these models, ultimately aiming to improve clinical decision-making and patient outcomes in bone marrow evaluation.

	Precision	*Recall*	*F1-score*	*Support*
MF 1	0.63	0.85	0.72	20.0
MF 2	0.00	0.00	0.00	5.0
MF 3	0.74	0.82	0.78	17.0
Accuracy	-	-	0.70	50.0

Malignant Hematology-Clinical (MHC) OP-MHC-30

Incidence of Cytogenetic Abnormalities and Recurring Mutations in Chronic Lymphocytic Leukemia – A Single Centre Study

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Introduction

Chronic lymphocytic leukemia (CLL) is an uncommon malignancy in India, compared to the west. Genetic aberrations & recurrent mutations in CLL have a pathogenic as well as prognostic significance in the disease biology. In this study, we present the incidence of genetic aberrations and recurring mutations in newly diagnosed CLL patients at our centre.

Aims & Objectives

To describe the incidence of specific cytogenetic abnormalities and targeted gene mutations in newly diagnosed CLL.

Materials & Methods

This study includes the data of 95 patients of newly diagnosed CLL in our institute from 2020 to 2024. Hematological parameters, and Rai & Binet staging were noted. Interphase Fluorescence in situ Hybridization (FISH) was performed in peripheral blood lymphocytes to identify specific cytogenetic abnormalities including deletion 13q, deletion 11q, trisomy 12 & deletion 17p. Next Generation Sequencing was conducted to identify the mutational status of Immunoglobulin Heavy Chain (IGHV), TP53, ATM, NOTCH 1, MYD88, SF3B1, & FBXW7 genes.

Result

Data of total 95 patients are available in this period. FISH study was done in 94 patients. The most common abnormality was deletion 13q (71% patients), followed by trisomy 12 (27%), & deletion 11q (21%), while deletion 17p was the least common (14%). All the four abnormalities were positive in one patient and 14% patients had no abnormality. Out of 82 patients, IGHV was hypermutated in 55% patients (n=45) & unmutated in 43% (n= 35) patients, and undetermined in 2. The incidence of TP53 mutation was 7%, NOTCH 1 was 17%,

Table 1: Clinical, genetic and mutational profile of patients

Number of patients			n = 95		
Median Age			61 (range 26-85) years		
Gender			Male: 69 (73 %) Female: 26 (27 %)		
Baseline haematological parameters:					
Total leukocyte count (x 10^9/L)			Median 85.7(range2.11 - 408.5)		
Platelet count (x 10^9/L)			Median 124 (range1.66- 512)		
Hemoglobin (g/dl)			Median 10.8(range3.6 - 15.4)		
Rai stage	n	%	**Binet stage**	N	%
0	17	18	A	27	28
1	14	15	B	28	30
2	23	24	C	40	42
3	23	24			
4	18	19			
FISH STUDIES (N=94)		N		%	
Deln 13q positive		60		64	
Deln 11q		20		21	
Trisomy 12		25		27	
Deln 17 p		13		14	
IGHV MUTATION STATUS (N=82) MUTATED – 55% (N=45) UNMUTATED – 43% (N=35) UNDETERMINED 2% (N=2)			**TP53 MUTATION STATUS** (N=70) MUTATED – 7 % (N=5) UNMUTATED – 93% (N=65)		
NOTCH 1 MUTATION STATUS (N=70) MUTATED – 17% (N=12) UNMUTATED – 83% (N=58)			**ATM MUTATION STATUS** (N=70) MUTATED – 5% (N=4) UNMUTATED – 95% (N=66)		
FBXW7 MUTATION STATUS (N=70) MUTATED – 4% (N=3) UNMUTATED – 96% (N=63)			**MYD88 MUTATION STATUS** (N=70) MUTATED – 3% (N=2) UNMUTATED – 97% (N=68)		
SF3B1 MUTATION STATUS (N=70) MUTATED – 9% (N=6) UNMUTATED – 91% (N=64)					

MYD888 was 3%, SF3B1 was 9%, ATM was 6% & FBXW7 was 4%. 50% of NOTCH 1 mutated & 66% of TP53 mutated patients had Rai III-IV stage at presentation. Details are given in Table 1.

Conclusion

There is limited data regarding the incidence of mutational abnormalities in CLL in India. In our study, deletion 13q followed by trisomy 12 were the most common cytogenetic abnormalities, in concordance with the western literature. However, more patients had deletion 17p and NOTCH1 mutations than those population from the west. Further studies are required to determine their effect on survival and response to treatment.

Malignant Hematology-Clinical (MHC) OP-MHC-31

A retrospective study of light chain Amyloidosis in the current era: A Tertiary Care center experience from Northern India

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Introduction

Despite significant progress and improving outcomes in the management of plasma cell disorders, AL amyloidosis remains diagnostically and therapeutically challenging. With the availability of serum-free light chain assay, more cases of AL amyloidosis are being diagnosed who were earlier missed as secondary amyloidosis. Novel agents like bortezomib are being used in almost all the patients. There is lack of published data from India about diagnosis and outcome of AL amyloidosis in current era.

Aims & Objectives

To study the clinical profile and treatment outcomes in AL amyloidosis.

Materials & Methods

A retrospective analysis of AL amyloidosis patients who were diagnosed in our hospital from January 2016 to September 2024 was done. Demographic, laboratory and treatment outcome data were collected from the departmental database. The haematological response was assessed as per international consensus guidelines for AL amyloidosis. The median follow-up and median overall survival of the patients was calculated in months.

Result

Sixty-nine patients were diagnosed with AL amyloidosis. Out of these 51 (74%) were males and 18 (26%) were females with a median age of 59 years (39-81 years). In 74% (51/69) of cases, the amyloid light chain type was lambda light chain while in 26% (18/69) it was kappa. The most common organs involved were the kidneys in 55% (38/69) cases, followed by heart in 51% (35/69), and two or more organs were involved in 38% (26/69) of patients. All were treated with bortezomib-based protocols.

Forty-nine patients (71%) who received treatment at our hospital were available for follow-up and were included in the survival analysis. A complete hematologic response was seen in 20/49 (41%), partial response in 18/49 (37%) and 11/49 (22%) had no response or progressive disease to first-line therapy. The median follow-up duration was 13 months (6 months to 76 months). Twenty-seven patients are alive; while 22 (47%) succumbed due to amyloid-related complications. The median OS was 35 months, with survival rates of 70%, 55% and 45% at 1, 2 and 3 years, respectively. Cardiac involvement (51 months vs. NR), Mayo stages III & IV (36 months vs. NR), and less than partial response to induction chemotherapy (3 months vs. 35 months) was associated with poorer survival. There was no difference in overall survival between AL amyloidosis with and without underlying myeloma.

Conclusion

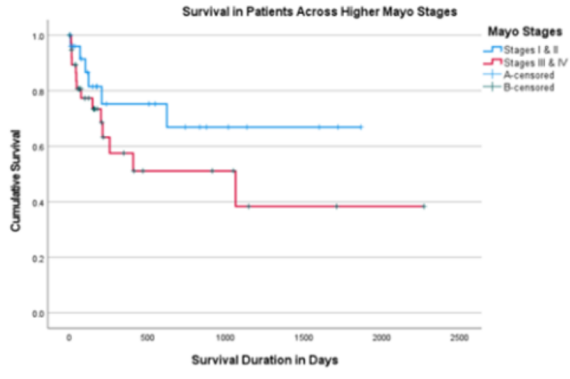
Serum free light chain assay in appropriate clinical syndrome setting clinches the diagnosis in majority of patients. Fat pad and rectal biopsy demonstration of amyloid deposit helps in tissue demonstration of amyloid if affected tissue biopsy is not available. The overall prognosis of patients with multi-organ involvement and patients with reduced cardiac ejection fractions remains poor. Patients who achieve complete hematologic response experience improved organ function and survival.

Figure 1 A Survival according to response to therapy

P=0.023 (1064 days vs. NR)

Figure 1B Survival across various Mayo stages

P=0.168, but, median OS 1064 vs. NR



Malignant Hematology-Clinical (MHC) OP-MHC-32

Venetoclax in Treatment of Refractory ETP-ALL: A single center experience

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Introduction

Early T-cell precursor acute lymphoblastic leukemia (ETP-ALL) is a highly aggressive subtype of T-ALL characterized by the abnormal expression of myeloid/stem cell antigens. ETP-ALL responds poorly to conventional induction chemotherapy and has a lower remission rate, higher recurrence rate, and worse prognosis than other types of T-ALL. Interestingly, cells from the ETP-ALL subtype are especially sensitive to BCL2 inhibition, suggesting that Venetoclax is a potentially effective drug for the treatment of this adverse risk subgroup.

Aims & Objectives

To study the role of Venetoclax in the patients of refractory ETP-ALL to achieve remission.

Materials & Methods

A retrospective review of patients diagnosed as ETP-ALL who were treated with adult ALL Chemotherapy protocol regimen along with Venetoclax was done and data was collected from inpatient records.

Result

All the 3 adult patients presented with fever, weakness and lymphadenopathy. On investigations, CBC showed Anemia with Leucopenia in all cases. Bone marrow aspiration and biopsy were performed in all the 3 cases, which showed presence of blast population with 78%, 62% and 80% respectively and diagnosis of ETP-ALL was made withImmunophenotyping.

With this diagnosis, all the patients were treated with adult ALL chemotherapy protocol which included weekly Daunorubicin, Vincristine and Dexamethasone. After 3 weeks of treatment, there was persistence of blasts in Peripheral blood smear with no hematological recovery. So in view of refractory disease, they were treated with Venetoclax.

One patient underwent haploidentical Allogenic HSCT and 14 months post transplant, he is in complete remission with negative MRD.

Second patient in the series had a complicated course with PCP Pnuemonia and succumbed to death.

The third patient went into complete remission with negative MRD and now planned for Allogenic HSCT.

Conclusion

As ETP-ALL is high risk disease, so to achieve remission,Venetoclax should be used as frontline therapy with conventional chemotherapy regimen.

There is need to conduct large, randomized control trials to compare Venetoclax with conventional chemotherapy regimen in ETP-ALL to validate the same.

Malignant Hematology-Clinical (MHC) OP-MHC-33

Practical Value of CD48 In T - Acute Lymphoblastic Leukemia MRD - Using 13-Color Multi Parametric Flow Cytometry

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Introduction

CD48 is an immunoglobulin superfamily receptor expressed on the surface of mature T-cells and NK-cells. It has been reported to be downregulated in T-ALL blasts and suggested to be useful marker in T-MRD. However, data on the utility of CD48 in T-ALL MRD monitoring is scarce and there is a need to evaluate its additional value in real world practice.

Aims & Objectives

To establish the practical value of CD48 in T-Acute lymphoblastic leukemia at diagnosis and MRD by using 13-colour multiparametric flow cytometry.

Materials & Methods

CD48 expression was studied in 217 samples including 27 diagnostic and 185 MRD from T-ALL patients. Samples were processed by bulk-lyse stain method, acquired using DxFLEX and analysed with Kaluza-software. Cells were stained with 13-color antibody panel that includes sCD3, cyCD3, CD4, CD5, CD7, and CD8, CD16/CD56, CD34, CD38, CD45, CD48, CD94 and CD161. Additional value of CD48 was studied and compared with conventionally standardized T-MRD approach.

Result

In 27 diagnostic samples, the CD48 expression was negative/downregulated in 24/27 cases (88.88%) with the median (range) proportion of CD48-negative blasts of 98.39% (62.23-100%).

Of 185 TMRD samples, 96 (51.89%) were MRD-positive using conventionally approach with median MRD of 0.23% (0.0009-87%). In MRD-positive samples, complete loss of CD48 expression was noted in 66/96(68.42%) and partial loss in 13/96(13.54%), thus supported the MRD detection in 81.96%. In 10 MRD-positive samples, the MRD was highly suspicious and loss of CD48 helped to confirm it. Notably, in 11 MRD-

positive samples, the downregulation of CD48 expression had identified MRD in false negative samples with conventionally approach and hence it was the main marker to identify MRD.

Of 90 MRD-neg samples,18/90(20%) showed downregulation of CD48 in normal T/NK cells with median of CD48-negative cells 0.44% (0.0002-3.38%) which could result in false-positive MRD and was avoided using conventional approach.

Conclusion

CD48 has a definite additional value in TMRD monitoring. It should be interpreted cautiously with conventional T-MRD panel that essentially includes CD4, CD5, CD8, and CD38.

Malignant Hematology-Clinical (MHC) OP-MHC-34

Immunophenotypic Characterization of Normal Hematopoietic Stem Cells using 16-color Multiparametric Flow Cytometry (MFC)

Sanjoli Chugh
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Introduction

A combination of CD34 and CD38(CD34p and CD38 pos/neg) allows evaluation of earliest hematopoietic precursors, referred to as hematopoietic stem cells(HSCs). Immunophenotypic aberrancies in stem-cell compartment, known as "leukemic stem cell–based MRD", is an extension of MFC-MRD in AML cases. Few recent publications have described the benefits of additional markers (CD45RA, CD371, CD7, CD56, CD22) to identify abnormal HSCs as a part of MRD evaluation.

Aims & Objectives

Immunophenotypic characterization of normal HSCs to differentiate from abnormal HSCs (LSC).

Materials & Methods

We studied immunophenotype of normal HSCs in uninvolved staging bone-marrows in 21 patients including lymphoma and solid malignancy cases. The samples were processed using bulk-lyse stain method, acquired using LSRFortessa and analysed with Kaluza-Version2.2.1.The HSCs were evaluated by using 16-colour MFC including CD7, CD10, CD15, CD19, CD20, CD22, CD33, CD34, CD38, CD45, CD45RA, CD64, CD117, CD123, CD371 and HLADR. However, CD45RA and CD22 are known to express in normal B-cell precursors, hence we studied the expression pattern of these markers in normal HSCs to avoid errors in MRD evaluation.

Result

Twenty-one patients aged(12-69 years) with M:F(1.3:1) were studied. The median and mean of CD34 positive hematopoietic precursors were 1.25% and 1.65%(0.08%-8.87%); of which 27.31% were HSCs. The hematogones were separated from CD34 hematopoietic precursors by using CD19. The HSCs express bright CD34, dim-negCD38, mod-dimCD117 and CD33, variable HLADR, negative CD7, CD123, CD15, CD64 and CD371. A subset of HSCs with mean and median of 10.11% and 5.52%, showed co-expression of CD45RA and CD22 in 100% cases along with dim-neg expression of CD10 in 90.4% cases with median MFI of 0.77 and dim-neg expression of CD20 in 76.2% cases with median MFI of 0.42. The mean and median MFI of CD45RA in CD22 positive HSCs was 3.32 and 2.49, while in CD22 negative HSCs was 0.59 and 0.3, respectively. The expression of CD45RA significantly correlated with positivity of CD22 ($p<0.0001$); thus indicating the HSCs of early lymphoid precursors (37706583, Chatterjee et al.)

Conclusion

In our study, we found that normal HSCs include a component of early precursors B-cells expressing CD45RA, CD22, dim-neg CD10 and CD20, hence these 4 markers should not be used as aberrancies to define abnormal HSCs.

Malignant Hematology-Clinical (MHC) OP-MHC-35

Minimal Residual Disease Assessment by Multiparameter Flow Cytometry and its Association with Cytogenetic Abnormalities in Cases of Multiple Myeloma

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Introduction

Cytogenetic abnormalities are crucial prognostic indicators in multiple myeloma. While patients with both standard- and high-risk cytogenetics exhibit similar treatment sensitivities, those with high-risk cytogenetics tend to have shorter survival times despite achieving comparable complete response (CR) rates. This raises concerns about using CR as a treatment endpoint, particularly for patients with high-risk cytogenetics, and suggests that minimal residual disease (MRD) assays, which quantify disease burden, may provide better prognostic insight. MRD negativity, especially in patients with high-risk cytogenetics, has been associated with improved outcomes. This study evaluates MRD responses using multiparameter flow cytometry in multiple myeloma patients with both standard- and high-risk cytogenetic profiles.

Aims & Objectives

To assess minimal residual disease using multiparameter flow cytometry in patients with multiple myeloma.

1. Correlation of MRD with cytogenetic abnormalities in multiple myeloma.

2. Correlation of MRD with International Myeloma Working Group (IMWG) response criteria.

Materials & Methods

This prospective observational study was conducted at Dr. B.L. Kapur Memorial Hospital between August 2022 and October 2023, involving 31 multiple myeloma patients post-induction chemotherapy or prior to HDT-ASCT. MRD was assessed using multiparameter flow cytometry, and data were analyzed using SPSS version 22.0. Logistic regression was not applied due to the sample size limitations.

Result

In this study of 31 patients with multiple myeloma, 80.64% were under 65 years, and 58.06% were male. IgG Kappa (48.38%) was the most common immunoglobulin subtype. There were significant associations between cytogenetic risk ($P=0.027$), IMWG response ($P<0.001$), IFE ($P<0.05$) and M band presence ($P=0.003$) with MRD status. Additionally, disease relapse was more frequent in MRD-positive patients ($P=0.023$), and plasma cell percentage in bone marrow was significantly higher in MRD-positive cases ($P=0.013$).

Conclusion

This study underscores the importance of MRD assessment, particularly in high-risk multiple myeloma. The findings suggest that MRD negativity correlates with better outcomes and serves as a more accurate measure of disease burden than CR. Further research with larger cohorts is needed to confirm these results and solidify MRD's role in treatment decision-making.

Malignant Hematology-Clinical (MHC) OP-MHC-36

MRD Assessment Post Induction Therapy in Acute Myeloid Leukemia – A Tertiary Care Center Experience

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Introduction

Acute myeloid leukemia is a clinically and genetically heterogeneous disease with a variable response to therapy. Currently risk stratification is determined by several factors assessed at diagnosis. Increasing evidence now indicates that the Measurable residual disease (MRD) is a measure of impending relapse and offers a therapeutic window to modify treatment

Aims & Objectives

Our study aims to assess the MRD Status in newly diagnosed AML patients at end of induction chemotherapy (standard 7+3 regimen) and its correlation with Overall Survival (OS) and Relapse free survival (RFS) in MRD positive and negative groups at one year.

Materials & Methods

We included 65 newly diagnosed adult AML patients (2021-2022). At the end of induction chemotherapy, BM samples were collected to monitor MRD by using three-Laser eight-color BD FACS CANTO II flow cytometer. Any level of MRD >0.1% was considered positive and <0.1% is negative. Patients were followed up for 1 year. Relapse free survival and overall survival were correlated with MRD status.

3.CORELATION BETWEEN MRD AND RELAPSE AT 1 YEAR

		MRD DAY 28		Total	P - value
		MRD NEGATIVE [N=41]	MRD POSITIVE [N=24]		
RELAPSE	No Relapse	36 (87.8%)	16 (66.7%)	52 (80%)	
	Relapse	5 (12.2%)	8 (33.3%)	13 (20%)	0.040*

4.CORELATION BETWEEN MRD AND OVERALL SURVIVAL AT 1 YEAR

		MRD DAY 28		Total	P - value
		NEGATIVE [N=41]	POSITIVE [N=24]		
OVERALL SURVIVAL	Alive	34 (82.9%)	17 (70.8%)	51 (78.5%)	0.252
	Dead	7 (17.1%)	7 (29.2%)	14 (21.5%)	

Result

Our cohort of patients included 33 males and 32 females. Of 65 patients, at the end of induction chemotherapy, 37% (n-24) were MRD positive and 63% (n-41) were MRD negative. Relapse at 1 year was 33 % (n-8) in the MRD positive group, compared to 12% (n-5) in negative group, (P value <0.040) which is significant. Overall Survival (OSS) and Relapse free survival (RFS) was 70% and 66% respectively, in MRD positive group, which is inferior when compared to (82%-OSS and 87%-RFS) MRD negative group. In our study, 31/65 patients (47%) underwent stem cell transplants and most were haplo-identical followed by Matched Sibling transplants.

Conclusion

Several factors influence MRD status and the subsequent outcomes of patients with AML, including the chemotherapy intensity, infection, HSCT application, donor availability and survival. In summary, our results indicate that MRD status could be used, not only as a potent predictor of outcomes, but also as an indicator of optimal subsequent treatment strategies for patients with de novo AML in CR1

Malignant Hematology-Clinical (MHC) OP-MHC-37

Study of Immunophenotypic Signature of Anti-CD19 Cart Cells During Initial Expansion Phase in Paediatric Ball Cases Receiving Cart Therapy

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Introduction

Chimeric antigen receptor (CAR)-T-cell therapy is considered as a major scientific breakthrough in cancer immunotherapy. Adoptive immunotherapy using CAR-T cells has achieved successful remissions in refractory B-cell leukemia and lymphomas. In order to estimate both success and side effects of CAR-T-cell therapies, monitoring of patient's immune profile including immunophenotypic signature of CAR-T cells is highly desirable. We analysed immunophenotypic signature of anti-CD19-CAR-T cells in the initial expansion phase of paediatric relapsed/refractory B-ALL cases receiving CAR-T therapy.

Aims & Objectives

To study the immunophenotypic signature of Anti-CD19 CART cells during initial expansion phase in paediatric BALL cases receiving CART therapy.

Materials & Methods

Immunophenotypic signature of anti-CD19-CAR-T-cells were studied in peripheral blood (n=60) and bone-marrow (n=12) samples from 12 B-ALL-patients using 14-color multi-parametric flow-cytometry (MFC) assay with CD3,CD4,CD8,CD19,CD20,CD45,CD62L, CD45RA,CD45RO,CD197 and Protein-L. We evaluated functional subsets of anti-CD19-CART-cells including naïve (Nv), effector memory (EM), central memory cells (CM) and terminal-effector-CD45RA+ (TERA) subsets in the product and patient's samples at different time-points i.e. Day-3,5,7,14 and 28 during first month of therapy.

Result

Median (range) of CAR-T-cells in the product, Day3, Day5,Day7,Day14 and Day28 was 44.54(13.04-96.51),15(1.11-29.02),15.35(6.33-60.95),40.81(6.8-84.48),65.14(7.65-99.19) and 16.53(8.42-47.73)% respectively. Similarly, the median CD4:CD8 CAR-T cells was 0.70,0.78,0.93,0.60 and 0.87. Fig.1a illustrated the dynamics of CAR-T cells, showing that their basal level (i.e.day 3-5) was minimum. However, the expansion started around 14th day and reduced at day 28. On further analysis of CAR-T functional subsets, we

noted that at all time points, majority of CAR-T cells belonged to EM cells(median across all time points were 57.29, 53.94 ,53.17 ,79.39 ,87.21 and 70.52) which was maximum during the peak expansion of CART cells. (Fig.1b).

Fig.1a

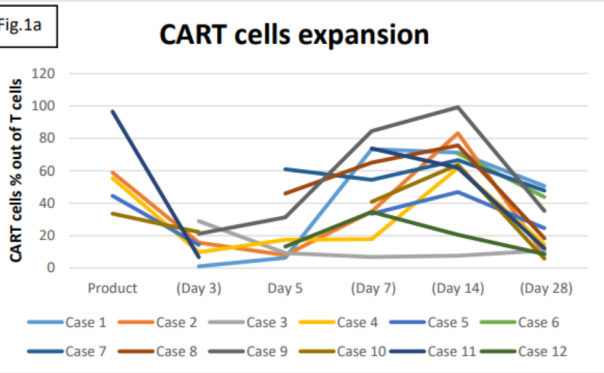
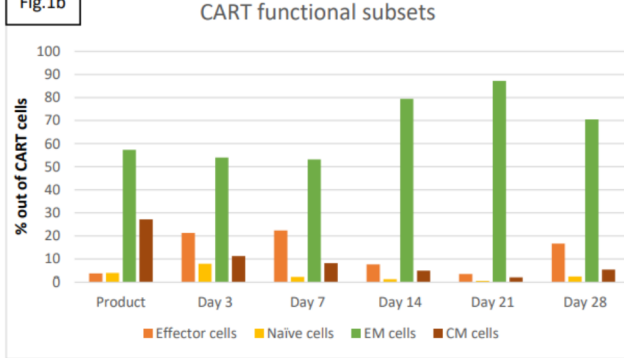


Fig.1b



Conclusion

Our study showed that the percentage of CAR-T cells was maximum around day 14-indicating that maximum expansion takes place in 2nd week of infusion. We also note that CAR-T cells are predominantly composed of functionally active EM cells during the peak expansion indicating its highest anti-tumor activity against CD19+ cells.

Malignant Hematology-Clinical (MHC) OP-MHC-38

Evaluation of Measurable Residual Disease by High Sensitive Multicolor Flowcytometry in a Newly Diagnosed Multiple Myeloma Following Induction Therapy in a Tertiary Care Center

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Introduction

Relapsing-remitting multiple myeloma (MM) is an incurable disease. It is typified by the neoplastic growth of clonal plasma cells that produce an excess of light chains, monoclonal immunoglobulin, or both, frequently leading to multiple target organ damage. Minimal Residual Disease (MRD) assessment has become a pivotal factor in the management and prognosis of multiple myeloma (MM), particularly for newly diagnosed patients. The depth of MRD negativity—meaning the degree to which these residual cells are reduced-has profound implications for predicting patient outcomes and guiding subsequent treatment decisions. Recent studies underscore that achieving MRD negativity is strongly associated with improved long-term survival and prolonged progression-free survival

Aims & Objectives

AIM :- to assess the utility of MRD in prognosticating the disease.

Primary objectives: 1) to assess the measurable residual disease in newly diagnosed patients of multiple myeloma by high sensitive flowcytometry

Secondary objectives: 2) to correlate it with serological response after 4cycles of therapy.

3) to correlate MRD levels with baseline clinical presentation, karyotype by FISH and conventional cytogenetics.

4) to correlate the MRD with event free survival (death, early relapse)and progression free survival of patients for 12months

Materials & Methods

Period of study – 1year

time period for assessment of MRD- at 4months and to have serological follow up at 8months and 12months

Inclusion Criteria:-
1) all patients attending OPDs and IPDs who are newly diagnosed as multiple myeloma.
2) Patients receiving different therapy like RVd, VTd, Rd, CyBorD, Dara based regimens.

Exclusion Criteria:-
1) those who are having secondary co-existing malignancy2) those who are having primary AL amyloidosis.

Result

Out of 85 patients evaluated, 3died before starting the treatment. Our study showed a male preponderance 46cases(54%), with a median age of 62yrs. Our study showed, IgG kappa (54%)being the most commonly involved Immunoglobulin and light chain. maximum patient had no cytogenetic abnormalities(44%), evaluated by FISH and conventional cytogenetics, followed by Del13q being the 2nd most common cytogenetic abnormality. At the end of 12months, 33 cases achieved sCR, 24 cases achieved VGPR,12 had partial response, 4had stable disease. 3cases had relapse, while on therapy. Out of 85 cases, MRD assessment was done on only 30cases due to financial constraints. of those 30cases 18were MRD negative and 12 are MRD positive. Of those MRD positive, 10cases were in VGPR and 2 are in sCR. Those with MRD negative all 18cases were in sCR.

Conclusion

Though a very small number but those with MRD negative had a good progression free and event free survival.

Malignant Hematology-Clinical (MHC) OP-MHC-39

Assessment of Early Outcome and Optimising Infrastructural Utilisation of The Dynamic Risk-Stratification Based ICICLE-Protocol for Management of Childhood All in Resource Poor Tertiary Care Centre

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Nil Ratan Sircar Medical College and Hospital

Introduction

Acute Lymphoblastic Leukemia (ALL)-the most common paediatric cancer with cure-rate exceeding 80% in developed countries, lags at around 50% in India. Induction mortality following high-dose chemotherapeutic regimen is an important contributor to dismal cure-rate in India, the other causes being relapse, treatment interruption and non- adherence to planned protocol. This is amplified by limited and poor infrastructure in resource-poor public hospitals. To overcome such predicament, the ICiCLe protocol employs a less-intensive regimen with customised intensification on the basis of FISH and MRD based restratification. Implementation of this protocol in resource constrained set-up of Nil Ratan Sircar Medical College and Hospital (NRSMCH) aims not only to evaluate improvement in outcome but to optimize the available infrastructure. Here we are presenting the early outcome of the said protocol.

Aims & Objectives

- To assess the early outcome of the ICiCLe protocol.
- To evaluate the available infrastructural utilisation.

Materials & Methods

1. Screening of patients (age: 1-18 years) with suspected acute leukemia
2. Confirmation of diagnosis by immunophenotyping 3. Restratification by triple-probe FISH 4. Initiation of ICiCLe protocol 5. Post-induction evaluation of patient outcome and MRD based final risk-stratification.

Result

Of the 29 enrolled patients, BCP-ALL comprised 93% and T-ALL-7%. By triple-probe FISH, 7% patients were positive for ETV6-RUNX1 and BCR-ABL1 respectively. At start, 39% of patients assigned to SRG, 43% to IRG and 18% to HRG. At Day 8, 93% showed prednisolone-good-response and 07% prednisolone-poor-response resulting in their restratification to the HRG. At end of induction, 96% had complete morphological remission, of which 48% were MRD positive. In SRG, 44.45% were MRD negative and 55.55% were MRD positive. In IRG and HRG, 44.45% and 40% were MRD positive respectively. The MRD positive cases were dynamically restratified to the HRG. Median days of hospitalisation during induction for SRG: 16 days, IRG: 28.5 days and HRG: 43 days.

Conclusion

Together, data reveals a substantial proportion of SRG patients became MRD negative with the less intensive regimen. The SRG group shows significant increase in bed turnover compared to IRG and HRG. These results support the early efficacy of the protocol with better utilisation of hospital beds.

Malignant Hematology-Clinical (MHC) OP-MHC-40

Retrospective analysis of outcomes of 7-day course of ventoclax with hypomethylating agent in newly diagnosed patients of AML – Single Centre Experience

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Introduction

Acute myeloid leukemia (AML) is an extremely heterogeneous hematological neoplasm. Patients may benefit from intense chemotherapy but still allogeneic hematopoietic stem cell transplantation (HSCT) is the only treatment option with curative potential. However, most patients cannot tolerate intensive chemotherapy or have lack of response and cannot receive HSCT. In middle and low income countries treating AML patients with intensive chemotherapy is difficult as most patients present with life threatening infections and at times salvaging with a low intensive regimen to achieve a response becomes more important.

Aims & Objectives

Retrospective analysis of efficacy and safety of the short course of venetoclax 7day regimen along with azacitidine in whom standard chemotherapy was not feasible, with the aim of providing real-world clinical practice evidence.

Materials & Methods

A total of 51 patients data was collected from database who have been diagnosed as Acute myeloid leukaemia according to WHO criteria between january 2022 to december 2023 and were classified according to ELN 2022

risk stratification. Patient related data were collected, how many cycles of chemotherapy received and response assessment post 2nd cycles. Complete hematological response along with complete response with incomplete count recovery, bone marrow morphological response along with MRD by flow cytometry were analysed.

Result

As of December 31 2023, 51 unfit AML patients were analysed. The median age of patients was 55 (21-76) years. Females patients were 32 and males were19. Normal CYTOGENETICS is seen in 33 patients. Complex karyotype is seen in 4 patients. Risk stratification was done using NGS findings. FR 13patients, IR 19patients and AR 19patients. Secondary AML is seen in 4 patients. Median time for transfusion independence was 36days. Platelet recovery was observed earlier with a median duration of recovery 28days. ORR in our population was 80.2%. CR+CRi was documented in 75.3% of study population. MRD negativity was observed in 69.5% of population. Median progression free survival in the study population was 15months. Median OS not reached.

Conclusion

Though the number of patients in our study were limited but our study strongly suggests reducing duration and dose of ventoclax for 7days with azole prophylaxis had better overall response and tolerability. In patients ineligible for intensive chemotherapy this regimen can be used for remission induction with minimal toxicity to before transplant.

Malignant Hematology-Clinical (MHC) OP-MHC-41

Occam's Razor or Hickam's Dictum: Myeloid Neoplasm with Disabling Musculoskeletal Pain

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Background

Chronic Myelomonocytic Leukemia (CMML) is a rare hematologic malignancy, sometimes associated with systemic inflammatory or autoimmune diseases. We present a unique case of CMML presenting with severe musculoskeletal pain and aortitis, raising the question of whether it represents a paraneoplastic syndrome or co-existing autoimmune pathology.

Case Presentation

A 49-year-old female presented with fever and severe upper back pain radiating to the upper limbs. She experienced significant weight loss (10 kg over two weeks). Initial evaluation showed anemia (Hb: 7.2 g/dL), leukocytosis (TC: 15730/µL), and thrombocytopenia (Plt: 60,000/µL). The patient was afebrile, with stable vitals but marked pallor. A whole-body PET-CT revealed diffusely increased FDG uptake throughout the bone marrow, suggestive of a myeloproliferative disease, and aortitis with thickening around the arch of the aorta.

Diagnosis

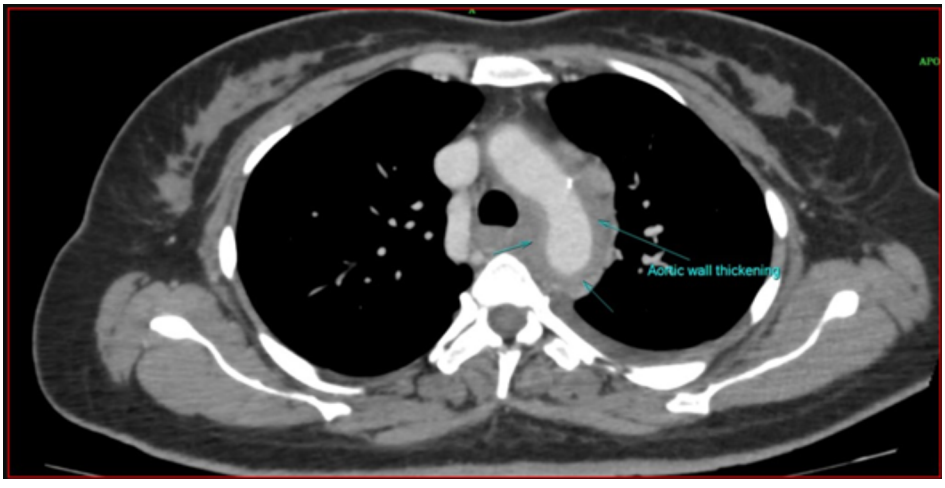
The clinical, imaging, and laboratory findings were consistent with CMML complicated by aortitis. Further investigations for autoimmune disease were negative, including vasculitis screening and IgG4 levels. Given the patient's hematologic and inflammatory findings, CMML with paraneoplastic large-vessel vasculitis was considered.

Treatment

The patient was started on dexamethasone (8 mg BD), which led to significant improvement in musculoskeletal pain. CMML-specific treatment was deferred due to the acute inflammatory presentation, and the patient was monitored for disease progression.

Follow-up

On follow-up, the patient's symptoms improved substantially on corticosteroids. Serial imaging showed stabilization of the aortitis, and further hematologic work-up confirmed the CMML diagnosis.



Conclusion

This case highlights the rare presentation of aortitis in CMML and raises the possibility of an overlapping autoimmune or paraneoplastic process. Clinicians should consider hematologic malignancies like CMML in patients presenting with unusual inflammatory syndromes. Further research is warranted to elucidate the underlying mechanisms linking CMML and aortitis.

Malignant Hematology-Clinical (MHC) OP-MHC-42

Clinical Experience and Short-Term Outcome of AML at A Tertiary Care Centre in Eastern India

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Introduction

Acute Myeloid Leukemia remains one of the most heterogenous and commonly diagnosed haematological malignancy encompassing an intensive treatment and financial burden in resource constraint settings. The current standard therapy for AML poses risk of high morbidity and treatment related mortality, along with delays in treatment initiation. In the current era of less intensive and targeted therapies, we set to explore the feasibility and efficacy of existing intensive chemotherapy regimens.

Aims & Objectives

1. To establish short term outcomes in patients with AML.

2. To assess treatment related mortality and toxicity profile in patients receiving AML therapy.

3. To appraise feasibility of Intensive Induction protocol in a resource poor Low-medium Income Country.

Materials & Methods

Retrospective and descriptive, single centre study, incorporating newly diagnosed cases of AML (excluding AML M3) who presented at the Department of Haematology , NRS Medical college and Hospital over a 9 month period, from January 2024 to September 2024. These patients were diagnosed and treated as per Institutional protocol, in line with the European Leukemia Network (ELN) 2019 guidelines. Baseline clinical and molecular parameters were recorded and outcomes were analysed.

Result

Total 56 patients were diagnosed and treated at our centre. Median age being 36 years (range 1.5 -75 years) with a female to male ratio of 14:13. There was an average delay of 19 days between diagnosis and treatment initiation. Of the 56 patients, 76% received 3+7 based intensive therapy, 4.5% received HAM, 7% received HMAs and 12.5% received Aza-Ven combination. Of the total patients receiving 3+7 induction, CR at end of induction was seen in 48.9% of patients, whereas 30% of the patients were not in remission. Induction related mortality was around 25%. The major complication was febrile neutropenia related sepsis (89%), burden of comorbidities (3%).

Conclusion

The standard therapy of AML is an intensive protocol practiced in a non-ideal setting in Low-Medium income Countries. This poses additional challenges in form of prolonged hospitalisation, severe sepsis, induction mortality and morbidity, as it does not replicate the cohort and set up of developed countries.

However, in light of high cure rates, this still remains the standard regimen. hence, our focus should be on enhancing the safety and efficacy of this therapy, optimisation of resources, reducing the time span between diagnosis and initiation of treatment. And also open avenues of less intensive and targeted therapies.

Malignant Hematology-Clinical (MHC) OP-MHC-43

Elevated Platelet Counts: Triple Negative Essential Thrombocytosis Hiding as Reactive Thrombocytosis

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Background

Thrombocytosis from excessive platelet counts is most commonly discovered on routine blood counts in asymptomatic patients. Most elevations are "Reactive" due to enhanced bone marrow production in response to causes including Iron deficiency anemia, Inflammation, Infection, or Malignancy. The increase in platelet count is typically less than 1,000,000/mm3. A minority of cases are due to MPNs like Essential thrombocytosis, polycythemia vera etc.

Case Presentation

A 65-year-old Female with Past co morbidities of type 2 Diabetes Mellitus and Hypertension presented to OPD with chief complaints of Pain in left upper quadrant abdomen and Fever for last 15 days. On examination mild tenderness was present in LUQ. Laboratory evaluations showed her Hb-8.0 g/dl, TLC-26k/mm3, Platelets-11.3 lakh/mm3, Creat-1.8 mg/dl, Urea-32 mg/dl, LDH- 996 and U.acid-7.2 mg/dl . PT/INR/aPTT- 15/1.2/31, BT/CT: 5.2 min/ 7.1 min. Her Iron studies showed Anemia of Chronic Disease. GBP was suggestive of Severe Thrombocytosis (MPN vs Reactive). Imaging of Abdomen revealed hypoechoic collection of 52ml with Perisplenic collection s/o Splenic abscess. The patient was started on empirical broad-spectrum antibiotics and

USG guided Pus Aspiration was sent for culture sensitivity. The patient showed clinical improvement after initiation of antibiotics and raised WBC counts declined. However, the platelet counts did not respond to treatment and were elevated (Platelet counts >10 lakh/mm3) even after resolution of abscess on imaging. The patient was further evaluated along the line of MPN. Repeat GBP showed clumps of giant platelets. Molecular studies BCR-ABL was negative, MPN panel (JAK2 EXON 12 AND 14, CALR, MPL) showed no mutation. Bone marrow aspiration and biopsy showed increased megakaryocytes, showing hyperlobation (staghorn pattern) with absent reticulin on biopsy s/o Essential Thrombocytosis.

Diagnosis

Triple negative Essential Thrombocytosis.

Treatment

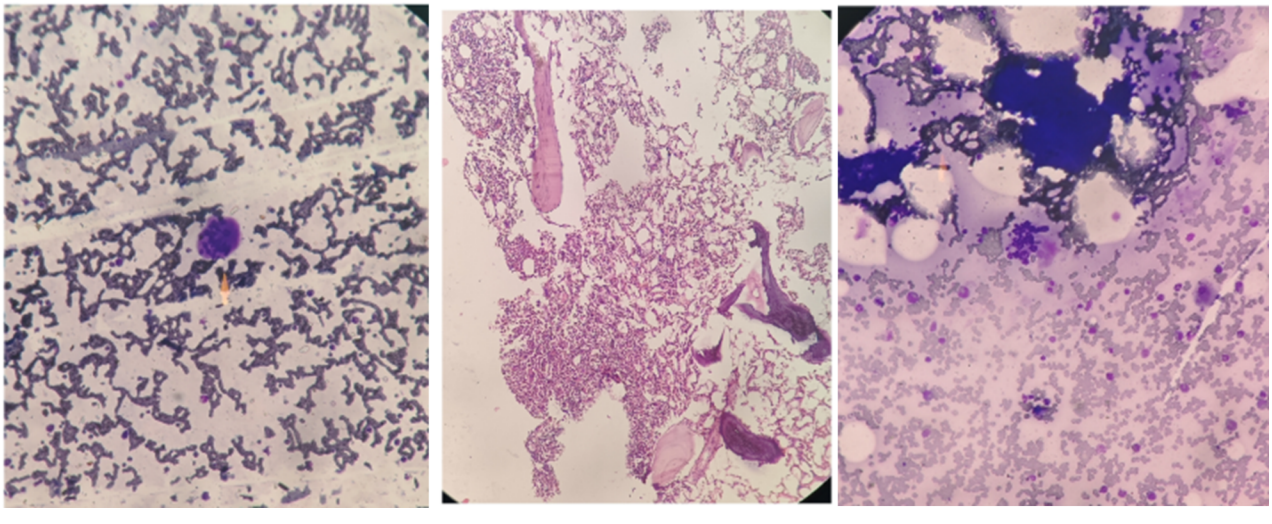
The patient was started on oral Aspirin (75mg) and Hydroxyurea (1000mg daily).

Follow-up

The patient showed response, and her platelet count improved to 6.2 lakh/mm3.

Conclusion

Reactive thrombocytosis does not exclude the possibility of ET. ET differentiation from reactive thrombocytosis and other MPN is clinically challenging.



Malignant Hematology-Clinical (MHC) OP-MHC-44

Outcomes of Chemoimmunotherapy in Treating Primary Central Nervous System Lymphoma: A Comprehensive Analysis

Rajkiran Emmadi
Bindu S Reddy, Tejeshwar N, Rachana Chennamaneni, Meher Lakshmi Konatam, Sadashivudu Gundeti

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Introduction

Primary central nervous system lymphoma (PCNSL) is a rare extranodal non-Hodgkin lymphoma affecting the brain, spine, cerebrospinal fluid, or vitreoretinal space, comprising 5% of extranodal lymphomas. Although highly responsive to chemotherapy and radiotherapy, relapse rates are high. The addition of Rituximab has

improved complete response rates, progression-free survival, and overall survival. This study analysed the outcomes of patients receiving chemoimmunotherapy.

Aims & Objectives

To determine the challenges and overall survival (OS) and progression free survival (PFS) rates in patients with PCNSL who received chemoimmunotherapy.

Materials & Methods

This was a single center, retrospective study. All consecutive patients with newly diagnosed histologically confirmed PCNSL who received chemoimmunotherapy were included in the study. Kaplan Meier survival was used to determine OS and PFS.

Result

Thirty-one patients were included in the study, with a median age of 50 years (15 – 65 years), and 67% were male. Eighteen (58%) patients had a PS ≥ 2. The majority (93.5%) of patients had CNS-related symptoms [headache (61.2%), hemiparesis (38.7%)], and two (6.4%) patients had ocular symptoms. The most common histology was DLBCL (96.7%), with the ABC/non-GCB type (80%) being the most common variant and high Ki67(mean 68%). Only seven (22.5%) patients underwent gross total excision. A total of 27(87%) patients received chemotherapy, and the MTR regimen (66.6%) was most commonly given. Consolidation RT was received by 8(26%) patients and ASCT was performed in 2(6%). Eight (25.8%) patients died during treatment. Complete response/near complete responses were seen in 8(26%) patients, mOS was 6 months while mPFS was 2 months. Among 19(61%) patients who completed chemoimmunotherapy, the relapse rate was seen in 7(26%), mOS was not reached while mPFS was 6 months.

Conclusion

Our study highlighted challenges such as mortality and a lower consolidative treatment rate during chemoimmunotherapy treatment. Our response rates and survival outcomes were comparable with those of other Indian studies. The outcomes in patients with PCNSL can be improved by addressing these challenges.

Malignant Hematology-Clinical (MHC) OP-MHC-45

Acute Promyelocytic Leukemia : Clinic-Pathological Analysis and Short - Term Treatment Outcome in a Tertiary Care Hospital in Eastern India

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Introduction

Acute Promyelocytic leukemia (APML) though constitutes approx. 10-15% of all Acute Myeloid Leukemia (AML) , is often recognized as a distinct entity due to its characteristic molecular pathology , presence of abnormal promyelocytes in peripheral blood and bone marrow,unique clinical features especially coagulopathy, relatively younger age of presentation and having high cure rate.

Aims & Objectives

1. To explore the clinico-pathological profile of all APML presented in our set in last 9 months

2. To ascertain the short term treatment outcomes and correlate with risk group ,morphology and demography.

Materials & Methods

In this retrospective cum prospective analytical study , all suspected APML cases presented to our set up was initially diagnosed morphologically and later confirmed by molecular study ; treated as per Institutional

protocol in line with European Leukemia Network (ELN) 2019 guidelines after stratification into appropriate risk group as per Sanz criteria. Baseline Clinical as well as laboratory parameters were assimilated and short term treatment outcomes were analysed. We have taken 26 cases, n =26.

Result

Median age was 28 years (range 3-64 years) with a female predominance 1.5: 1. Fever was the most common of all symptoms (73%) followed by bleeding (69%). Most common clincal sign was pallor (96%). In hematological parameters anemia & thrombocytopenia were present in 100% of cases. Most patients belong to intermediate Risk group (IRG) followed by High risk (HRG) and standard risk (SRG).Morphologically hyper granular variant is the most common variant observed. Early death (induction mortality) was observed in 11% of cases due to bleeding related complications, and all patients who survived induction achieved morphological remission. One patient relapsed within 5 months , being a ZBTB-RARA variant, treated in line with AML like protocol and expired in relapse. Antracyclines was associated with significant instances of febrile neutropenia and ATO was associated with ECG changes. DS seen in 8 out of 26 patients. Most of them are IRG.

Conclusion

APML is a medical emergency and prompt treatment alters the prognosis significantly. In view of above clinicians and pathologists should have a high index of suspicion as early diagnosis and supportive care remains the cornerstone of management. However, in light of high cure rate, now our focus should also include long term follow-up and treatment related complications.

Malignant Hematology-Clinical (MHC) OP-MHC-46

Pediatric precursor B -Cell Acute Lymphoblastic Leukemia with Bulky Mediastinal Mass with Malignant pleural and pericardial effusion with Superior vena Cava Obstruction Syndrome with KRAS missense mutation along with CDKN2A and CDKN2B deletion: A case report

Prisla maria Dalton
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Background

Superior Mediastinal syndrome is a life threatening emergency which is often challenging yet rewarding to treat.In a study by Prateek et al, the most common malignant cause of mediastinal syndrome is found to be Hodgkin lymphoma followed by T cell lymphoblastic lymphoma.However B cell Acute Lymphoblastic leukemia presenting with mediastinal syndrome is rare.In cases where molecular screening for B cell ALL is negative ,genome-wide technologies gives an insight about the prognosis and nature of the disease and hence is useful in treatment selection.

Case Presentation

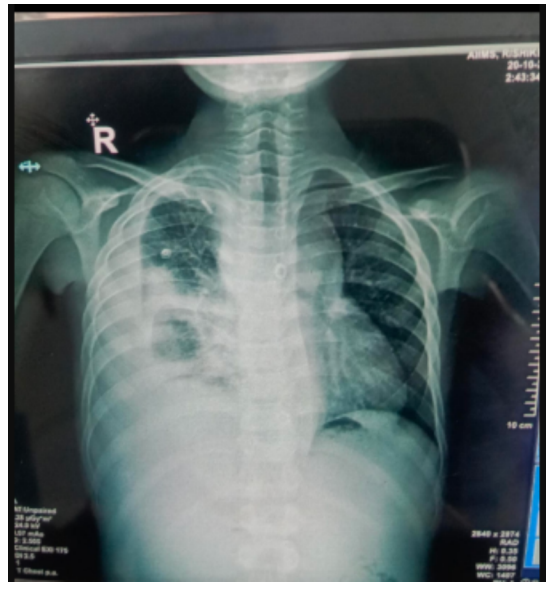
8 year old child presented to pediatric emergency with abdominal distension for 1 month,generalised weakness for 1 month,swelling in right side of cheek for 4 to 5 days,B/L pedal edema for 2 days.O/E he had multiple cervical lymphadenopathy with distended neck veins .On auscultation right sided air entry was markedly reduced.Abdominal examination revealed splenomegaly and hepatomegaly and shifting dullness.

Diagnosis

Complete blood count at presentation revealed Hemoglobin of 7.7 g/dl , white blood count of 72370/cumm and platelets of 81000/cu mm.His peripheral smear examination revealed 67 % blasts.Chest Xray showed massive right sided pleural effusion with bulky mediastinal mass.High dose steroids was started immediately after sending Flow-cytometry in view of Mediastinal syndrome.Immunophenotyping of peripheral blood was

positive for Cluster of differentiation 19 (CD 19),CD 10,CyCD 79 A,SCD 22,Human Leukocyte Antigen -DR isotype (HLA-DR),CD 34,Anti Terminal deoxynucleotidyl transferase (TDT)which was suggestive of precursor B cell ALL.His cytogenetics was normal showing 46 XY.ALL polymerase chain reaction was negative.Next generation sequencing was positive for CDKN2A ,CDKN2B deletions and KRAS missense mutations.Ultrasound abdomen revealed hepatosplenomegaly with bilateral enlarged kidneys with raised echogenicity with bilateral pleural effusion and ascites.Echocardigraphy revealed moderate pericardial effusion with ejection fraction of 60 %.Fundus examination showed multiple roth spots and pre retinal bleeds.

Treatment



Right side Intercostal Drainage Tube was inserted in view of massive right sided pleural effusion with mediastinal shift.Child was treated in Pediatric Intensive Care Unit in view of respiratory distress requiring High flow Nasal Cannula support.Computed Tomography imaging of Thorax was planned but was not done as child was too sick to get shifted for CT scan.He received 1 dose of rasburicase in view of Tumour lysis syndrome. After informed and written consent he was started on modified BFM 2009 induction regimen: Dexamethasone arm..His day 8 steroid response was poor .Day 15 Measurable residual disease was negative - <0.01%.He also developed Methicillin-resistant Coagulase negative Staphylococcus Aureus sepsis and was treated with susceptible antibiotics.His clinical condition improved.

Follow-up

Day 33 MRD was negative and hence achieved disease remission post induction.He then received early intensification and day 78 MRD post early intensification was negative.He is currently receiving High risk Consolidation Chemotherapy (HR blocks)as per BFM protocol and is doing well in disease remission status.

Conclusion

B cell Acute Lymphoblastic leukemia with Mediastinal syndrome can be salvaged with timely initiation of steroids.In the background of CDKN2A and CDKN2B deletions which are adverse independent prognostic marker in ALL patients ,high intensity chemotherapy regimen has to be used to prevent disease relapse and to achieve favourable outcome.

Malignant Hematology-Clinical (MHC) OP-MHC-47

Molecular Profile by Next Generation Sequencing and its Impact on Risk Stratification and Outcomes of Acute Myeloid Leukaemia - A Tertiary Care Centre Experience from India

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Introduction

Mutation profile of acute myeloid leukaemia (AML) is heterogeneous and complex. With the availability of next generation sequencing multiple mutations are being detected with prognostic and therapeutic relevance. Published date from India is scarce here we report our single centre experience of using NGS to better characterize our patients.

Aims & Objectives

To study molecular profile and its prognostic relevance in adults with acute myeloid leukemia.

Materials & Methods

Retrospectively study of AML patients diagnosed from November 2021 to September 2024. Details of AML-PCR panel (NPM1, FLT3-ITD, FLT3-TKD, AML1: ETO, inv16) and next-generation sequencing (NGS), karyotyping, ELN risk stratification and survival was collected.

Result

94 patients, median age 56 years (18 to 85); 43 (46%) males and 51 (54%) females. 81 (86%) were de-novo AML (3 myeloid sarcoma - one of the GI tract, one ocular and one paravertebral mass). Median haemoglobin, leucocyte and platelet counts were 8.1 g/dL, 7.8 x 109/L and 44 x109/L, respectively, median BM blasts of 65% (range 12 to 96%).

Karyotypes reports were available in 87 patients; mutation panel by PCR and NGS was available in 94 and 61 patients, respectively. Median of 2 mutations per patient (range 0-5) as in table 1. AML1: ETO translocations were seen in 8; inv16 in 3 patients. C-kit mutations were seen in 5 patients - 4 with t(8;21) and one with inv16. NPM1, FLT3-ITD and FLT-3 TKD and CEBPA mutations were seen in 24, 15, 7 and 11 patients, respectively. MDS related mutations (RUNX1, ASXL1, SRSF2, STAG2, ZRSR2, BCOR1) were seen in 21 (22%). TP53, IDH1 and IHD2 mutations were seen in 7, 5 and 9 patients, respectively. Accordingly, 30 (32%) fell in the ELN adverse, 44 (47%) intermediate and 20 (21%) in favorable risk category.

Table 1 Overall response rates to therapy and median OS among various mutations.

	n	*ORR (%)*	*p value*	*Median OS (months)*	*p value*
t(8;21)	8	88	0.310	NR	0.821
inv16	3	67	0.999	NR	0.914
FLT3-ITD	15	73	0.794	44	0.924
FLT3-TKD	7	57	0.415	45	0.198
NMP1	24	71	0.397	NR	0.611
CEBPA	11	91	0.194	77	0.199
TP53	7	43	**0.040**	20	**0.009**
RUNX1	9	56	0.251	11	**0.048**
ASXL1	9	67	0.735	30	0.935
IDH1 & 2	14	86	0.103	45	0.510

With 21 deaths during the study period, the median OS was 49 months with 2-year and 5-year survival rates of 70% and 45%, respectively. Patients in ELN adverse risk category had poorer

OS (p=0.011, hazard ratio 4.15), however, there was no difference in response to first-line therapy. Presence of RUNX1 mutations were also associated with poor OS (p=0.048), while TP53 mutation was associated with both poor OS (p=0.009) and poor response to first-line therapy (p=0.040).

Conclusion

In the present era, detection of few mutations by PCR is inadequate as multiple mutations are seen in AML patients which have prognostic and therapeutic implications. We recommend use of NGS for mutation and fusion detection in a newly diagnosed patient with acute myeloid leukemia.

Malignant Hematology-Clinical (MHC) OP-MHC-48

A Study to Analyse Bone Health in Multiple Myeloma Patients Using Radiological and Bone Turnover Markers

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Introduction

The pathophysiology of multiple myeloma (MM) involves an imbalance in bone remodeling. Increased osteoclast activity and decreased osteoblast function result in bone resorption and the development of skeletal-related events (SREs), such as fractures and severe pain. Bone turnover markers (BTMs) have emerged as critical tools for monitoring this imbalance, providing insights into the dynamics of bone remodeling in MM patients. BMTs include bone resorption markers (N-telopeptide) and bone formation markers (bone-specific alkaline phosphatase (BSAP) and Procollagen I Intact N—terminal (PINP)). Imaging studies don't provide detailed information on the dynamic status of bone health, which are otherwise routinely used for assessing bone disease. So, BTMs using serum/urine samples may be an alternative option for monitoring bone health in MM.

Aims & Objectives

To compare the radiological and BTM for assessing bone health in MM patients.

Materials & Methods

We performed a single-center, cross-sectional observational pilot study that included 50 patients diagnosed with MM in a tertiary care center in Western India from October 2022 to September 2024. The study was done in accordance with the Declaration of Helsinki and after obtaining Institutional Ethical Clearance. All patients were subjected to PET-CT, DXA-BMD, and BTMs, irrespective of the stage of the disease and the treatment regimen. The BTMs and radiological parameters were correlated.

Bone Health Marker	DXA Femur Neck (BMD)	DXA Lumbar Spine (BMD)	PET-CT Score (PET-DS)
PINP Levels	Moderate positive correlation (r=0.12), p-0.06	Weak positive correlation (r=0.04), p-0.42	No correlation (r=0.01), p-0.99
BSAP Levels	Weak correlation (r=0.02), p-0.71	Moderate correlation (r=0.10), p-0.1	Weak correlation (r=0.04), p-0.81
NTX Levels	No significant correlation (r=0.01), p-0.84	Weak correlation (r=0.07), p-0.22	Weak correlation (r=0.05), p-0.7

Result

BSAP was generally low in patients with lower PET-DS scores, reflecting reduced bone formation in early-stage disease or stable disease. In contrast, positive BSAP and PINP levels were found in patients with higher PET-DS scores, suggesting ongoing bone remodeling in response to disease progression. Similarly, N-telopeptide showed a notable decrease, with lower levels and reduced variability among BMT patients.

Conclusion

The study concludes that combining BTMs is particularly relevant for identifying early-stage bone disease, where BTMs like NTX can detect bone resorption before significant BMD loss is evident on DXA scans. The findings emphasize that regular monitoring of BTMs can help guide treatment decisions, especially in patients at high risk of bone complications. Expanding the use of BTMs in routine clinical practice, combined with imaging, enables early intervention in bone disease progression.

Malignant Hematology-Clinical (MHC) OP-MHC-49

Hematopoietic Stem Cell Transplant Outcomes in Patients with Acute Myeloid Leukemia –A Single Center Study

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Introduction

Allogenic hematopoietic stem cell transplantation (Allo-HSCT) is only curative therapy for intermediate and high-risk acute myeloid leukemia (AML) . The intensity and type of post remission therapy is generally tailored according to risk profile, whereby chemotherapeutic consolidation is favored in favorable risk AML and allo-HSCT is favored in intermediate and adverse risk AML

Aim & Objective

1) To estimate the overall survival and regimen related toxicities in AML patients who underwent Allo-HSCT.
2) To compare the progression free survival in intermediate and high risk groups.

Material & methods

This is a retrospective cohort study of Acute Myeloid Leukemia patients who underwent Allo HSCT at our center from 2019 to 2024. A total 20 patients with adverse risk ,intermediate risk and relapse refractory disease who underwent Allo-HSCT during this study period were included (ELN 2022 risk stratification). Data was collected from the hospital electronic medical records (EMR). Kaplan Meier method, log rank test were used to evaluate overall survival and progression free survival.

Results

Mean age of all AML patients was 46.8 ± 12.4 years, and male : female ratio was 1.2 :1. Out of 20 patients, 11 (55%) were intermediate risk and 9 (45%) were adverse risk according to ELN 2022 risk stratification. Overall survival was 53 months (95% CI: 1, 112.1). Overall survival was longer in intermediate risk (46.68 months; 95% CI: 32.45, 60.91) compared to adverse risk group (34.6 months; 95% CI: 5.21, 24.39; p=0.908). The progression free survival was also longer in intermediate risk (43.24 months; 95% CI: 29.16, 56.72) compared to adverse risk group (31.8 months; 95% CI: 5.01, 20.12; p=0.842). Common complications included CMV reactivation (70%) and GVHD (45%), grade 1/ 2 GVHD (30%) and grade 3 (15%). Mortality occurred in 5 (25%) patients.

Conclusion

The overall survival and progression free survival at our institute was 53 months. The progression free survival was longer in Intermediate risk as compared to adverse risk in Allo-HSCT. The conditioning regimen is associated with few toxicities for which prophylaxis should be given.

Malignant Hematology-Clinical (MHC) OP-MHC-50

Clinical outcomes of Multiple Myeloma post Autologous Hematopoietic Cell transplant: A Single Centre Study

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Introduction

Multiple myeloma (MM) is characterized by clonal proliferation of malignant plasma cells in the bone marrow, monoclonal protein in blood or urine & associated organ dysfunction.Induction therapy followed by Autologous Hematopoietic cell transplantation (AHCT) is the standard of care for consolidation therapy in patients with multiple myeloma.

Aim & Objectives

To determine overall survival, progression free survival and transplant related mortality in patients undergoing Autologous HCT (AHCT) at our Institute.

Materials & Methods

This is a retrospective study of MM patients who underwent AHCT at our center from 2019 to 2023. Data was collected from the hospital electronic medical records (EMR). Kaplan Meier analysis was done to determine overall survival (OS) and progression free survival (PFS). Bortezomib based induction therapy was given in most of the cases. Pretransplant response was assessed. Complete response (CR) was defined as no M protein in serum & urine protein electrophoresis, Immunofixation & < 5% plasma cells on bone marrow & very good partial response (VGPR) as > 90% reduction in serum and urine protein electrophoresis. Injection Granulocyte Colony stimulating factor and Plerixafor was used for stem cell mobilization.

Results

Sixty-three percent (26/41) cases of MM underwent HCT at our centre. The age range was 38-69 years. Most common type was IgG kappa (27%) followed by light chain disease (23%) followed by IgG Lambda (11.5%). Pre transplant thirty-eight (10/26) and thirty four (9/26) percent patients were in CR & VGPR respectively.

Fifteen percent (4/26) had renal failure before transplant. Median duration of follow up was 32.87 months (95% CI: 15.85, 47.88). OS was 47.19 months (95% CI: 39.37, 55.03) and PFS was 43.32 months (95% CI: 35.73, 51.50). One year & two-year OS was 83.7% and 69% respectively. One year & two-year PFS was 83.7% & 44.4% respectively. Complications included infections (bacterial in 5 cases and viral in 3 cases). No transplant-related mortality was observed.

Conclusion

AHCT for multiple myeloma is associated with good overall survival and progression free survival justifying its use as consolidation therapy for multiple myeloma patients.

Malignant Hematology-Clinical (MHC) OP-MHC-51

An audit to assess safety and efficacy of Generic Dasatinib in Chronic Myeloid Leukemia (CML)

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Introduction

Dasatinib is approved in India for newly diagnosed chronic myeloid leukemia-chronic phase (CML-CP) patients. It has deeper and faster molecular response than Imatinib. Generic Dasatinib formulations offer alternative, low-cost treatment for patients in LMICs such as India. This study aimed to evaluate the safety and efficacy of generic Dasatinib as a first-line treatment in CML-CP in our institute.

Materials & Methods

A retrospective audit of medical records was carried out from (June 2023 to January 2024) of CML patients and patients were categorised based on SOKAL score. Data on patients who had dose reduction, dasatinib withdrawal/interruption were captured with reasons and CTC criteria were used to assess safety. Efficacy outcomes were- Complete Cytogenetic Response (CCyR), Early Molecular Response (EMR) and Major molecular response (MMR).

Results

Of the 108 patients, 89/108 (82.4%) met the selection criteria. The mean[±SD] age of patients was 39.3[±11.5] years. 63%(n=56/89) were males. Sokal risk was high in 47% (n=42/89), intermediate in 33% (n=29/89) and low in 20% (n=18/89). The starting dose of dasatinib was 100 mg/day for 84% (n=75/89) participants, 50 mg in remaining 16%. Dasatinib was interrupted in 39% (n=35/89) primarily due to pleural effusion [n=11/35, 32%], of which 54% (n=6/11) were moderate grade, thrombocytopenia [n=12/35, 34%] and diarrhoea (n=8/35, 23%). 12% of the patients (n=11/89) required dose reduction, main reasons being thrombocytopenia (n=5/11) and diarrhoea (n=4/11). 6% (n=5/89) patients were lost to follow up. At 3 months, n=75/89 (84%) achieved EMR. CCyR was achieved in 73% by 12 months (65/89). Data was not available for 5.6% patients. 76% (n=68/89) achieved MMR, of which 14%(n=13/89) achieved it within 3 months, 41% (n=37/89) by 6 months, 47% by 12months [n=42/89]. Data was not available for 7% of the patients. Around 16% (n=15/89) required TKI change in view of various reasons: increasing RQPCR, repeated episodes of pleural effusion, Grade 4 thrombocytopenia and diarrhoea.

Conclusion

Generic Dasatinib is highly efficacious however pleural effusion, thrombocytopenia and diarrhoea led to significant drug interruptions and change of TKI in small number of patients.

Malignant Hematology-Clinical (MHC) OP-MHC-52

Clinicoepidemiological study of Newly diagnosed Multiple Myeloma with Special Reference to Prognosis

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Introduction

Multiple Myeloma (MM) is a disorder of clonal plasma cells characterized by monoclonal proteins in the serum and organ damage. Prognosis is based on staging and cytogenetics. Treatment includes combination of drugs with autologous stemcell transplant in eligible patients.

Materials and methods

Evaluation of patients attending Clinical Hematology OPD, GMCH with suspected diagnosis of MM by clinical, biochemical and immunological tests, bone marrow examination, imaging and cytogenetics.

Results

Total 79 patients with 51 males and 28 females and median age of 60 years. Fatigue and backache were the most common symptoms. Kappa was the predominant light chain involved. Cytogenetic evaluation done in 31 patients showed high risk cytogenetics in 15 patients. Overall treatment response was seen in 95% of patients.

Discussion

MM is characterized by serum monoclonal proteins, bone marrow plasmacytosis, organ damage and low risk and high-risk cytogenetics. In this study, high risk cytogenetics was more frequently associated with poor prognostic markers with less response to therapy.

Conclusion

MM was evaluated in this study and was found to have inverse relation prognostically with high-risk cytogenetics.

Malignant Hematology-Clinical (MHC) OP-MHC-53

Real World Outcomes of AZA/VEN Induction Followed by Intermediate Dose Cytarabine Based Consolidation Therapy AML

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Introduction

Acute myeloid leukemia (AML) is a malignant disorder of hematopoietic stem cells characterized by clonal expansion of abnormally differentiated blasts of the myeloid lineage. In the early cooperative group trials of 3 + 7 in highly selected younger patients (usually 55 years or younger), the 5-year survival rates range from 40% to 50%. Later trials included patients up to 60–65 years of age and reported lower long-term survival rates of 30–40%. Both elderly acute myeloid leukemia (AML) patients and those with baseline infections, when treated with intensive chemotherapy, are associated with high induction mortality. VIALE A reported a ORR of 66.4 % with median PFS of 14 months in the AZA/VEN arm versus 9 months in AZA arm.

Aims & Objectives

To assess the efficacy of patients receiving induction with AZA/VEN and consolidation with Cytarabine based therapy

Materials & Methods

We conducted a retrospective analysis of AML patients deemed unfit for intensive chemotherapy (by virtue of age >60 years, ECOG-PS 3-4, or those with non- resolving infections at baseline), treated with azacytidine-venetoclax combination as induction chemotherapy and later received Intermediate dose @1500mg/m2 based consolidation therapy for 3 cycles using electronic database of hospital (Paras)

Results

We identified 24 patients treated from 2018 to 2023. Median age 48.08±13.18. 41% were males. Overall 70 % patients had co-morbidities and 41% had baseline infections. 27% had ECOG PS of 2 or more. As per ELN 2022 classification 54% were standard risk, 31% were intermediate risk and 22% were adverse risk patients. 68% patients achieved CR+Cri composite CR at day 30. Induction Mortality was zero. Median follow up is 9.5 years. 2 year PFS is 47.3 % and 2 year OS is 53% respectively

Conclusions

Aza/VEN induction is a safe and efficacious induction strategy in young unfit patients and Cytarbine consolidation may be given to patients who do not wish to continue AZA/Ven or undergo HSCT.

Malignant Hematology-Clinical (MHC) OP-MHC-54

Outcome of High Dose Imatinib versus Imatinib plus Decitabine in Patients with Accelerated Phase or Imatinib Resistant Cases of Chronic Myeloid Leukemia

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Aims and Objectives

To compare therapeutic effect of high does Imatinib versus standard dose Imatinib in combination with Decitabine among patients with Imatinib resistant cases of CML in both Chronic and Accelerated Phase

Material and Methods

50 Imatinib resistant patients of CML divided in two arms High dose Imatinib and other being standard dose Imatinib plus Decitabine 25 patients each in both arm of which 20 patients were with secondary imatinib resistance while 12 with Primary imatinib resistance and 18 with secondary imatinib resistance

Results

It was found that patients with Primary Imatinib resistance and Accelerated phase patients respond better to Imatinib with Decitabine

Miscellaneous/Molecular Hematology (MH) OP-MH-1

Molecular Landscape of Precursor-T Lymphoblastic Leukemia: A single centre experience from Eastern India

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Introduction

T- Lymphoblastic Leukemia accounts for approximately one-fourth of acute lymphoblastic leukemia cases. Sequencing approaches have identified >100 genes that can be mutated in T-ALL. However, the revised WHO 2022 edition of lymphoid neoplasms still does not incorporate molecular signatures into the T-ALL subgrouping unlike B-ALLs and AML, which are classified mainly based on molecular landscapes.

Aim and Objectives

1) To establish the molecular landscape of patients with T-lymphoblastic Leukaemia at diagnosis.

2) To study their correlation with MRD status and survival outcomes. 3) To derive the utility of NGS in T-ALL.

Methods

This retrospective observational study included all newly diagnosed patients of T-lymphoblastic leukemia of all age groups who presented in the OPD during the period between January 2022-October 2023 in whom complete baseline diagnostic work-up was available including flow cytometry, FISH and NGS studies.

Results

There was lower frequency of karyotypic abnormalities in adult ETP-ALLs than other sub-groups. Non-ETP ALLs showed significant association with NOTCH1 mutations (p=<0.00001), followed by JAK3 (p=0.01), FBXW7 (p= 0.066) and PHF6 (p=0.09) mutations. There was no difference between adult and pediatric patients, in terms of genomic profiling except in PHF6 gene. There was no significant difference between NOTCH1-mutated and NOTCH1-wild T-ALL patients as well as NOTCH1-HD versus NOTCH1-PEST mutated patients in terms of MRD, RFS and/or OS. 45.1% of all TALL patients harboured ≥3 mutations. However, the complex molecular profile did not correlate significantly with MRD positivity and poor RFS and/or OS rates.

Conclusion

Molecular profiling of TALLs do not significantly impact long-term survival outcomes. In resource-constrained settings, we can get away by not doing comprehensive molecular profiling of TALLs at baseline and restrict the sequencing assay to only those cases which are persistently MRD positive or have relapsed.

Miscellaneous/Molecular Hematology (MH) OP-MH-2

Clinico-Hematological Profiles of Myelodysplasia Related Mutations in Acute Myeloid Leukemias

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Introduction

MR (Myelodysplasia related) mutations in ASXL1, BCOR, EZH2, SF3B1, SRSF2, STAG2, U2AF1, and ZRSR2 genes, as per the 2022 ELN recommendations are an independent marker of adverse risk in AML irrespective of prior history of MDS or MDS/MPN. The WHO and ICC classifications see these as mutations defining AML with myelodysplasia-related (AML-MRC) genetic changes and they reflect myelodysplasia. This study aims to provide a comparative analysis of MR mutation in different AML.

Methods

In this retrospective study, 277 AML cases over a 6-year duration (Jan 2018- May 2024) diagnosed and treated at our centre and were risk stratified according to genetic mutations analysed by targeted NGS Panel, Oncomine™ Myeloid Research Assay (ThermoFisher Scientific). 59 AML cases harbouring MR mutations were identified and their clinico-hematological data including morphology, immunophenotyping, cytogenetics and clinical profiles were evaluated.

Result

59 of 277 AML cases harbored MR mutations, of which 40 cases were de-novo AML, 16 cases AML cases had prior history of MDS/MPN (AML-MR), and 3 therapy related AML (t-AML). Majority cases were adults (55 patients), with median age of presentation 51 year for both AML-MR and de-novo AML. Dysplasia in peripheral blood (PB) and bone marrow (BM) sample was observed variably at 35% vs 82% in AML-MR and 21% vs 26% in de-novo AML, respectively. Cytoplasmic MPO positivity was seen in 47% AML-MR vs 67% de novo AML cases. NGS revealed a prevalence of mutations in transcription factors gene, (RUNX1) in all 3 AML subgroups, however truncating variants in RUNX1 gene were common in de novo AML (71%) vs AML-MR (57%). De novo AML had noteworthy mutations in epigenetic regulators, ASXL1 gene and spliceosome pathway gene, SRSF2 at 26% (n-10) each. On follow-up, the AML-MR cases showed relapse in 1 case and 6 alive patients (37%) while de novo AML cases showed relapse in 9 cases and 16 alive patients (55%).

Conclusion

The MR mutations confer a poor prognosis in both, cases of AML-MR and de-novo AML. The cases of de-novo AML harboring MR mutations are candidates for escalated chemotherapy and hematopoietic stem cell transplant as per their performance score as there is a higher risk of relapse.

Miscellaneous/Molecular Hematology (MH) OP-MH-3

Not Everything Hairy is a Hairy Cell - Evading the Trap, A Case Series of Seven Cases

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Background

Cases with this hairy cell morphology are important to differentiate as the therapy is different for each of these cases

Case Presentation

A case series of 07 cases

1. 60yrs Male presented with Weakness fatigability x 3 months with clinical diagnosis of Hairy cell Leukemia
2. 81yrs Male Evaluated for Leucocytosis, mild thrombocytopenia with clinical diagnosis of Hairy cell Leukemia variant.
3. 52 yrs Male presented with Fever, night sweats and weight loss,Splenomegaly,Rapid raising TLC and with clinical diagnosis of Splenic lymphoma/leukemia with prominent nucleoli.
4. 48 yrs Male presented with early satiety and abdominal distention with massive splenomegaly and falling blood counts; clinical diagnosis : Splenic diffuse red pulp small B cell Lymphoma.
5. 76 yrs Female presented with Pallor, fatigability and body aches with Hb 6.7g/dL, TLC 6.5 x 109/L Lymphocytes 5.1 x 109/L and Platelets 11 x 109/L; Clinical diagnosis : Plasma cell Leukemia
6. 70 yrs Male presented with Fever associated with chills and night sweats since 1.5 months,Retroperitoneal lymphadenopathy and Splenomegaly; Clinical diagnosis :Mantle cell Lymphoma
7. 20 yrs Male presented with Left sided upper abdominal mass, fever, generalized weakness since 3 months; Clinical diagnosis : T-acute Lymphoblastic Leukemia

Diagnosis

Hairy cell leukemia and mimickers of HCL

Treatment

Treatment based on differentiating Hairy cell leukemia with other mimickers of HCl

Follow-up

Follow up of cases after differentiating each entity based on molecular workup

Conclusion

Distinction of these different entities is possible through careful evaluation of morphologic, immunophenotypic, cytogenetic, and molecular features, as well as peripheral blood and bone marrow specimens. This is necessary for accurate diagnosis leading to optimal patient management.

Miscellaneous/Molecular Hematology (MH) OP-MH-4

Quantitation of Leukemic Stem Cell-like Cells (LSC) Burden at Diagnosis Identifies Clinical Heterogeneity in European Leukemianet 22 (ELN22) Risk Stratification of Acute Myeloid Leukemia (AML)

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ACTREC, Navi Mumbai

Introduction

Relapse in AML is thought to originate from chemo-resistant, dormant LSC populations. Evidence exists that the LSC burden at diagnosis may play an important prognostic role, however current risk stratification schema for AML such as the ELN22 classification do not consider this.

Aims & Objectives

To evaluate LSC burden at diagnosis in ELN22 risk categories and to correlate with outcomes.

Materials & Methods

A total of 150 adult AML patients receiving "3 + 7" induction chemotherapy were accrued. Patient characteristics and morphological remission status were evaluated. Flow cytometric assessment of measurable residual disease (MFC-MRD) was performed post-induction (PI). CD34+/CD38- progenitors were analysed and a cut-off of 0.1% as described by Terwijn et al to discriminate between LSC^{high} and LSC^{low} groups. Diagnostic samples were sequenced using 135-gene myeloid panel and risk-stratified as per ELN22 recommendations. Correlation of these groups with PI MFC-MRD and morphological remission status was performed using odds ratio. Overall survival (OS) and relapse-free survival (RFS) were endpoints analysed using log-rank test and Cox proportional hazard regression model.

Result

Median age was 37 years (M:F = 1.7). Median follow-up was 34.8 months. The median OS was not reached whereas the median RFS was 44.6 months. According to ELN22 risk stratification, patients were classified as favorable (47.3%), intermediate (38%), and adverse (14.6%) risk. Median LSC% of 150 cases was 0.2. Majority were classified as LSChigh (57.3%). Post-induction, 46.7% were MFC-MRD+, of which 71.4% were LSC^{high}. High LSC burden at diagnosis predicted for PI MFC-MRD positivity (p=0.0013). LSC^{high} AML had significantly inferior OS (p=0.01) and RFS (p=0.004), compared to LSC^{low} group. LSC status significantly impacted RFS (p=0.003) and OS (p=0.017) in intermediate risk group. Median OS of ELN22 intermediate group with LSC^{high} was similar to adverse risk group. On multivariate analysis, ELN22 adverse risk group and LSChigh (0.1%) were independent predictors of OS.

Conclusion

Quantitation of LSC at diagnosis has an important role in predicting outcomes in AML and ELN22 intermediate risk group with diagnostic LSC^{high} has comparable outcomes with adverse risk group.

Miscellaneous/Molecular Hematology (MH) OP-MH-5

Molecular Characterisation of Beta-thalassemia in Antenatal Screening Samples at a Tertiary Care Centre in Central India

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Introduction

Hereditary hemoglobinopathies constitute a group of heterogeneous autosomal recessive disorders. Beta-thalassemia, the most common autosomal recessive single-gene disorder of haemoglobin synthesis is characterized by hypochromic microcytic hypochromic anaemia. The disease runs a chronic course requiring repeated blood transfusions that usually leads to iron overload, and no other effective therapy is presently available. If left untreated, affected individuals manifest failure to thrive and shortened life expectancy.

Aims & Objectives

AIM: To assess the burden of beta-thalassemia and its molecular characterisation in antenatal samples.

OBJECTIVES:

1. To assess the burden of heterozygous beta thalassemia amongst the antenatal screening samples
2. To determine the spectrum of common beta-thalassemia mutations in the carriers detected during antenatal screening.

Materials & Methods

The present cross sectional study was conducted at AIIMS Bhopal from October 2023 to June 2024. Fifty consecutive cases of heterozygous beta-thalassemia amongst the antenatal screening samples received for HPLC were included in the study. Mutation analysis was performed using ARMS PCR for five common mutations in India IVS 1-5 (G-C), IVS 1-1 (G-T), Codon 8/9 (+G), Codon 41/42 (-TCTT), 619bp deletion

Result

A total of 3618 patients were screened for Beta thalassemia from October 2023 to June 2024. Out of these 102 were found to be Beta thalassemia trait by HPLC. From the 102 samples consecutive 50 samples were taken for mutation analysis by ARMS PCR for five common mutations.

Out of the 50 cases the most common mutation was IVS 1-5 (G-C) in 34 (68%) females followed by with Cd8/9 (+G), with Cd41/42 with two cases (2%) each. Rest 14 (28%) cases were negative for the five common mutations.

Conclusion

To conclude IVS1-5 (G-C) is the most common mutation for Beta thalassemia in our study population. A significant (28%) of cases did not show any of the five mutations.

Miscellaneous/Molecular Hematology (MH) OP-MH-6

Molecular Work Up of Unexplained Erythrocytosis in Young Patients of Indian Origin, a Study Conducted at Tertiary Centre in North India

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Introduction

Erythrocytosis is a rare disorder characterized by increased red cell mass and elevated hemoglobin concentration and hematocrit. Several genetic variants have been identified as causes for erythrocytosis in genes belonging to different pathways including oxygen sensing, erythropoiesis and oxygen transport.

Aims & Objectives

Aim of the study is to study the molecular basis of congenital erythrocytosis for the patients presenting at department of hematology, AIIMS, New Delhi.

Materials & Methods

Study was conducted at Department of Hematology, AIIMS, New Delhi. It was a prospective study. Patients included were less than or equal to 40 years with Hemoglobin level >165gm/l or hematocrit>48%. Exclusion criteria included patients who were positive for JAK2 V617F mutation or mutations in Jak2 Exon 12. Also patients with secondary causes of erythrocytosis such as those with smoking history, high altitude residents, abnormal pulmonary function tests, renal artery stenosis, congenital heart disease, and splenomegaly were excluded. Sanger sequencing was performed for all exons of HBB gene, exon 8 of EPOR gene, exon 2 of VHL gene, Exon 1 and 2 of BPGM gene, all Exons of HBA gene. A total of 100 patients were included in the study.

Result

Hemoglobin range is 166 to 200 gm/dl. Hematocrit range is 49 to 60.8. Serum erythropoietin levels ranged from <0.1 to 67.2 mU/mL. Three patients showed mutations in Exon 2 of VHL gene, One showed mutation Homozygous NM_000551 (VHL) C.598 C>T (p.Arg200Trp), Chuvash polycythemia. Two other cases showed mutation at same site in VHL gene but in heterozygous state. One case with heterozygous mutation in exon 8 of EPOR, NM_000121.4 (EPOR):c.1460A>G (p.Asn487Ser) in a 26 year old male patient who had cerebrovascular thrombosis at young age and during workup for CVT found to have erythrocytosis.

Conclusion

Study of genetic basis of idiopathic erythrocytosis at a tertiary centre in India might provide a small insight into genetic basis of erythrocytosis in Indian patients which is not widely explored and will aid in the therapeutic advancements in cases of idiopathic erythrocytosis.

Miscellaneous/Molecular Hematology (MH) OP-MH-7

Impacts of WT1 Gene Genomic and Epigenomic Aberrations on Prognosis in Acute Myeloid Leukemia Within the Indian Population

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Introduction

Acute myeloid leukemia (AML) is a complex hematologic malignancy marked by the abnormal proliferation of myeloid progenitor cells due to various genetic and epigenetic changes. The Wilms tumor 1 (WT-1) gene, a crucial regulator of hematopoiesis, encodes a zinc-finger transcription factor that modulates cell growth, apoptosis, and differentiation. Despite its significance, the specific role and clinical relevance of WT-1 in AML remain underexplored.

Aims & Objectives

This study investigates the RNA expression, methylation levels, and molecular functions of the WT-1 gene in AML patients.

Materials & Methods

Bone marrow (BM) and peripheral blood (PB) samples were collected from 112 AML patients (112 at diagnosis and 105 post-induction chemotherapy) and 20 non-malignant controls. WT-1 expression and promoter methylation were assessed using real-time PCR and methylation-specific PCR. We also conducted Gene Set Enrichment Analysis (GSEA) to explore WT-1's biological functions and examined its correlation with immune checkpoints using the Sangerbox 3.0 database. Kaplan–Meier survival analysis assessed WT-1's prognostic significance.

Result

Among the 112 patients, 65.17% were male and 34.83 female. Notably, 86.60% exhibited WT-1 overexpression at diagnosis compared to remission or control samples ($p < 0.001$). Robust hypermethylation of the WT-1 promoter was observed in 68.75% of cases at diagnosis ($p < 0.001$). WT-1 expression and methylation inversely correlated with normal hematopoiesis, showing positive associations with age, high marrow blast counts, M4 subtype, adverse cytogenetics, and poor outcomes. GSEA indicated that WT-1 is involved in transcription misregulation and several molecular functions related to cell growth and apoptosis. Immune checkpoint analysis revealed a positive correlation between WT-1 expression and several immune markers (e.g., CD28, CD40). Survival analysis indicated that higher WT-1 expression correlated with poorer overall survival.

Conclusion

The overexpression and hypermethylation of the WT-1 gene are linked to the leukemic burden in AML, suggesting that it may serve as a promising molecular marker for early diagnosis, measurable residual disease detection, and as a potential therapeutic target in AML.

Benign Hematology-Laboratory (BHL) PP-BHL-1

Post Bone Marrow Transplant Colitis- Histopathological Clues to Differentiate Primary GVHD from CMV Colitis

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Background

Histopathology has played a major role in understanding the pathophysiology and aiding in the diagnosis and management of graft-versus-host disease (GVHD). For all the cases undergoing transplant the post-transplant recovery depends on a multitude of factors and one of the common problems that may impede recovery is acquiring infections like CMV or drug induced injuries(mycophenolate mofetil) etc. GVHD reactions affect almost all the organ systems. The department received biopsy samples of 2 cases of Colitis post bone marrow transplant ,suffering from thalassemia and aplastic anemia. We aimed this study in highlighting the histopathological findings which differentiate cases of primary GVHD colitis versus CMV colitis.

Case Presentation

Case 1:Patient was 10-year male, case of aplastic anemia who underwent a bone marrow transplant and presented with diarrhea. A histopathological biopsy sample from duodenum was sent to the department. Microscopic examination of the biopsy tissue showed biopsy fragment with large areas showing crypt drop out, focal ulceration, crypt destruction with apoptotic bodies and regenerative atypia focally. This was accompanied by fair number of eosinophils in Lamina propria, lymphocytes and neutrophils. Occasional intranuclear inclusion mimicking CMV inclusion was also seen.A diagnosis of CMV colitis with GVHD was rendered and IHC advised for confirmation.

Case 2:8 year male case of Thalassemia post BMT suffering from persistent diarrhea. Biopsy sent twice from rectal and colonic mucosa showed variable degree of crypt dropout, apoptotic debris and reactive atypia. Lamina propria showed inflammation comprising of lymphocytes, plasma cells and few eosinophils .No viral inclusions were noted in both the biopsy specimens. IHC for CMV was negative in both the cases. The first biopsy specimen from colon was Modified Lenner Sale Grade 1,Myersons Grade 1 while the follow up biopsy was Modified Lenner Sale Grade 1,Myersons Grade 2,indicating persistent GVHD features on histopathology.

Diagnosis

On comparing the histopathological features of the 2 cases it is clear that while features like crypt loss, crypt destruction, reactive atypia can occur in both CMV and GVHD inflammation comprising of neutrophils and viral inclusions are seen with CMV infection per se while absence of neutrophils favours GVHD.IHC is confirmatory for CMV infection. Presence of eosinophils may be there in GVHD as well as drug induced injury as in case with Mycophenolate mofetil.

Treatment

Since this is a histopathological correlative study treatment of the cases is not discussed in detail

Follow-up

Case 2 shows persistent GVHD histopathological features

Conclusion

Histopathological clues on biopsy specimen are extremely useful diagnostic tool with specific features which can help a histopathologists in diagnosing GVHD from CMV colitis in patients post bone marrow transplant.

Benign Hematology-Laboratory (BHL) PP-BHL-2

DKMS Access to Transplantation (ATT) Program: Giving Hope for a Healthy Future

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Introduction

Healthcare in India remains challenged by affordability, accessibility and availability. Several NGOs seek to address these challenges and help the patients find relief and improve the relevant clinical outcome. DKMS's Access to Transplantation (ATT) program is designed to bring value to patients with blood cancer and blood disorders by removing barriers to access hematopoietic stem cell transplantation (HSCT) in resource-limited settings, particularly low- and middle-income countries (LMICs).

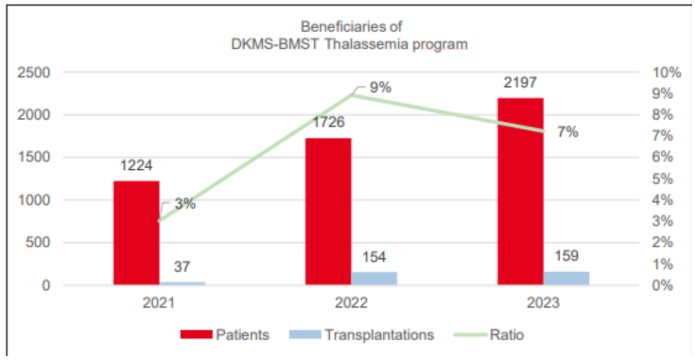
Aims & Objectives

In India, the DKMS-BMST Thalassemia program and the DKMS BMST Patient Funding program seek to facilitate access to transplantation for - patients in need, by

- Raising awareness among patient families about HSCT as a treatment option for blood cancer and blood disorders.
- Providing free high-resolution HLA typing for Thalassemia patients and their potential family donors (siblings, parents).
- Offering free searches for matched unrelated donors when no matched related donors are available.
- Guiding on treatment options and potential sources of financial support.
- Assisting patients from lower socio-economic backgrounds by offsetting substantial treatment costs through the Patient Funding program.

Materials & Methods

Impact of Access to Transplant (ATT) program in India from 2021-2023:



- DKMS-BMST Thalassemia program in collaboration with 18 partner organisations, provided 14,214 free HLA typing, leading to 961 perfect family matches. 350 patients received an HSCT by the end of 2023.
- DKMS BMST Patient Funding program received 215 applications from 21 transplant centers. Funding was confirmed for 161 patients (74.8%), who required a transplantation as a potential cure. Among these, 77 patients were diagnosed with blood cancer and 84 with blood disorders.

Conclusion

DKMS ATT programs in India have significantly improved access to transplantation for patients with blood disorders. By providing free HLA typing and financial aid, they've helped many patients receive life-saving HSCT. This has not only saved lives but also motivated families to consider transplantation and improved compliance with supportive care. DKMS aims to expand these programs to remove socioeconomic barriers to transplantation.

Benign Hematology-Laboratory (BHL) PP-BHL-3

Bone Marrow Metastasis as Presenting Feature of Follicular Thyroid Carcinoma

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Background

Bone marrow metastasis is a common site for distant metastasis in cases of thyroid cancer (2-15?ses). The rate of bone metastasis is three times higher for follicular thyroid cancer (7-28%) in comparison to papillary thyroid cancer (1-7%). The axial skeleton (spine and pelvis) is the most common site. Hereby, we discuss a case of a patient presenting with a chest wall lesion with metastatic carcinomatous deposits, which, when retrospectively investigated, came out to be a metastasis of follicular thyroid carcinoma.

Case Presentation

A 73-year-old female presented with a chest wall lesion. Routine investigations revealed a normocytic normochromic blood picture with mild rouleaux formation, raised ESR, and RFT within normal limits. Serum electrophoresis showed no M-band. β 2 microglobulin was raised. The scan showed a lytic lesion involving L1 and D12 vertebral bodies involving the right 9th rib and left 6th rib. Based on the above investigation, a provisional diagnosis of Multiple myeloma was made.

Diagnosis

A biopsy of the chest wall lesion was performed, which revealed tumor cells arranged in variable-sized follicles. The individual tumor cells exhibit mild nuclear pleomorphism, hyperchromatic nuclei, inconspicuous nucleoli, and a moderate amount of cytoplasm. Nuclear crowding and overlapping were noted. The follicles are filled with colloid-like material. The final impression was given as metastatic carcinomatous deposits, with the possibility of thyroid origin not being ruled out. A bone marrow biopsy was also done on this patient, which also revealed a similar morphology as a chest wall lesion. An immunohistochemistry TTF1 marker was applied to the blocks, and the result was positive, confirming thyroid origin.

Treatment

The patient was referred to the Department of Oncology and was given two cycles of chemotherapy.

Follow-up

Unfortunately, patient was lost to follow-up after that.

Conclusion

Bone marrow metastasis can be a presenting feature of follicular thyroid carcinoma and can mimic multiple myeloma clinically. Histopathology and bone marrow biopsy remain the gold standard for diagnosis. Further immunohistochemistry can confirm the primary.

Benign Hematology-Laboratory (BHL) PP-BHL-4

Utility of Peripheral Blood Immune Subset Enumeration in The Evaluation of Lupus Nephritis

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Introduction

Systemic lupus erythematosus (SLE) is a systemic autoimmune disease characterized by generation of autoantibodies leading to multiorgan dysfunction, particularly the kidneys. Immune cells, including T cells, B cells, dendritic cells, and others, are implicated in the pathogenesis of LN. . The role of specific immune cells in predicting the activity of lupus nephritis (LN) and outcomes not widely studied.

Aims & Objectives

To study the association of the peripheral blood immune subsets with severity of LN and with autoimmune serology

Materials & Methods

A retrospective study of 4 years (May 2021 to April 2024) was performed after ethical clearance including all cases with established diagnosis of SLE who have undergone autoimmune serology, renal biopsy and immune subset evaluation at diagnosis after excluding cases with pre-existing immune deficiency disorders and malignancy. The histopathological classification of LN was based on the criteria established by the International Society of Nephrology (ISN) and the Renal Pathology Society (RPS). Independent t test and one way ANOVA was used to assess the change in mean values. Chi square test was used to assess the association between the variables. Pearson correlation was used to assess the strength of the linear relationship between two variables. The statistical significance was determined at a 5% level of significance.

Result

A total of 28 patients of LN were identified. The mean age of the patients was 32.3 ± 16.6 years with female: male ratio of 8.3:1. Patients with Class 3, 4 and 5 LN had a significantly lower CD3, CD4 and CD8 counts. Class 4+5 LN had strong associations with CD3+, CD4+ and CD8 + T cells. Anti-cardiolipin antibodies showed significant association with CD3+, CD4+ and CD8 + cell counts.

Conclusion

The involvement of T cell subsets and anti-cardiolipin antibodies suggests their importnat role in the inflammatory process of LN. Dysregulated lymphocyte subpopulation ratios is associated with the paroxysm of LN and might provide insights to pathogenesis of LN. The study underscores the importance of comprehensive immune profiling in patients with LN. Understanding the relationship between immune subsets and disease activity can lead to better disease monitoring and targeted therapies.

Benign Hematology-Laboratory (BHL) PP-BHL-5

Multiple Myeloma-Stem Cell Transplant Experience at Our Centre

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Divya Krishna

Paras HMRI Hospital, Patna

Introduction

Multiple myeloma is a non-curable disease in which autologous stem cell transplant plays an important role.

Aims & Objectives

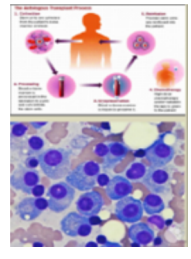
Sharing our experience from a two tier centre.

Materials & Methods

Restrospective data study

Result

70% remission rate with autologous stem cell transplant.



Conclusion

Autologous stem cell transplant offers long term remission in myeloma patients.

Benign Hematology-Laboratory (BHL) PP-BHL-6

PRCA Secondary to ABO incompatibility in Post Allogenic Stem Cell Transplant Patient

Avinash Kumar Singh
Santosh Kumar, Anis Akhtar

Paras HMRI Hospital, Patna

Background

Case Report

Case Presentation

44 years old male post Allogenic stem cell transplant with persistent anaemia.

Diagnosis

Parça secondary to ABO incompatability post Allogenic transplant.

Treatment

Bortezomib weekly for 4 weeks+ steroid

Follow-up

In Remission

Conclusion

Post Allogenic transplant with ABO incompatible donor prca can be a complication.Bortezomib can be treatment of choice.

Table 1
Types of Donor–Recipient ABO Incompatibilities

Mismatch Type	ABO Blood Type		Potential Clinical Consequence	Etiology	Potential Interventions
	Recipient	Donor			
Major	O	A, B, AB	• Acute hemolytic episode • Delayed RBC engraftment	• Transfusion of incompatible red blood cells • Recipient anti-donor isohemagglutinins	• Red blood cell reduction of stem cell product
Major	A	AB	• Pure red blood cell aplasia	• Loss of immature stem cells from processing with ABO antigens expressed on granulocytes and platelets	• Therapeutic plasma exchange in recipient to reduce isohemagglutinins before transplantation (uncommon in United States)
Major	B	AB	• Delayed granulocyte and platelet engraftment		• Promote donor erythropoiesis via erythropoietin administration
Minor	A	O	• Acute hemolytic episode secondary to passenger lymphocyte syndrome	• Donor plasma with elevated isohemagglutinin titers/small blood volume recipient • Passenger lymphocytes producing isohemagglutinins	• Plasma reduction • Continual clinical monitoring between days +5 and 15 for signs/symptoms of hemolysis (including laboratory monitoring with LDH, bilirubin, CBC, DAT)
Minor	B	O	• Delayed hemolysis		
Minor	AB	O, A, B			
Bidirectional	A	B	• Combination of major and minor consequences	• Combination of major and minor etiologies	• Combination of major and minor interventions
Bidirectional	B	A			

LDH indicates lactate dehydrogenase; DAT, direct antiglobulin test.

Benign Hematology-Laboratory (BHL) PP-BHL-7

Post Allo-SCT Membraneous Nephropathy

Avinash Kumar Singh,
Divya Krishna Santosh Kumar

Paras HMRI Hospital, Patna

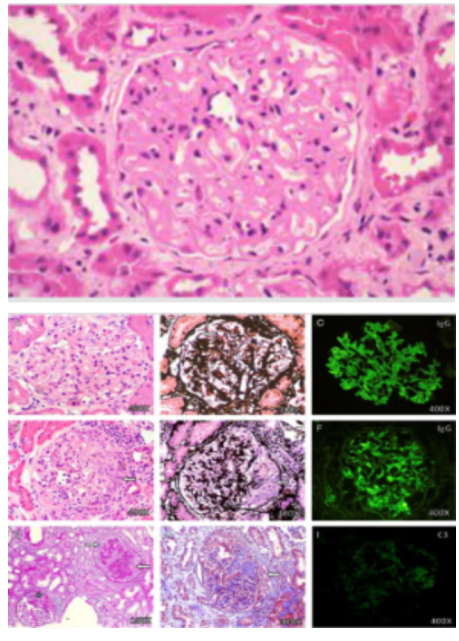
Background

Case report

Case Presentation

45 years old male a case of relapsed aml ,post Allogenic SCT evaluated for swelling of b/l lower limbs found to have significant proteinuria.

13 years olde male a case of aplastic anemia post Allogenic SCT evaluated for b/l lower limbs swelling was found to have significant proteinuria.



Diagnosis

Membranous Nephropathy -complication of chronic GVHD

Treatment

Steroid + Jakavi

Follow-up

In remission

Conclusion

Chronic GVHD affecting kidneys needs detailed evaluation including renal biopsy. Treatment with Jakavi and steroid has shown very good response.

Benign Hematology-Laboratory (BHL) PP-BHL-8

A Rare Presentation of Cardiac Amyloidosis with Pericardial Effusion

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Background

A serving soldier presented with facial puffiness and pedal oedema and diagnosed as a case of amyloidosis after extensive workup.

Case Presentation

49 years old male without any co-morbidities presented in Apr'21 with facial puffiness, painless pedal edema and pleuritic chest discomfort without any constitutional symptoms.

Diagnosis

He had muffled heart sounds with low-voltage ECG and moderate pericardial effusion on 2D echocardiography in presence of normal CBC, LFT, RFT, TFT, lipid profile with presence of sub-nephrotic proteinuria. Pericardial fluid analysis showed exudative effusion with raised ADA and he was treated empirically with ATT. However, he was evaluated at our hospital after 1 year in view of persistent chest heaviness with echo showing presence of pericardial effusion. 2D Echo showed moderate, deep-seated pericardial effusion (24 mm lateral to RV, 19 mm posterior to LV) without features of tamponade, which could not be aspirated for repeat study. CT chest-abdomen showed moderate-to-severe pericardial effusion, cardiomegaly and mild bilateral pleural effusion. Auto-immune workup negative, serum ACE level normal. Protein electrophoresis showed M band of 0.17 g/dL (SIFE – IgG lambda with normal FLC, serum β2microglobulin and neg myeloma FISH panel). Bone marrow study showed 3% plasma cells. Abdominal fat pad biopsy showed eosinophilic extracellular amorphous material deposition around dermal vessels, congophilic in congo red stain and apple-green bi-refringence under polarized lights. Cardiac MRI showed hypertrophied LV with delayed enhancement in myocardium and sub-endocardium. NGS panel for whole exome sequencing was negative.

Treatment

He was provisionally diagnosed as AL amyloidosis and treated with diuretics, ACE inhibitors and SGLT 2 inhibitors to which he has responded.

Follow-up

Patient is on regular follow up with CHEC kolkata

Conclusion

Amyloidosis is a protein misfolding disorder characterised by deposition of randomly oriented non-branching protein-fibrils in extracellular space presenting as multi-system disease. Heart is the second most-common organ involved in systemic amyloidosis. However diagnosing a case of amyloidosis is challenging due to its varied presentations.

Benign Hematology-Laboratory (BHL) PP-BHL-9

Donor-Specific Antibody Profiles in Patients Undergoing Haploidentical Hematopoietic Stem Cell Transplantation: Insights from a Tertiary Care Cancer Center in Eastern India

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Introduction

Allogeneic hematopoietic stem cell transplantation (allo-HSCT) with haploidentical donors presents challenges, especially regarding the presence donor-specific anti-HLA allo-antibodies (DSAs). These DSAs can lead to primary graft failure, a significant risk factor for transplant outcomes.

Aims & Objectives

This study aims to analyse the profile of donor-specific anti-Human Leukocyte Antigen (HLA) antibodies (DSA) in patients undergoing haploidentical HSCT at a tertiary care cancer centre in eastern India.

Materials & Methods

According to institutional policy, all the patients undergoing haploidentical HSCT were screened for the presence of anti HLA antibodies as a pre-transplant work up using Lifecodes Lifescreen Delux ® Kits from Immucor. The patients screened positive are subjected to a solid phase assay to check for the presence of donor specific antibody (DSA) using Lifecodes Lifescreen Single Antigen Assay ® Kits (Class I and Class II). Results were interpreted as mean fluorescence intensity (MFI) against DSA mismatch.

Result

Between August 2014 and 2024, 253 patients (Male: Female ratio-1.97:1) undergoing haploidentical HSCT were screened for anti-HLA antibodies. The most common diagnoses were acute myeloid leukaemia and aplastic anaemia in malignant and benign disorders respectively. All patients had received multiple transfusions prior to transplantation. Among those screened, 54 patients (21.34%) tested positive for anti-HLA antibodies. Of these, 35 patients (13.83%) had antibodies against both Class I and II. Fifteen patients (5.92%) had antibodies against Class I only and four patients (1.58%) tested positive for antibodies against Class II. Out of 54 patients screened positive, 27 patients were tested with Single Antigen Assay. Among them 15 (62.5%) were found to have donor-specific antibodies (DSA), with 10 (66.66%) having DSA against both Class I and II. Additionally, 3 (2.6%) were positive for Class I DSA, and 2 (1.33%) for Class II DSA. For two patients due to the absence of specific beads for the DSA allele in the assay kit, testing with cell-based assays (Flow crossmatch/CDC) was performed.

Conclusion

Our result of DSA positivity is concordant with the data in the published literature. It is important to screen for DSA as it might affect the outcome of transplant. Understanding the presence and levels of these antibodies can inform clinical strategies to improve graft acceptance and minimize complications, ultimately enhancing patient management and survival rates.

Benign Hematology-Laboratory (BHL) PP-BHL-10

Haemophagocytosis in The Bone Marrow: Is it Always Haemophagocytic Lymphohistiocytosis?

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Introduction

Haemophagocytic syndromes result from macrophage activation and commonly present with symptoms like hepatomegaly, splenomegaly, rash and fever. They are more commonly secondary to infection or malignancies, and are rarely primary. Although haemophagocytosis itself is not diagnostic of Haemophagocytic lymphohistiocytosis (HLH), it is an important component of the diagnostic criteria and is identified on bone marrow aspirates (BMA) by the haematopathologist.

Aims & Objectives

To observe the morphological findings in BMA smears showing haemophagocytosis, and to study the association of haemophagocytosis with other components of the HLH-2004 criteria.

Materials & Methods

BMA reports from the past 30 months were retrieved, and a search for 'haemophagocytosis' yielded 60 results. The clinical details (fever, splenomegaly) and laboratory results (haemogram, triglyceride, fibrinogen, ferritin) were obtained from hospital database/ requisition forms. The slides were retrieved and examined by two pathologists. The extent of haemophagocytic activity and where possible, the ingested cells were categorised (RBC or its precursors, granulocytes, lymphocytes and plasma cells).

Result

A total of 60 cases showing haemophagocytosis in BMA were retrieved. On correlating with HLH-2004 criteria, the most consistent criterion to be fulfilled was fever (85%) followed by 'raised ferritin' (83%) and 'cytopenias' (77%). In many cases HLH was not suspected clinically, and hence some parameters (especially triglycerides) had not been ordered. This was especially prominent in cases of Acute leukemia which showed haemophagocytosis in 18/60 cases but these could not meet the sufficient number of criteria, since HLH was not suspected clinically and the relevant tests were not ordered. Table 1 elaborates the underlying etiology in all the cases. Cases with greater extent of haemophagocytosis encountered in smears were more likely to fulfil the criteria for HLH.

Conclusion

Haemophagocytosis is often encountered in the BMA smears and may not necessarily indicate HLH. In the present study, apart from HLH, haemophagocytosis was commonly encountered in acute leukemia, acute febrile illness, leishmaniasis and sepsis. However, in unsuspected cases, it should alert the clinician to evaluate the patient for other biochemical and clinical parameters of HLH, so that a prompt and timely treatment can be started, which can be life-saving for the patient.

Table 1: Underlying etiology in cases showing evidence of haemophagocytosis on bone marrow aspirate smears

HLH (n=13)		Non HLH (n=47)
Primary (n=1)	**Secondary (n=12)**	Infective (n=17)
	Infective (n=5)	Acute leukemias (n=18)
	Sepsis (n=6)	Sepsis (n=2)
	Autoimmune (n=1)	Malignancies on treatment (n=3)
		Autoimmune/ Drug-induced (n=5)
		MDS (n=2)

Benign Hematology-Laboratory (BHL) PP-BHL-11

Enhancing Lab Performance: Essential Quality Indicators in Hematology

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Introduction

Quality indicators (QI) are measurable, objective, quantitative measures of key system performance. They can indicate the quality of the key, strategic, and support processes. Quality indicators must address all three key processes in the laboratory: pre-examination, examination, and post-examination. Besides self-evaluation, quality indicators can also be used for benchmarking. It helps to capture information about quality indicators in the haematology laboratory and to evaluate laboratory quality performance over time as a strategy for continuous quality improvement efforts.

Aims & Objectives

Our aim is to enhance lab performance and better patient care by using quality indicators in the haematology department

Materials & Methods

A retrospective analysis of the following quality indicators for July 2023-July 2024 was carried out:

a) Sample Rejection,

b) Equipment Breakdown,

c) Critical Alerts Reporting,

d) Turn-around-Time(TAT),

e) External Quality Assurance Scheme (EQAS) and

f) Internal Quality Assurance Scheme (IQAS).

Result

A total of 147664 haematology samples were received. 561 samples were rejected based on criteria clotted, mismatch, unlabelled, etc. Equipment breakdown occurred 27 times, 99.9% of critical alerts were informed telephonically; in addition system system-generated short message service(sms) was sent to patients. 2% of reports were beyond the given TAT. Out of 13 CBC EQAS challenges comprising 156 tests 2 were outliers and of 13 Coagulation EQAS challenges comprising 65 tests none of them were outliers. Necessary corrective actions were taken. Internal quality control was performed routinely; results were within the laboratory-defined ranges.

Conclusion

The use of quality indicators to assess and monitor the quality system of the clinical laboratory services is an extremely valuable tool in keeping the total testing process under control systematically and transparently.

Benign Hematology-Laboratory (BHL) PP-BHL-12

Demystifying the Evaluation of a 'Dry Tap'

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Introduction

Failure to yield any hematopoietic tissue on bone marrow aspiration (BMA) is known as 'dry tap', in which either only blood or no material is obtained. Faulty technique is frequently blamed for a dry tap. While an inaccurate technique does result in a dry tap, more often than not, the dry tap is associated with an underlying bone marrow pathology.

Aims & Objectives

This study aimed to evaluate the causes of dry tap, and to assess its clinical relevance.

Materials & Methods

This was a retrospective observational study, which included all bone marrow aspirates (BMA) and corresponding biopsies performed at our Institute from July 2023 to June, 2024. Out of these, only the aparticulate/ grossly hemodiluted smears were selected for review. The definitive diagnosis was determined by examining the trephine biopsy.

Result

A total of 1136 BMA smears and corresponding biopsy slides were reviewed for this retrospective analysis. Of these, 267 aspirates yielded no marrow particles. 76 of these aspirates were excluded from the study as in these cases, either the trephine biopsy was sub-optimal, or in some cases only aspiration had been performed. Moreover, 66 of the 267 aspirates yielded few hematopoietic elements despite being aparticulate and hence, these were also excluded. Finally, 125 (11.8%) cases had aparticulate aspirates which were grossly hemodiluted and these were attributed to a 'dry tap'. Of these, only 20 (16%) of the dry tap could be attributed to improper/ faulty technique, because their trephine biopsy was adequate and satisfactory for evaluation. The rest 105 (84%) patients had an underlying bone marrow pathology which had resulted in the dry tap. The causes of dry tap are elaborated in table 1

Table 1: Causes of dry tap in the 125 bone marrow aspirates

Sno.	Cause	Number (percentage)
1.	**Hematological malignancies**	
	Acute leukemia	41 (32.8%)
	Myeloproliferative neoplasms	22 (17.6%)
	Chronic lymphoproliferative disorders	10 (8%)
	Plasma cell dyscrasia	4 (3.2%)
2.	**MDS / MPN**	
	MDS	1 (0.8%)
	MDS/ MPN	2 (1.6%)
3.	**Benign haematological disorders**	
	Aplastic anemia	6 (4.8%)
	Hemophagocytosis	1 (0.8%)
	Nutritional anemia	5 (4%)
	Hemolytic anemia	1 (0.8%)
	Hypocellular marrow with non-specific findings	7 (5.6%)
4.	**Non haematological disorders**	
	Metastatic disease	4 (3.2%)
	Hyper cellular marrow with granuloma	1 (0.8%)
5.	**Faulty technique of aspiration**	20 (16%)

Conclusion

The laboratories should periodically review the cases yielding a dry tap, and if the corresponding biopsies are adequate, then one must focus on improving the technique of BMA. More importantly a dry tap should serve as a diagnostic alert, rather than a basis for disregard of the operator's technique. Cases of dry tap should be thoroughly investigated, as it is often associated with an underlying bone marrow pathology.

Benign Hematology-Laboratory (BHL) PP-BHL-13

Secondary Graft Failure F/B Second HSCT

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Background

Cast report

Case Presentation

7 years old girl diagnosed case of very severe aplastic anemia underwent hsct at our centre with brother as donor and bone marrow as stem cell source.Developed secondary graft rejection and underwent second hsct at our centre with the same donor and peripheral blood as stem cell source.

Diagnosis

Secondary graft failure in a case of very severe aplastic anemia post Allogenic stem cell transplant.

Treatment

Second hsct

Follow-up

In remission

Conclusion

In graft failure second hsct is an option of choice for treatment but has many challenges and high TRM.

Benign Hematology-Laboratory (BHL) PP-BHL-14

Evaluation of Short Tandem Repeat Markers for Chimerism Analysis: A Tertiary Center Experience

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Introduction

Chimerism analysis is a genetic test to monitor bone marrow engraftment and assess risk of graft failure. Different methods have been reported for this purpose, however multiplex PCR-based procedures with fluorescence detection using short tandem repeat (STR) analysis, especially commercially available multiplex assays, are frequently used, since they are independent of gender mismatch, are highly sensitive and able to generate accurate and reproducible report with very low amounts of DNA.

Aims & Objectives

The objective of the study was to assess the utility of the commercially available 16 STR marker kit for routine Chimerism analysis at tertiary cancer Center.

Materials & Methods

We did retrospective analysis of 335 chimerism samples at different time point from 134 HLA-matched related and 9 HLA-matched unrelated (MUD – from international registry) transplant, received at our laboratory during three years (January 2017 to December 2019). Chimerism analysis was performed by Promega PowerPlex® 16 HS System kit. Analysis was performed as per technical recommendations from UKNEQAS-LI Chimerism working group.

Result

The mean number of fully informative markers in the 143 cases analysed was 6 out of 16 and mean number of partially informative markers was 3 out of 16.

Most common informative markers were D8S1179 (88%, n=126) followed by THO1 (87%, n=124). Least informative marker was CSF1PO (25%, n=37).

At D+28 complete chimerism (100% Donor cell) noted in 96 noted in 96% cases (137/143) and D+90/D+100 complete chimerism noted in 91% (130/143) cases. Mixed chimerism (Donor cell < 95%) at D+90/D+100 observed in 12% (17/143) recipient. 6% (9/143) cases showed only 3 informative markers.

Conclusion

Our study highlights the importance of use of 16 STR markers for chimerism analysis. The 16 markers STR kit is sensitive and useful to detect, at least 3 informative markers for chimerism analysis.

Benign Hematology-Laboratory (BHL) PP-BHL-15

Stem Cell Transplant Experience in Aplastic Anemia from a Two Tier City

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Introduction

Allogenic stem cell transplant is the choice of treatment in aplastic anemia patients.We share her our experience in this field from a centre at a two tier city.

Aims & Objectives

Discuss experience of Hsct from a two tier city.

Materials & MethodsRetrospective data collection

Result

Around 64% patients who underwent hsct are in remission till date.

Conclusion

Allogenic stem cell transplant should be first choice of treatment in eligible aplastic anemia patients.

Benign Hematology-Laboratory (BHL) PP-BHL-16

DNTS have a High Negative Predictive Value but a Low Positive Predictive Value for The Diagnosis of ALPS

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Introduction

Autoimmune Lymphoproliferative Syndrome is a rare genetic disorder characterized by chronic lymphoproliferation and autoimmunity. One of the hallmark features of ALPS is the presence of elevated levels of Double Negative T cells (DNTs), which lack CD4 and CD8 surface markers. The criteria for diagnosing ALPS was first established in 1999 and later modified in 2009, consisting of two required and six accessory criteria. DNTs, one of the required criteria, is often mistaken to be a pathognomonic feature of ALPS.

Aims & Objectives

In this study, we aim to evaluate the predictive value of DNTs in diagnosing ALPS.

Materials & Methods

All the samples received for the Primary Immunodeficiency screening panel in the Department of Haematology, Christian Medical College, Vellore, between January 2022 and December 2023, were included in the study. Demographic, clinical and genetic details were retrieved from patients' electronic medical records.

Result

387 cases were screened for PID by flow cytometry with a median age of 7 years and a male-to-female ratio of ~1. Of these, 168 samples were received with a clinical query of ALPS. Increased TCRab+ DNTs were seen in 103/168 cases and were absent in 65/168 cases. As per the 2009 criteria, the required criteria were satisfied in 27/103 cases, 1/27 had a primary accessory criterion, and 25/27 had secondary accessory criteria. Of the 103 with DNTs, 69 had genetic testing performed at our centre. 42/69 showed variants – 22 VUS and 20 Pathogenic/ Likely pathogenic. Of the 20 significant variants, only 7 were related to ALPS and ALPS-like diseases. Among the 65 without DNTs, 31 had genetic data – 17 showed variants – 3 VUS and 14 pathogenic/ likely pathogenic variants. Of the significant variants, only 2/14 showed ALPS-like mutations. With the current cut-off values of DNTs being >1.5% of total lymphocytes and 2.5% of CD3+ lymphocytes, it had a sensitivity of 84.6% in diagnosing ALPS/ ALPS-like diseases. In comparison, the specificity was only 33%. PPV was 15.9% and NPV was 93.5%.

Conclusion

An increased percentage of TCRab+ double negative T cells has a good negative predictive value and sensitivity in diagnosing ALPS but very poor specificity and positive predictive value.

Benign Hematology-Laboratory (BHL) PP-BHL-17

Insight in Diagnostic Criteria, Lab Findings and Prognostic Factors in Patient of Hemophagocytic Lymphohistiocytosisisis in Critical Care

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Background

Hemophagocytic lymphohistiocytosis (HLH) is a hyperinflammatory syndrome with high mortality even with appropriate treatment. This condition, which shares features with sepsis and systemic inflammatory response syndrome (SIRS). It is a clinical spectrum taking place in many underlying conditions involving all age groups. HLH is a consequence of a severe, uncontrolled hyperinflammatory reaction that is many cases triggered by an infectious agent. Acquired HLH is more common than primary HLH but later is more fatal and has worst prognosis. HLH represents the extreme end of the spectrum of inflammatory reactions and is characterized by the magnitude of the clinical and laboratory abnormalities and the progressiveness of the symptoms.

Case Presentation

A 60 year female presents to the emergency and casualty department of Hamidia Hospital, Bhopal on 29/09/24. She was referred from district hospital, Sehore.

Patient presented with complaints of high grade fever since 10 days associated with chills and rigors. There was no documented diurnal variation in this patient. Patient also complained of pain in abdomen from last 7 days associated with loss of appetite and generalised weakness. There was swelling noted in bilateral arms and legs since 7 days.

There is no history of type 2 Dm, HTN, No other known medical and surgical history. Drug history is negative.

Diagnosis

Based on her clinical work up and radiological findings which showed ARDS on HRCT.

Lab findings, P.S comments, and bone marrow aspiration revealed it to be a case of Hemophagocytic Lymphohistiocytosis.

Treatment

The patient is treated conservatively on grounds of acute febrile illness.

Steroids (Dexamethasone), Antibiotics, Antipyretics, I.V fluids are given to the patient

Follow-up

The patient is continuously monitored for her vitals, clinical outcome.

Lipid profile tests, ferritin levels, follow up P.S comments and other markers are being assessed.

Conclusion

HLH is a dangerous hyperinflammatory syndrome with highly characteristic, but nonspecific, symptoms and laboratory findings. A high level of awareness is necessary to consider HLH in patients with prolonged fever, hepatosplenomegaly, and cytopenias. Genetic causes identified to date affect cytotoxic function of NK and cytotoxic T cells.

Benign Hematology-Laboratory (BHL) PP-BHL-18

Enhancing Diagnostic Accuracy Through External Quality Assessment - A Five-Year Review

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Introduction

The laboratory keeps an eye on how well its examination procedures are working by comparing the findings of other laboratories, which may involve taking part in EQA programs and finding suitable alternatives that are suited for the examinations and the interpretation of the examination results.

Aims & Objectives

For fifteen years, we have been participants in two EQA programs for parameters like CBC, reticulocyte count, peripheral smears, PT/INR, APTT, fibrinogen, and D-Dimer quantitative, and our alternates include split sample testing for the D-Dimer semiquantitative method and myeloperoxidase test. The purpose of this study is to demonstrate how effective it is to identify accuracy failures in testing techniques by involvement in EQA and other alternates.

Materials & Methods

In the last five years of data evaluation, for CBC, reticulocyte count, and peripheral smears, a total of 22 EQA samples were run for AIIMS-ISHTM, 66 samples of BIORAD EQA, which included CBC, PT/INR, APTT, fibrinogen, and D-Dimer quantitative, and 10 samples of split sample testing were done for the D-Dimer semiquantitative method and myeloperoxidase test. Data from these five years was reviewed to evaluate the outcome of the performance of test parameters with these EQAs and alternates.

Result

Z-score acceptability for AIIMS-ISHTM showed for WBC:95.5%, RBC:86.4%, MCV:95.5%, RDW:95.5%; remaining CBC parameters, reticulocyte count, and peripheral smear showed 100% satisfactory results; for BIORAD, CBC showed WBC:95.5%, RBC:97%, hemoglobin:98.5%, hemocrit:97%, MCH:98.5%, RDW:98.5%, and remaining parameters showed 100%; for BIORAD, coagulation parameters, PT:95.5%, INR:95.5%, APTT:100%, fibrinogen:98.5%, D-Dimer:100% z-score acceptability. Root cause analysis showed the most probable reason for unacceptable results, which were related either to typographical errors (12%), calibration needs (25%), equipment under repair (23%), sample handling (18%), or unexplained random errors (22%).

Conclusion

Participation in the EQA program or alternate methods helps in detecting errors, which may be directly linked to affecting the accuracy of the examination methods. Outliers of EQA tell us that the calibration of the methodology may be compromised. Prompt action taken against the root cause analysis findings helps in retrieving the accuracy and thus improves the reliability of the examination methods.

Benign Hematology-Laboratory (BHL) PP-BHL-19

Critical Insights into Bone Marrow Involvement in Neuroblastoma and Ewing's Sarcoma: Case Studies and Implications

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Background

Bone marrow involvement in neuroblastoma and Ewing sarcoma is pivotal for understanding prognosis, treatment strategies, and the underlying biology of these malignancies. Accurate assessment of marrow status can guide therapeutic decisions and influence patient outcomes.

Case Presentation

Case1: A 2-year-old male presented with a mass in the left hypochondrium and left iliac region for one week. Tru-cut biopsy from renal lesion and bone marrow aspiration were performed. Results indicated bone marrow involvement, prompting initiation of cytoreductive chemotherapy (COJEC). After receiving treatment, patient showed improvement.

Case 2: A 15-year-old girl presented with forehead swelling since 6 moths, with history of prior surgery for similar lesion. Additionally, she had knee swelling and altered sensorium. After neuroimaging and PET scan, surgical intervention was done. Postoperatively, bone marrow examination was performed for suspected metastasis.

Diagnosis

Case 1: Histopathological analysis of trucut biopsy revealed malignant round cell tumor. Subsequent immunohistochemical (IHC) analysis showed positivity for NSE, synaptophysin, and chromogranin, confirming the diagnosis of left paraspinal neuroblastoma. Bilateral bone marrow aspiration and biopsy suggested Stage 4 disease due to marrow involvement.

Case 2: Histopathological analysis performed indicated malignant small round cell tumor with possibility of Ewing Sarcoma/ PNET. For further confirmation, immunohistochemical analysis performed showed positivity for CD99 and FLI-1. Following this, FDG PET scan showed a mixed lytic-sclerotic lesion in the proximal epi-metaphysis of the left tibia, indicating a primary malignant lesion with features of Ewing Sarcoma. Bone marrow aspiration and biopsy confirmed bilateral marrow metastasis.

Treatment

Case 1: Patient with metastatic neuroblastoma underwent cytoreductive chemotherapy.

Case 2: Patient underwent surgical resection for her forehead lesion, followed by chemotherapy for metastasis.

Follow-up

Case 1: Patient is tolerating treatment well, with ongoing chemotherapy cycles.

Case 2: Follow-up of patient is pending.

Conclusion

Detection of bone marrow involvement mandates multimodal treatment approach integrating chemotherapy, surgery, and radiation. Evaluating the response of marrow disease to systemic therapy is crucial for optimizing treatment efficacy and assessing novel therapeutic strategies.

Benign Hematology-Laboratory (BHL) PP-BHL-20

Role of Cytochemical Myeloperoxidase (MPO) Stain in Detection of Myelodysplasia on Morphology

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Introduction

The MPO-stain is a histochemical stain used to identify myeloperoxidase enzyme activity in polymorphonuclear neutrophils and their precursors. The expression of MPO is used extensively as it is sensitive, easily available, rapid, economical and convenient way to diagnosis and subtype various leukemias. A positive MPO-stain indicates presence of myeloid lineage cells, while a negative result can suggest lymphoid lineage cell or other cell types. However, the negative stain in granulocytic lineage helps in detecting the abnormality which indicates dyspoiesis.

Aims & Objectives

To establish the role of MPO-stain in detection of myelodysplasia like features which gives a strong clue to diagnose MDS(myelodysplastic neoplasm) and AML-MR(AML-myelodysplasia related) on morphology and guide further ancillary techniques.

Materials & Methods

We assessed the intensity of MPO cytochemical stain in bone marrow aspirate smears of 73 patients, of which 31-MDS patients, 22 AML-MR, 10 cases with t(8;21) and 10 controls included negative staging marrows. The aspirate slides were stained with Benzidine dihydrochloride after fixation and counter stained with wright stain. The reaction product was black and coarse. The normal neutrophils and its precursors-stained black color uniformly and the myeloid blasts show polar staining. The absence of the black color staining in cytoplasm was considered as abnormality in granulocytes.

Result

Of 31 MDS cases, 15 cases (48%) showed absence of myeloperoxidase staining in neutrophils and its precursors and 11 cases (35.48%) showed weak positive stain. Of 22 AML-MR cases, in 18 cases (81%) the neutrophils showed weak to negative MPO stain, and blasts in 54% (n=12) were MPO positive. The expression of MPO stain was compared to the 10 control samples where the normal neutrophils and its precursors showed uniform MPO staining. The blasts in AML cases with t(8;21) showed strong polar MPO positivity while there was comparative weak to negative MPO stain in dysplastic myeloid cells. Thus, the negative and weak expression of MPO was considered as abnormal and stated as dysplastic neutrophils.

Conclusion

MPO stain is a sensitive, rapid and easily available way to look for intensity of positive staining to detect dysplastic features in granulocytic cells in cases of MDS and AML-MR.

Benign Hematology-Laboratory (BHL) PP-BHL-21

Diagnostic Accuracy of 'Scatter Fluorescence Cube Technology' for Detecting Blasts in Peripheral Blood

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Introduction

Scatter fluorescence cube technology used in Mindray BC6800 is a relatively newer technology which in addition to a five part differential leucocyte count and 37 routine parameters has 17 research parameters which includes flagging of abnormal cells like nucleated red blood cells (NRBC), immature granulocytes (IMG), infected red blood cells, blasts and atypical lymphocytes. This study was conducted to assess its utility in a routine hematology laboratory to see if it could reliably detect and distinguish blasts and atypical lymphocytes with enough accuracy that it could reduce the need for manual microscopy.

Aims & Objectives

To determine the sensitivity of 'Scatter Fluorescence Cube Technology' in Mindray BC 6800 automated hematology analyser in identifying blasts in peripheral blood.

Materials & Methods

A cross-sectional study was conducted on samples which came for complete blood count in the routine hematology laboratory of a tertiary care hospital. The Mindray BC 6800 automated hematology analyser was used. CBC parameters of samples which were flagged for "? blasts", "? atypical lymph/blasts" and "? atypical lymph" were evaluated and their peripheral smear was seen for confirmation of blasts. Even the presence of 1% blasts was considered positive on peripheral smear.

Result

Out of the 8336 samples which were evaluated, 1131 were flagged. Out of these 40 were flagged for "? blasts" with a sensitivity of 12.42% and specificity of 97.28%; 103 were flagged for "? atypical lymph" with a Sn of 31.9% and Sp of 64.4%; 175 were flagged for the non-specific flag "? abn lymph/blasts" with a Sn of 54.35% and a Sp of 42.47%. Four cases which were signed out as hematological malignancy were not flagged at all.

Conclusion

SF Cube technology has high sensitivity in detecting blasts and abnormal lymphocyte but it does not have 100% Sensitivity. Also it failed to reliably distinguish atypical lymphocytes from blasts. While most cases of hematological malignancies were flagged with at least one of these flags, not all were reliably flagged as "? blasts". We conclude that while these flags are good indicators and should raise the need for peripheral smear evaluation, it lacks accuracy and cannot be considered a standalone for diagnosing hematological malignancies.

Benign Hematology-Laboratory (BHL) PP-BHL-22

In The Shadows: A Study of Bone Marrow Metastasis of Solid Tumours in Paediatric Population

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Introduction

While the bone marrow is an established site of origin of primary haematological malignancies, it is also an important site for involvement by metastatic solid malignancies. Bone marrow aspiration and biopsy are essential to determine marrow metastasis, aid in clinical staging, risk stratification, and therapy selection, understand the response to treatment, and predict relapse. In patients with an unknown primary, the study of histomorphological features of metastatic deposits may also point us in the direction of the primary non-hematopoietic solid malignancy.

Aims & Objectives

This study aims to review the incidence and histopathological features of metastatic deposits of solid tumours in bone marrow in the paediatric population.

Materials & Methods

A retrospective study was conducted, and an institutional database was searched to identify paediatric cases with solid tumours who underwent bone marrow aspiration and biopsy from January 2017 to October 2024. Their slides were retrieved and examined to identify the cases that showed evidence of metastatic deposits.

Result

Seventy-eight cases were identified, out of which twenty-one cases showed metastatic deposits. Of these, fifteen were diagnosed cases of neuroblastoma; two were afflicted with Ewings sarcoma, and one patient had medulloblastoma. One of the cases had an unknown primary. On microscopic examination of bone marrow aspirate smears, the tumour deposits had characteristic small, round blue cell morphology. None of the diagnosed cases of rhabdomyosarcoma showed evidence of bone marrow invasion.

Conclusion

To conclude, bone marrow is an important and commonly involved site of metastasis for solid tumours in paediatric population. Bone marrow aspiration and biopsy is a relatively simple and cost-effective procedure to look for such deposits and guide further treatment and monitor the prognosis.

Benign Hematology-Laboratory (BHL) PP-BHL-23

Thalassemia Transplant Experience From A Tertiary Care Center - South India

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Introduction

The Thalassemia and structural hemoglobin disorders are the commonest monogenetic disorders globally. India has a huge burden with estimated 100,000 patient with beta Thalassemia Syndrome. Majority of these children lack the facilities even for proper blood transfusion and chelation therapy. However, currently the only curative treatment is still the Allogenic stem cell transplantation. Selecting the right patient and considering intense chelation and Pretransplant immunosuppressive therapy would be much helpful for these children to have high cure rate post-transplant. In this study we are projecting our experience about allogenic stem cell transplantation in Thalassemia children.

Aims & Objectives

This is a retrospective study evaluating the outcome of Thalassemia children at a our center between Jan 2022 – May 2024

Materials & Methods

The data were retrieved from the case records and tabulated analyzed.

Result

We have done total 27 Thalassemia Allogenic HSCT during this period, median age was 7yrs, in our series there were 10 (37%) children belongs to class III and 17 children were class II(63%). Mean baseline ferritin was 3700ngm/ml. All these children received 2 cycles of Pre-transplant conditioning therapy. Type of transplant Full matched family donor -5 (18%), Haplo HSCT 21 (77.7%) and MUD transplant -1(3.7%). Conditioning therapy FTT in full matched children and FTTA in haploidentical HSCT and MUD children. Overall Mortality was 22%; 2 (7.4%) children died before engraftment due to gram negative sepsis and 4 (14.8%) children post engraftment due to GVHD grade IV, Refractory CMV infection. One child had graft rejection at day +180 he is alive planned for second transplantation. Overall survival in our series was 78%. No engraftment related issues.

Conclusion

Our series has unique data having high number of class III children and predominate Haplo transplanted children. Meticulous selection of children and intense chelation pre transplantation would help in preventing the graft rejection and peri transplant related issues. Our data having similar survival as western data

Benign Hematology-Laboratory (BHL) PP-BHL-24

Hemophagocytic Lymphohistiocytosis (HLH) - A Rare Case Report

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Background

Hemophagocytic lymphohistiocytosis is a rare and aggressive life-threatening syndrome of excessive immune activation, immune dysregulation and inflammation. This condition can occur as primary or secondary to infections, autoimmune diseases and malignancy. Its incidence is estimated to be 1.2 cases per 10,00,000 individuals per year.

Case Presentation

We present a case of 50 years male with complaints of high-grade fever, generalized weakness, loss of appetite and weight loss since 2-3 months. Routine blood counts and peripheral smear examination revealed microcytic hypochromic anaemia with pancytopenia.

Biochemical investigations revealed raised blood urea levels(91.9mg/dl) and raised LDH levels (1735 U/L), elevated AST-79 U/L, elevated ALT- 68 U/L and elevated serum triglyceride-399 mg/dl.

Bone marrow aspiration showed markedly hypercellular marrow with decrease in erythroid and myeloid cells, relative lymphocytosis with marked increase in RE cell and histiocytes, also seen in clusters. Few of these cells revealed hemophagocytosis of platelet/white cells/normoblasts. Occasional mitotic cells also seen.

BM biopsy revealed hypercellular marrow with focal and diffuse lymphohistiocytosis. The erythroid and myeloid precursor were markedly decreased. Occasional clusters of histiocytes with pink granular cytoplasm also seen. The erythroid and myeloid precursors are markedly decreased.

Immunohistochemistry findings showed positivity for CD68 and CD163.

USG abdomen and pelvis revealed mild splenomegaly.

Diagnosis

Based on above findings a diagnosis of hemophagocytic lymphohistiocytosis was made on the basis of Diagnostic criteria for hemophagocytic lymphohistiocytosis HLH-2004.

Treatment

Patient was started on dexamethasone and supportive care.

Follow-up

The patient was continued with the above treatment but eventually succumbed to multi-organ failure after one week of hospital course.

Conclusion

This case report enlighted physicians and haematologists for further similar type of cases so that timely diagnosis and management of patients can be done. The mortality rates in adults are high due to delayed diagnosis and multiorgan involvement.

Benign Hematology-Laboratory (BHL) PP-BHL-25

The Many Faces of Sitosterolaemia

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Background

Sitosterolaemia is an uncommon disorder of lipid metabolism that is inherited in an autosomal recessive manner. It is characterized by an increase in absorption of dietary sterols, especially the phytosterols. Patients may develop hypercholesterolaemia, xanthomas, premature atherosclerosis, deranged liver function tests and a variety of haematological abnormalities, including haemolytic anaemia and macrothrombocytopaenia.

Case Presentation

We present two cases of sitosterolaemia that were diagnosed at our institution in the last 2 years. The first case was a 64 year lady referred with cytopaenias noted more than 3 years ago. She had a history of Coronary artery disease and CABG. More recently, she was treated with steroids for suspected ITP, prior to presentation to us with little benefit. There was history of consanguinity in the parents and she had xanthelesmas. The CBC at presentation showed: Hb: 10, WBC 9.7, Platelets 37, Reticulocyte count 3%. She had mild unconjugated hyperbilirubinaemia (Bilirubin 2.0, unconjugated Bilirubin 1.6) and mildly raised LDH (241, ULN 234). The second patient was a 39 year female referred with anaemia and splenomegaly. Splenomegaly was apparently first noted more than 10 years ago. She was unsuccessfully treated as autoimmune haemolytic anaemia (AIHA) with steroids on a few occasions prior to presentation to us. She too gave a history of consanguinity in the parents. The CBC at presentation showed: Hb 9.2, MCV 102.4, WBC 5.8, Platelets 90, Reticulocyte count 5.5%. Bilirubin was normal but LDH was marginally elevated (242, ULN 234)

Diagnosis

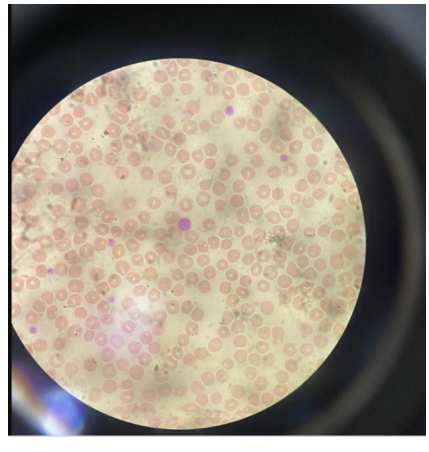
Both patients had certain characteristic abnormalities on the peripheral smear, which raised suspicion for sitosterolaemia. The most obvious features were significant anisothrombia with several giant platelets (some almost as big as neutrophils!), red cell abnormalities in the form of polychromasia, stomatocytes, spherocytes and an occasional nucleated red blood cell. History of consanguinity in the parents and lack of response to steroids added weight to our suspicion. Patients underwent Next Generation Sequencing (NGS) and were found to harbour the homozygous mutation for the ABCG5 gene at exon 9.

Treatment

Both patients were given dietary advice regarding avoidance of plant sterol rich foods such as vegetable oils, nuts, etc. The first patient who had a history of coronary artery disease and xanthelesma, was started on Ezetimibe.

Follow-up

Both patients have been advised to attend the outpatient department for regular follow up, every 3-4 months.



Conclusion

Sitosterolaemia is considered a rare metabolic disorder, but its prevalence may be significantly underestimated. The suspicion in both cases was raised on peripheral smear examination, which is readily available. Eliciting thorough history, good clinical examination and proper peripheral smear examination offer valuable clues towards a diagnosis of sitosterolaemia, which can be confirmed by genetic testing. Prompt diagnosis will help patients take necessary dietary precautions and lipid lowering medications to minimize the risk of premature atherosclerosis.

Benign Hematology-Laboratory (BHL) PP-BHL-26

HSCT For Adults with Sickle Cell Disease - Attempting to Fulfill the Void

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Introduction

Hematopoietic stem cell transplantation (HSCT) offers a potential cure for sickle cell disease (SCD). HSCT is currently indicated in persons with severe vaso-occlusive complications or end-organ damage related to SCD. Retrospective studies have shown that children have better outcomes in SCD HSCT. Paradoxically, many sickle phenotypes worsen with age, as end-organ damage accumulates, making them theoretically eligible but medically unfit for transplantation in adulthood. Thus, deciding to proceed with HSCT in an adult patient is complex. The need for more adult sickle cell transplants in our country and to explore expanded donor pool options is a pressing necessity.

Aims & Objectives

To assess the feasibility and outcomes of HSCT for adults with SCD

Materials & Methods

Fourteen patients aged 18 years or more who underwent allogenic stem cell transplants at our institution between 2018 and 2024 have been included in this retrospective case series. This series includes both matched donor and haploidentical donor transplants for adults with sickle cell anemia.

Result

14 adults with SCD with severe phenotypes, ranging from 18 -29 years of age underwent HSCT from 2018 to 2024 at our institution. All of them underwent myeloablative conditioning and received PBSCs. 5 patients had haplo-identical donors while 9 patients had matched sibling donors. The follow-up period ranged from 6 to 80 months, with a median follow-up of 31 months. The haploidentical donor transplant patients received pretransplant immunosuppressive therapy. 2 patients developed acute gut GVHD and 1 developed chronic skin GVHD. One patient developed primary graft failure precipitated by early CMV reactivation (autologous rescue done). 2 patients who underwent MSD and one patient who underwent a haplo transplant had died. 2 patients developed PRES beyond day 100. At present 10/14 (71 %) of these patients are on follow-up and without sickle-related complications

Conclusion

Stem cell transplantation in adult sickle cell patients is feasible and should be considered in adult sickle cell patients with significant sickle-related impairment in quality of life. The decision to transplant in adult SCD remains a complex one. Given these challenges, there is a void in the arena of adult sickle cell transplantation in our country, that we endeavor to fulfill.

Benign Hematology-Laboratory (BHL) PP-BHL-27

Hemeteam India : Together Everyone Achieves More

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Introduction

Interprofessional team-based care has been often reported in cellular therapy settings in order to promote quality care and amalgamation of knowledge in the best interest of the patient and the hospital. Myriad terms are in vogue which all signify team-based care: transdisciplinary, cross-disciplinary, interdisciplinary and multidisciplinary, to name a few. However, they are not interchangeable as they all exist within different frameworks. For example, multidisciplinary care implies different disciplines working collaboratively but within their clinical limits, whereas interdisciplinary means synthesis and harmonization of knowledge under one integrative approach within one team.

Aims & Objectives

AIM: This is a single centre retrospective experience to depict the effectiveness of team based interdisciplinary care (HemeTEAM India) in a BMT unit in India.

OBJECTIVE: Comparison of outcomes in transplant patients in terms of mortality, infection rates as well as administrative aspects related to length of intensive care unit (ICU) and average length of hospital stay, and financial implications.

Materials & Methods

This study is a descriptive retrospective analysis of performance of the BMT unit at the department of Hematology and bone marrow transplant at Fortis Memorial Research Institute, Gurugram, India. This is a private sector hospital in urban area of National Capital Territory of Delhi catering to 150-200 transplant cases per year. The transplant unit was established in the year 2017.

The conceptualization of an integrative approach and development of HemeTEAM India began in 2020, and implementation in 2021. The evaluation of outcomes was performed on 31 December, 2020, and on 31st July, 2024 to compare the differences in outcomes after implementation of HemeTEAM India.

Result

The recruitment and team building began in 2021, and expert from interdisciplinary fields were on-boarded on a staggered approach. A total of 550 transplants were conducted before 2021. From 2021 to 2024, 500 more transplants were done. The length of hospital stay was shortened by 2+/-1 day from an average length of 21 days to 19 days, with ICU stay shortening from an average of 7 days to 3 days. This resulted in increased hospital bed turnover. The recruitment of financial coordinator reduced the turnaround time of discharge procedures by 80% (from 12 hours to 2.6 hours) and faster insurance reimbursement and bill settlement.

The cost of one allogeneic BMT before 2021 was $30000 which is now $22000, giving the patient a financial benefit of $8000. The cost of cross referraland visits was $3000 which is now brought down to $500.

Conclusion

This is a prototype model which can be replicated not only in BMT units, but also across other specialties offering better patient focused care eventually resulting in better outcomes. This model rationalizes interdisciplinary care, delegation of duties and caters to unmet needs for the aggrieved both medically and financially.

Benign Hematology-Laboratory (BHL) PP-BHL-28

Cytogenetics-Based Characterization of Acute Myeloid Leukemia (AML)

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Introduction

Cytogenetic analysis in Acute myeloid leukemia (AML) is an essential key element in classifying AML subtypes and has important implications for clinical management. Cytogenetic abnormalities define 3 AML categories: AML with recurrent genetic abnormalities (AML-RGA), AML with myelodysplasia-related changes (AML-MRC), and AML-not otherwise specified (AML-NOS). We aimed to describe the chromosomal abnormalities in newly diagnosed AML and reclassify them according to the 5th edition of the World Health Organization(WHO-HAEM5) and International Consensus Classification (ICC) of acute leukemias.

Objectives

To classify cytogenetic abnormalities in AML as per WHO- HAEM5 and ICC.

To risk stratify the cytogenetic abnormalities in AML as per the 2022 edition of the European Leukemia Network of AML-2022 (ELN-2022).

Patients And Methods

The newly diagnosed AML cases at Christian Medical College, Vellore, between 2018 and 2023, were retrospectively looked for conventional karyotyping. Cytogenetic analysis was performed on unstimulated overnight cultures of bone marrow using standard protocols, and results were reported as per ISCN. Patients who had received chemotherapy relapsed, and those with incomplete karyotype study were excluded. We also excluded APML and secondary-AML cases.

Results

We received 986 cases of AML. After exclusion, 668 cases (60%) were used for further analysis. The median age was 37 years (range: 0-80 years), of which 397(59.4%) were males and 271(40.6%) were females (Table 1). The abnormal karyotype was seen in 399 (59.7%) patients, while 269 (40.2%) showed normal karyotype. Of 399 cases, solitary abnormalities were seen in 170 (42.6%) and two in 93(23.3%), while 136(34.1%) patients showed ≥3 chromosomal abnormalities. The most common RGAs were t(8;21)(n=84, 53.8%), inv(16) (n=25, 16%), and 11q23 rearrangements (n=26, 16.7%). The most common numerical abnormalities were trisomy 8 (n=24,-39.3%), loss of Y (n=23, 37.7%), and monosomy 7 (n=14, 22.9%). The cases were classified according to WHO-2022 and ICC-2022 (Table 2). Based on ELN-2022 risk stratification, 16% of AML cases were classified as favourable-risk, 59.4% as intermediate-risk, and remain 24.6% as adverse-risk%.

Table 1: Overview Of 668 AML Cases

Characteristic	AML Cases	Median Age	Males	Females
All karyotype details	668	37 (0-80)	397 (59.4)	271 (40.6%)
Normal karyotype	269 (40.2%)	37 (0-75)	166 (61.7%)	103 (38.2%)
Abnormal karyotype	399 (59.7%)	38 (1-79)	231 (57.8%)	168 (42.1)
Details of Abnormal karyotype (n=399)				
Based on the number of karyotypic abnormalities				
Single abnormality	170(42.6%)	37(0-79)	91(17.7%)	79(15.1%)
Two abnormalities	93(23.3%)	38(2-72)	62(66.6%)	31(33.3%)
Complex karyotype (≥ 3 abnormalities)	136(34.1%)	37(1-71)	78(57.3%)	58(42.6%)

Table 2:Classification of AML As per WHO-HAEM5 and ICC-2022

AML (n=668)	WHO-2016	WHO-HAEM5	ICC-2022
RGA	156 (23.3%)	156 (23.3%)	156 (23.3%)
AML-MRC	124 (18.5%)	120 (17.9%)	163 (24.4%)
AML-NOS	388 (58.1%)	392 (59.4%)	349 (52.2%)

Conclusion

The frequency of abnormal karyotype in our AML cohort was 60%, which is in concordance with the available literature. The incorporation of the molecular profile is needed to characterize the intermediate risk further.

Malignant Hematology-Laboratory (MHL) PP-MHL-1

Myeloid Sarcoma: An Uncommon Presentation of Myeloid Neoplasms - A Case Series of 4 Rare Cases Reported in a Tertiary Care Institute

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Background

Myeloid sarcoma (MS) is a neoplasm of the myeloid cells and can arise before, concurrent with or following haematolymphoid malignancies. It is an uncommon extramedullary manifestation commonly associated with AML. We report 04 cases of MS, diagnosed in this institute over a period of 6 years, during various phases of their respective hematolymphoid malignancy.

Case Presentation

Case 1: A 13yr/female; a known case of AML (in remission) presented with lump right breast

Case 2: A 70 yr/male, with no previous known co-morbidities or h/o neoplasia presented with an enlarged cervical lymph node

Case 3: A 5yr/male, a newly diagnosed case of APML presented with swelling in left temporal region since 15 days.

Case 4: A 49 yr/female, a known case of MDS-EB2 with monosomy 7 (in remission) presented with abnormal uterine bleeding and clinical signs and symptoms of Anemia

Diagnosis

Case 1:

1. FNAC - Features of hematolymphoid neoplasm.
2. Concurrent PBS: 8% blasts
3. Concurrent Bone marrow studies: 61% myeloid blasts
4. Histopathology of breast lump: Myeloid sarcoma
5. Final diagnosis: Myeloid sarcoma presenting as a relapse of AML with additional molecular changes

Case 2:

1. Lymph node excision biopsy: NHL
2. Concurrent PBS: High TLC with immature polymorphonuclear cells and 15% blasts
3. Bone marrow studies: 70% myeloid blasts s/o CML with blast crises
4. Review of Lymph node biopsy with PBS and bone marrow study features (final diagnosis): CML in blast crises presenting as Myeloid sarcoma

Case 3:

1. FNAC: Features of cutaneous hematolymphoid neoplasm in a k/c/o APML
2. PBS: 33% blasts with promyelocytes
3. Bone marrow studies: 28% hypergranular promyelocytes
4. CECT head: Extensive periosteal reaction involving skull base and mandible with overlying enhancing soft tissue swelling extending into extradural space favouring a granulomatous etiology, with differential diagnosis of Hypervitsminosis A, Late onset Caffey's disease and infiltration by leukaemia/lymphoma or a small round cell tumour.

5. MRI brain: Possible extramedullary hematopoeisis with a differential diagnosis of a Myeloproliferative disorder
6. Histopathology of temporal lesion: Myeloid sarcoma
7. Final diagnosis: Myeloid sarcoma in a k/c/o APML

Case 4:

1. Gynaecological examination: Uterocervical mass
2. TAH + BSO done with its histopathology: Features s/o hematolymphoid neoplasm in cervix
3. PBS: 15% blasts
4. Bone marrow studies: 24% blasts with promyelocytes
5. Final diagnosis: Secondary AML following transformation of MDS EB2 presenting as Myeloid sarcoma of Uterine cervix

Treatment

Case 1: FLAG-ida regimen of salvage chemotherapy

Case 2: Ponatinib + FLAG-ida therapy

Case 3: ATRA therapy

Case 4: Decitabine therapy

Follow-up

Case 1: Death after 04 months of diagnosis of MS

Case 2: Initial remission followed by relapse and subsequent death after 08 months of diagnosis of MS

Case 3: Death within 01 month of diagnosis

Case 4: Death after 09 months of disgnosis of MS

Conclusion

MS is an uncommon neoplasm associated with myelogenous neoplasms. It can present at any site of the body and during any stage of the disease. It is a marker of unfavourable prognosis and indicates poor survival. Due to versatility of its clinical presentation, it is important to consider a differential diagnosis of MS in haematological neoplasia, small round cell tumours and undifferentiated carcinomas/sarcomas, even in the absence of a clinically apparent evidence of a haematolymphoid malignancy. Early intervention along with timely diagnosis, including complete staging of the disease coupled with accurate molecular study and appropriate management is crucial to improve survival. Additionally, newer therapeutic markers can also be used in assessment of the disease, which can further accentuate the survival.

Malignant Hematology-Laboratory (MHL) PP-MHL-2

Primary Thyroid Lymphoma: A Report of 4 Cases with Cyto-histopathological Correlation

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Background

Primary thyroid lymphoma (PTL) is an uncommon entity that comprises less than 5% of thyroid malignancies and 2-3% of extranodal lymphomas.[1] PTLs have a female predilection, with Diffuse large B-cell lymphoma (DLBCL) being the commonest subtype, followed by mucosa-associated lymphoid tissue (MALT) lymphomas.[2].

Case Presentation

Total thyroid FNACs performed in the cytology laboratory, and the number of cases diagnosed as categories V and VI of TBSRTC and PTLs were calculated. The proportion of PTLs over total thyroid FNACs and PTLs over categories V and VI of TBSRTC was calculated. Clinico-radiological data, FNAC, histopathology (HPE), and immunohistochemistry (IHC) data were retrieved from the hospital & departmental database.

Case presentation/Result: A total of 734 thyroid FNACs were performed in two years (September 2022-August 2024), of which 30 cases belonged to categories V and VI of TBSRTC, and 4 cases of PTLs were identified, constituting 0.54% of total thyroid FNACs and 13.33% of primary thyroid malignancies. A female predilection (M: F= 1:3) was found with age ranging from 58-78 years.

Diagnosis

On CECT, 2 of 4 cases showed homogenous enlargement of both thyroid lobes, 1 showed solitary exophytic nodule, and 1 showed multiple nodules involving entire thyroid. On FNAC, all 4 cases were diagnosed as non-Hodgkin`s lymphoma (NHL), with 3 of 4 cases showing the morphology of large cell lymphoma and 1 case showing plasmacytoid morphology. 1 of the 4 cases exhibiting solitary exophytic nodule on CECT also had cytological features of co-existing lymphocytic thyroiditis. On HPE and IHC, all 4 cases turned out to be DLBCL, with 2 cases each of geminal center B-cell subtype (DLBCL, GCB) and activated B-cell subtype (DLBCL, ABC).

Treatment

On modified Ann Arbor staging 2 cases each of stage IE and stage IIE were found. All the cases were treated with chemotherapy only.

Follow-up

3 of the 4 cases are on regular follow-up after completion of chemotherapy. However, 1 succumbed to the disease during the second cycle of chemotherapy.

Conclusion

FNAC is an incredible diagnostic tool for diagnosing PTL with high sensitivity and specificity. DLBCL is the most common NHL among PTLs.

Malignant Hematology-Laboratory (MHL) PP-MHL-3

Infant's Genetic Battle: Familial Hemophagocytic Lymphohistiocytosis Revealed

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Background

Hemophagocytic Lymphohistiocytosis (HLH), first described in 1939, represents a severe, often fatal, immune disorder driven by excessive inflammatory cytokine release. HLH is characterized by multi-organ infiltration, hematological suppression, and hemophagocytosis. Primary HLH includes Familial HLH (FHL) and primary immunodeficiency syndromes, with FHL frequently linked to genetic mutations such as those in the PRF1 gene, leading to impaired cytotoxic cell function and uncontrolled cytokine production.

Case Presentation

We present a 6-month-old female infant from a consanguineous family, initially born with low birth weight but otherwise healthy. At 4 months, she experienced recurrent fever and seizures, diagnosed as meningitis elsewhere. Symptoms persisted, including persistent fever, projectile vomiting, abdominal distension, developmental regression, and neurological abnormalities. Clinical examination revealed hepatosplenomegaly, microcephaly, and developmental delay. Laboratory findings included bicytopenia, elevated LDH, hyperferritinemia, hypertriglyceridemia, hypoalbuminemia, and hyponatremia. Imaging showed hepatosplenomegaly and brain abnormalities. Bone marrow aspiration demonstrated hemophagocytosis, and whole exome sequencing confirmed FHL type 2 due to a homozygous missense PRF1 mutation.

Diagnosis

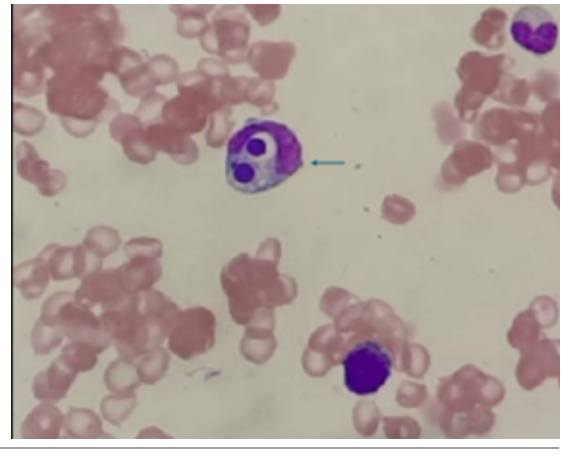
The diagnosis of HLH was confirmed by meeting six out of eight HLH-2004 diagnostic criteria: fever, splenomegaly, bicytopenia, elevated LDH, hyperferritinemia, and hemophagocytosis. Whole exome sequencing revealed a homozygous missense variant (c.1489T>C, (p. Cys497Arg)), {Amino acid conserved by GERP++ PhyloP}, favoring the diagnosis of Familial Hemophagocytic Lymphohistiocytosis 2 (FHL2).

Treatment

Initial management included broad-spectrum antibiotics, intravenous dexamethasone, anti-epileptic medications, electrolyte correction, and blood transfusions. Despite these interventions, the child's condition did not improve. The addition of chemotherapeutic agents and HSCT was considered; however, due to the severity and lack of response, the parents opted for discharge after 6 days, and the child was lost to follow-up.

Follow-up

The prognosis and outcome could not be documented as the patient was lost to follow-up.



Conclusion

FHL, particularly Familial HLH 2 due to PRF1 mutations, is a life-threatening condition requiring prompt diagnosis and treatment. Early initiation of treatment, including chemotherapy and hematopoietic stem cell transplantation, is crucial for improving survival outcomes. This case highlights the importance of genetic testing and adherence to diagnostic criteria in managing this complex disorder.

Malignant Hematology-Laboratory (MHL) PP-MHL-4

Experience With Ark Methotrexate Assay in Cancer Care

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Introduction

Methotrexate, abbreviated as MTX, is anti-metabolite and anti-folate drug. Methotrexate test is used for the measurement of methotrexate in human samples, typically serum or plasma. The measurement thus obtained are used in monitoring levels of methotrexate to ensure appropriate drug therapy. The degree of methotrexate cytotoxicity is related to the drug's concentration and to the duration of exposure. The use of lecovorin "rescue" permits relatively safe administration of very high doses of methotrexate to achieve maximum antineoplastic activity. Monitoring methotrexate concentrations & rate of decline in serum during high-dose therapy is essential when designing adequate leucovorin rescue dosages for several reasons

Aims & Objectives

The goal of this study was to establish Methotrexate Assay quantitation and validation by using the ARK assay technology on Siemens Dimension Biochemistry Analyser

Materials & Methods

We established Ark Diagnostics Methotrexate Assay on the Siemens Dimension ExL analyser for Methotrexate evaluation. All the quality parameters like CV%, Precision, Linearity, Limit of detection, limit of blank, inter-lab comparison were assessed for the assay

Result

We observed CV% 6.4, Linearity 0.04-1.2umol/L, Limit of detection 0.0206 µMol /L and Limit of blank 0 µMol/L were observed

Conclusion

Ark Methotrexate Assay can be successfully established on Siemens Dimension EXL analyser and used in the evaluation of Methotrexate levels.

Malignant Hematology-Laboratory (MHL) PP-MHL-5

Does Ploidy Status by Flowcytometry Correlate with Cytogenetic Studies : A Single Centre Experience

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Introduction

FxCycle is a DNA selective dye that preferentially stains dsDNA and can be used to analyze DNA ploidy in B-ALL cases, based upon isolation of leukemic populations from normal counterparts by flowcytometry. FxCycle based ploidy results is known to correlate with cytogenetic ploidy status in B-ALL.

Aims & Objectives

To assess the Ploidy status by flowcytometry in B-ALL patients and correlate with cytogenetics and clinical profile.

Material and methods

It was a retrospective observational study which included newly diagnosed B-ALL patients in whom both ploidy status by cytogenetic and flowcytometry studies were available. Their correlation was studied with post induction Minimal residual disease, RNA sequencing/ Reverse Transcriptase PCR and survival outcomes.

Results

Among our B-ALL patients 41.9%, 38.7% and 18.2% were diploid, near hyper-diploid and hyperdiploid by FxCycle flowcytometry respectively. One patient showed masked hypodiplody with endoreduplication. High hyperdiploidy (>50 chromosomes) by cytogenetics corresponded to hyperdiploidy by FxCycle method. Concordance between the two modalities of ploidy assessment was 64.7% and 76.9% for high hyperdiploidy and diploidy respectively. However, Near-hyperdiploidy by flowcytometry was found to be an unreliable factor showing concordance with cytogenetic studies in only 25% of the patients. Fusion transcripts coexisting with hyperdiploidy was significantly uncommon in comparison to the diploid subset ($p=0.02$). More importantly, Ploidy status did not correlate with MRD-PI, Relapse free survival as well as overall survival in our study.

Conclusion

Hypodiploidy is rarely seen in our subset of B-ALL patients. Masked hypodiploidy required FxCycle flow analysis for correct assessment. Ploidy status does not impact the survival outcomes in the present study.

Malignant Hematology-Laboratory (MHL) PP-MHL-6

Assessing Mitochondrial Priming in AML by BH3 Profiling : A Flow Cytometry-based Approach

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Introduction

BCL-2 family of proteins are key regulators of the intrinsic/mitochondria-mediated apoptotic pathway. Mitochondrial priming reflects a cell's ability to undergo apoptosis in response to treatment with chemotherapy and agents targeting the mitochondria. BH-3 profiling is a flow cytometry-based functional assay that measures the loss of MOMP, using its surrogate marker, Cytochrome C. The amount of Cytochrome C released determines the priming of a cell, higher the cytochrome C release; higher the priming and vice versa.

Aims & Objectives

To assess the mitochondrial priming of AML samples by flowcytometry based BH3 profiling and evaluate the priming status among different risk groups and molecular subtypes.

Materials & Methods

AML cell lines (U937, THP-1, Kasumi-1, and NB4), mononuclear cells from allogenic healthy donor PBSC and primary AML samples (n=83) were used. Briefly, the cells were stained with fixable viability dye and CD45 antibody/ CD34 antibody. After digitonin permeabilization, the cells were exposed to BIM peptide (a pan pro-apoptotic protein) and stained overnight with Cytochrome C antibody. The release of cytochromeC (%BIM response) was assessed by flow cytometry, using DMSO as a negative control and Alamethicin as a positive control.

Result

All AML cell lines (U937, THP-1, Kasumi-1 and NB4) showed significant loss of cytochrome C (p-<0.0001). In CD34 positive population from allogenic healthy donor PBSC samples, the mean±SD was 56±16.2%. This mean value was used as the threshold for classifying mitochondrial priming in primary AML samples. Among the 83 AML samples, 68% had higher priming, while 30% had low priming. There was also significant heterogeneity in the priming within different ELN-defined risk groups. Though limited by numbers, there was an apparent increase in the priming of intermediate group compared with other risk groups. Additionally, distinct priming patterns were noted in the molecularly defined AML subtypes, with NPM1 and FLT3 ITD mutated AML having significantly higher priming (p-0.0046) than other subtypes in comparison to CD34 positive cells.

Conclusion

We have standardized BH3 profiling in our laboratory and observed significant heterogeneity in primary AML cells. We plan to evaluate the role of this assay in predicting response to therapy, especially with agents targeting the mitochondria, such as Venetoclax.

Malignant Hematology-Laboratory (MHL) PP-MHL-7

Evaluating the Expression Patterns of PAN-NKG2DL in AML : A Flow Cytometry-based Approach

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Introduction

It is recognised that there is a potential role for Natural Killer (NK) cell-based therapy in the treatment of acute myeloid leukemia (AML). The activatory receptor NKG2D on NK cells recognises stress-induced ligands (NKG2DLs-MICA, MICB, ULBP1-6) selectively expressed on tumor cells; the quantum of expression of these ligands on AML blasts could potentially have a bearing on response to therapy and relapse.

Aims & Objectives

To determine the expression of NKG2DLs on leukemic cell lines and AML patient-derived BM blasts using a flow cytometry-based assay.

Materials & Methods

Recombinant human NKG2D Fc chimera protein (R&D Systems, Minneapolis, USA) was biotinylated using a one-step biotinylation kit (Miltenyi-Biotech, Germany) according to the manufacturer's protocol. Leukemic cell lines (K562, U937, THP-1, NB4) and BM blasts from AML patients (n=58) were exposed to biotinylated NKG2D and were detected with Streptavidin PE. AML blasts were gated as CD45dim, while LSCs were identified as CD34+CD38-. Mean Fluorescence Intensity (MFI) was measured to quantify pan-NKG2DL expression. Cells were acquired in Navios flow cytometer (Beckman Coulter, California, USA) using Kaluza analysis version 2.1 (Beckman Coulter, California, USA).

Result

Among the leukemic cell lines evaluated, THP-1 had the lowest (mean=1336.44±758.4) and K562 the highest (mean=9938.54±2655.93) expression of NKG2DL in comparison with other cell lines. In AML(n=58) cells, LSCs showed lower ligand [removed]median=102.10; range: 0.0-786.6) compared to blasts (median=129.06; range: 20.45-1237). High NKG2DL in K562 correlated with the highest cytotoxicity (mean=52.68%), while THP-1, despite its low NKG2DL levels, had a mean cytotoxicity of 50.41%. We categorized AML patients according to ELN risk stratification and observed no significant differences in NKG2DL expression between blasts and LSCs across the risk categories (Adverse: n=9; Intermediate and Favorable: n=35).

Conclusion

Our study highlights heterogeneity in NKG2DL expression among leukemic cell lines and AML patient-derived BM cells. The lack of association between ligand expression and cytotoxicity in cell lines suggests other factors may play a role in tumor recognition beyond the NKG2D/NKG2DL axis. Further studies and follow-up evaluations are required to assess any associations with clinical outcomes.

Malignant Hematology-Laboratory (MHL) PP-MHL-8

Exploring Steroid Resistance and its Impact on Chemotherapy Response in ETP-ALL

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Introduction

Early T-cell precursor acute lymphoblastic leukemia (ETP-ALL) represents a high-risk subtype of T-ALL characterized by a distinct immunophenotype and gene expression profile. It demonstrates greater steroid resistance and inferior event-free survival than T-ALL, highlighting the critical need for alternative therapeutic strategies.

Aims & Objectives

To study the impact of steroids-dexamethasone (DEX) on the chemosensitivity to other drugs commonly used in ALL treatment regimens.

Materials & Methods

The sensitivity of DEX was evaluated on T-ALL cell lines (Jurkat and CCRF-CEM), ETP-ALL cell line (Loucy), as well as bone marrow mononuclear cells (BM-MNCs) derived from T-ALL, near-ETP ALL, and ETP ALL patients by treating the cells with increasing concentration of DEX from 20nM – 1000nM for 48hours. To evaluate the impact of DEX on other chemotherapeutic drugs, we standardized the concentration and exposure time of DEX, with DEX-resistant cell lines (Jurkat and Loucy) treated with 10 µM DEX for 7 days and DEX-sensitive cell lines (CCRF-CEM) treated with 2.5 nM DEX for 24 hours. Patient-derived samples were pre-treated with 100 nM DEX for 24 hours. Following DEX pre-treatment, the cells were exposed to other chemotherapeutic drugs commonly used in standard ALL treatment regimens.

Result

The IC50 of DEX-treated CCRF-CEM (DEX-sensitive) cell line was 630.95 nM, whereas the Jurkat and Loucy (DEX-Resistant) cell lines were >1000 nM (Figure 1a). In patient-derived BM-MNCs, 51.85% of nETP & ETP-ALL (n=27) and 36.84% of T-ALL cases (n=19) had IC50 values >1000 nM, showing greater steroid resistance in nETP and ETP-ALL (Figure 1b). In-vitro DEX exposure did not significantly affect the sensitivity of other drugs used in ALL treatment regimens in cell lines and patient-derived BM-MNCs (Figure 1c). We also observed that primary nETP-ALL and ETP cells are sensitive to venetoclax, consistent with the literature (Figure 1d).

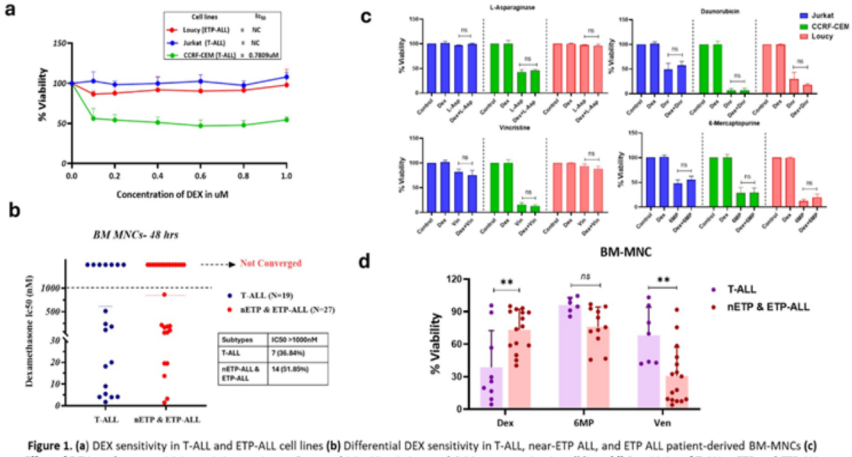

Figure 1. (**a**) DEX sensitivity in T-ALL and ETP-ALL cell lines (**b**) Differential DEX sensitivity in T-ALL, near-ETP ALL, and ETP ALL patient-derived BM-MNCs (**c**) Effect of DEX on chemosensitivity to L-Asparaginase, Daunorubicin, Vincristine, and 6-Mercaptopurine in cell lines (**d**) Sensitivity of T-ALL, nETP and ETP ALL patient-derived BM-MNCs to Dexamethasone, 6-Mercaptopurine and Venetoclax

Conclusion

ETP-ALL cells exhibit greater resistance to DEX than T-ALL cells, and pre-treatment with DEX does not significantly alter the sensitivity to other chemotherapeutic drugs. Additionally, ETP-ALL cells demonstrate sensitivity to venetoclax and 6-MP. The potential of adding venetoclax in treating ETP-ALL and removing steroids needs to be explored further.

Malignant Hematology-Laboratory (MHL) PP-MHL-9

Primary CNS Lymphoma

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Paras HMRI Hospital

Background

Case Report from two tier city

Case Presentation

Case-1 weakness of left part of body for 1 month.

Case-2 altered sensorium for last 2 months.

Diagnosis

Primary CNS lymphoma

Treatment

HD Mtx + Rituximab +ITMtx

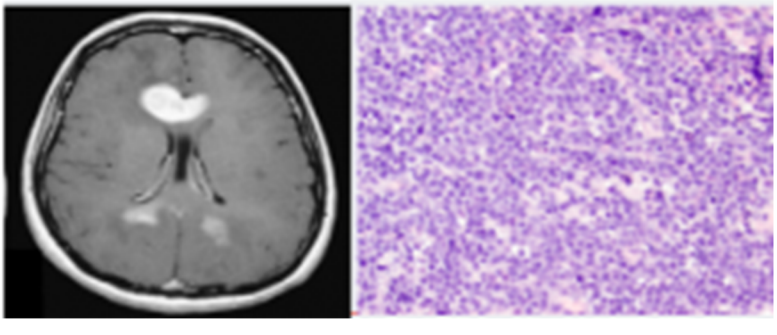
Follow-up

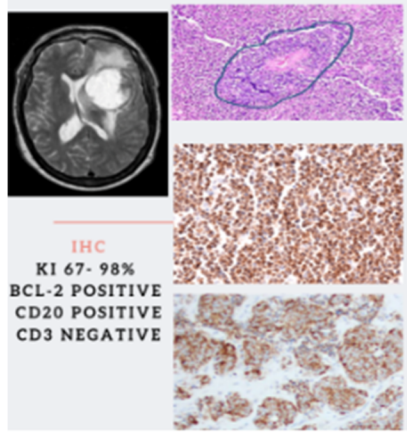
Case-1 In remission 2 years post treatment

Case-2 succumbed to disease within 1 month.

Conclusion

Primary CNS lymphoma a very rare presentation.Early detection and treatment can offer long term survival.





Malignant Hematology-Laboratory (MHL) PP-MHL-10

Pathological Insights of Primary Renal Lymphoma in a Suspicious Case of Renal Cell Carcinoma

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Background

Primary renal lymphoma (PRL) is a rare neoplasm which accounts for less than 1 % of all renal neoplasms and is an uncommon type of Non-Hodgkin's lymphoma, Diffuse large B cell lymphoma is the most common subtype.

Case Presentation

A 70 year hypertensive male presented with dull aching right flank pain associated with voiding difficulty and weight loss. On investigating,Urine for cytology was not conclusive of any pathology. USG showed Soft tissue(5.39x5.09cm) noted in lower pole right kidney.CT scan showed possibility of neoplastic mass lesion(6.2x6.4x5.2cm) in relation to right lower pole of kidney and peri renal space,small nodular lesion in the medial lip of right adrenal gland, possibility of Metastasis. Grossly received right partial nephrectomy specimen,cut surface showed white to tan yellow mass. On Microscopy,diffuse proliferation of monomorphic lymphoid cells in the interstitium with intact glomeruli and tubules was noted.Individual cells are larger,round to oval,scant cytoplasm,regular nuclei,fine to vesicular chromatin,prominent nucleoli. IHC-Tumour cells are membranous CD45-Positive,CD20-Diffusely positive,CD3 and CD5- Scattered positive,Kappa restriction present. Post op PET CT scan showed lower and upper pole of right kidney likely residual disease,conglomerate lymph nodal mass encasing IVC and abdominal aorta likely spilling of residual disease into regional area. Retrograde hematological parameters was found normal.

Diagnosis

Primary renal B cell Non Hodgkin's lymphoma

Treatment

Post op 6 cycles of chemotherapy of ABVD regimen was given

Follow-up

After completion of treatment patient's prognosis is good without any residual disease in form of superficial lymphadenopathy and B symptoms and under regular follow up.

Conclusion

The exact pathophysiology of PRL is not very clear as the kindey lacks lymphoid channels.Several theories proposed are from the lymphatics of renal capsule the PRL arises and invades into renal parenchyma or hematogenous dissemination or arises from extension of inflammatory tissue or originates from MALT tissue found in the kidney.PRL is critical in differentiating from other renal masses especially in unilateral lesions that mimic RCC.Hence histopathological diagnosis with subsequent IHC and diagnostic imaging is very essential.In this study the patient was diagnosed incidentally by diagnostic imaging,highlighting the rarity of PRL and emphasizing importance of early diagnosis and treatment.

Malignant Hematology-Laboratory (MHL) PP-MHL-11

Diagnostic Utility of Body Fluid Flow Cytometry in Patients with and Without Prior Haematolymphoid Malignancy

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Introduction

Effusion in body cavities can occur as a complication of benign and malignant disease. Presence of malignant cells in effusion is associated with advanced stage of disease. Involvement of body fluid by neoplastic cells can occur at time of diagnosis or during the course of the disease. Flow cytometry is an important tool for evaluation of body fluids involvement by a haematological malignancy.

Aims & Objectives

- To demonstrate the utility of multiparameter flow cytometry in the diagnosis of malignant body fluids.
- To determine the category of haematolymphoid malignancies involving the body fluids.

Materials & Methods

We reviewed cases of body fluids processed for flow cytometry in Hematology laboratory . Samples of peripheral blood and bone marrow were excluded from our study. All the necessary details (specimen type, clinical history, previous diagnosis, demographic details) were recorded. In this retrospective study, total 54 cases were analyzed.

Result

Among 54 cases, 38 (70%) were from patients with a prior history of haematolymphoid malignancy of which 21 cases (55%) were abnormal by flowcytometry. Of the remaining 16 cases (30%) from patients with no prior history of haematolymphoid malignancy, only one was abnormal by flowcytometry. Pleural fluid involved in majority of cases (12 cases; 22.2%) followed by cerebrospinal fluid (CSF) (10 cases; 18.5%). There were 13 cases of B cell neoplasms, 6 cases of T cell neoplasms, 2 cases of myeloid neoplasms and 1 case of acute leukemia of ambiguous lineage involving positive body fluid effusion.

Conclusion

Multiparametric flowcytometry has an important role in detecting body fluid involvement in haematolymphoid malignancy as it can detect small malignant cells that may be missed out by routine microscopy.

Malignant Hematology-Laboratory (MHL) PP-MHL-12

Utility of CD180 in Classification and Identification of B-Cell Non-Hodgkin Lymphomas

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Introduction

CD180, also known as RP105 (Radioprotective 105), is a toll-like receptor (TLR) family member primarily involved in B-cell activation and innate immune response. Studies have shown that over-expression of CD180 is associated with Marginal Zone Lymphomas (MZL), and under-expression, in association with under or over-expression of other markers, is associated with Chronic Lymphocytic Leukaemia (CLL) and Mantle Cell Lymphoma (MCL).

Aims & Objectives

In this study, we aim to evaluate the expression of CD180, as a single biomarker, among the types of B-NHLs and its utility in the classification of B-NHLs.

Materials & Methods

We analyzed the CD180 expression in the cases of B-NHLs diagnosed at the Department of Haematology, Christian Medical College, Vellore, between June 2023 and June 2024. The expression of CD180 was classified into 5 tiers of bright, moderate, dim, heterogenous and negative. These were grouped into 3 groups with negative, heterogenous and dim being grouped as under-expression, bright as over-expression and moderate as equivalent expression to mature lymphocytes. Wherever available, bone marrow reports and other clinical details were retrieved from the patients' electronic medical records.

Result

A total of 165 cases were included in the study, with a median age of 57 years and a male-to-female ratio of 2.7. Of the 165, CLL were 77, MCL were 18, MZL were 17, Diffuse Large B-cell Lymphomas (DLBCL) were 15, Hairy Cell Leukaemia (HCL) were 8, Burkitt Lymphoma (BL) were 5, Follicular Lymphoma(FL) were 4, Lymphoplasmacytic Lymphomas (LPL) were 3, small cell B-NHL – unclassified were 15 and large cell B-NHL – unclassified were 3. Under-expression of CD180 was seen in 121/165 (73%) cases, over-expression was seen in 12/165 (7%), and equivalent expression was seen in 32/165 (20%). Among the underexpressors, CLL>MZL>DLBCL and among the overexpressors HCL=Low-grade NHL>MZL=DLBCL. Equivalent expression was predominantly seen in MCL. Under expression of CD180 had a positive predictive value(PPV) of 87% in detecting CLL among CD5+ B-NHLs. Among MZL, under-expression of CD180 was seen in 12/17 cases, over-expression was seen in 2/17 cases and the rest showed equivalent expression. CD180 did not show any significance in classifying other types of B-NHL in our study.

Conclusion

Under-expression of CD180 is a helpful marker in identifying B-NHL. Among CD5+ B-NHLs, under-expression of CD180 has a PPV of 87% in identifying CLL.

Malignant Hematology-Laboratory (MHL) PP-MHL-13

Unraveling Congenital Leukemia: A Case Study and Insights into Early Diagnosis and Management

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Background

Congenital leukemia is a rare hematologic malignancy presenting in neonates, characterised by the presence of leukemic cells in the peripheral blood or bone marrow within the first month of life. Its clinical presentation often overlaps with other neonatal conditions and prognosis varies significantly based on early diagnosis and tailored treatment strategies, highlighting the importance of prompt clinical intervention.

Case Presentation

A 29 years old booked primigravida, underwent emergency LSCS at 36+6 weeks of gestation in view of Absent End Diastolic Flow with FGR (<3rdcentile) and fetal distress and delivered a baby boy. Baby did not cry immediately after birth and required PPV for 30 seconds with an APGAR score-6/8/9 and was admitted to nursery in view of respiratory distress. On physical examination, child had a Down's Phenotype with Halls-criteria 7/10 and hepatomegaly(liver-5cm BCM).Routine blood investigation at day 1 of life revealed TLC of 2,69,800/mm3 with Hb-14.5g/dL & Platelet-2.57L. Peripheral smear examination revealed Hyperleukocytosis, with 88% blasts, micromegakaryocytes and megakaryoblasts along with features of myelodyspoeisis: nuclear disjunction,binucleation,abnormal granulation. Cytochemistry showed positivity for PAS and NSE and negativity for MPO. On flowcytometry these cells were positive for CD61,CD71,CD42a,CD42b,CD56,CD45,CD34, CD33 and Negative for CD19,cCD3,cMPO,cCD79A,CD13,HLADR and CD56,overall immunophenotyping suggestive of Acute Megakaryocytic leukemia–M7(AML-M7).

Diagnosis

Possibility of AML-M7 associated with Down's syndrome was suggested, and karyotyping along with JAK2 and GATA-1 gene mutation analysis was adviced.

Treatment

Child was started on low dose Cytorabine at 1.5mg/kg/day along with other supportive measures. Gradually the TLC decreased along with blast cells. At the end of the course, blast cells decreased to 2%(Day-8). Baby was weaned off from ventilator to CPAP support and RT feeds were established.

Follow-up

Regular monitoring was instituted. Baby was weaned off from CPAP support, but continued to require oxygen support with persistent enlarged and firm liver and is on follow-up.

Conclusion

Congenital leukemia, while rare, requires a high index of suspicion for early detection and effective treatment. This case highlights the importance of comprehensive diagnostic approach and necessity for personalized treatment plans. Continuous follow-up is vital to ensure long-term health and to address potential complications associated with treatment.

Investigations:

Cytarabine

Date	26/8	28/8	29/8	4/9	5/9	7/9	9/9	12/9
Hb/hct	14.5/44	14.4/43.4	15.8/43	13.2/39	9.7/26.6	17.8/43.5	11.4/33.6	10.5/30.2
TLC	269800	57600	1.78 L	1.22 L	80570	36400	18210	8400
DLC	My25 Mmy 20 P30 L8 B10	My6 B24 P45 L8	B43 P13 L42	B87 P3L3	B58P21		60/30	P50L45 B2
Blasts	88%	86%						2%
Plt	2.57 L	2.43 L	76000	69000	52000	37000	26000	67000
Bil T/D	1.9/0.3	4.1/0.4				8.1/4.9		
Urea/Cr	13/0.9		26/1.0			31.0.3		
Na/ k	131/3.7		127/4.2			141/5.4		
OT/PT	110/32					20/12		
INR		1.7		2.1				
Ca	7.7					8.2		
Blood c/s			NG	NG			NG	
CSF	WNL					WNL		

Malignant Hematology-Laboratory (MHL) PP-MHL-14

Generation of Efficient Lentiviral Transduction Vectors for Therapeutic Correction of Fanconi Anaemia Pathway

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Introduction

Fanconi Anaemia (FA) is a genetic disorder arising from defective DNA interstrand cross-link repair, predominantly due to biallelic mutations in any of the 22 genes constituting the FA pathway. Mutation screening of Indian FA patients revealed that approximately 60% of cases harbor mutations in FANCA, while around 20% have mutations in FANCL. Clinically, FA is characterized by congenital abnormalities, a predisposition to malignancies, and, most notably, progressive cytopenia leading to bone marrow failure (BMF) in 70-80% of patients within the first decade of life. Hematopoietic stem cell transplantation (HSCT) is the only curative treatment for BMF in FA; however, it is fraught with challenges such as the availability of HLA-matched donors and the need for myeloablative conditioning, which poses heightened risks of cytotoxicity in FA patients due to their inherent DNA repair deficiencies. To address these limitations, We have constructed lentiviral vectors expressing FANCA or FANCL using three different promoters, which are first being evaluated for their efficiency in fibroblasts from FA patients before advancing to transduction studies in CD34+ HSPCs.

Aims & Objectives

AIM: To evaluate the robustness of various eukaryotic promoters in driving overexpression of Fanconi Anaemia (FA) genes in fibroblasts derived from FA patients.

Objective: Lentiviral mediated gene complementation of FANCA and FANCL in FA patient's fibroblasts respectively, to evaluate restoration of functional FA pathway.

Materials & Methods

We designed lentiviral vectors containing different mammalian promoters to control the expression of FANCA or FANCL. For this study, we selected the EF1α, MND, and HPGK promoters. The lentiviral vectors were used to transduce normal fibroblasts (BJ-36) to assess the transduction efficiency of each promoter. Flow cytometry was used to evaluate the efficiency of transgene expression. The same lentiviral vectors were subsequently used to transduce fibroblasts from FA patients with confirmed mutations in FANCA or FANCL (identified by next-generation sequencing). Gene complementation was confirmed by Western blotting, which assessed FANCD2 ubiquitination, a critical marker of functional FA pathway restoration.

Result

Preliminary results indicate that all three promoters—EF1α, MND, and HPGK—efficiently drove transgene expression in normal fibroblasts. The transduction efficiencies across the different vectors were comparable. In FA patient fibroblasts, successful gene complementation was achieved, as demonstrated by the restoration of FANCD2 mono-ubiquitination, indicating reactivation of the FA pathway.

Conclusion

The lentiviral vectors employing EF1α, MND, and HPGK promoters demonstrated efficient transgene expression and functional gene comple mentation in FA patient fibroblasts. Our next step is to assess the performance of these lentiviral vectors in FA patient-derived CD34+ hematopoietic stem cells, where promoter choice will be critical for ensuring sustained gene expression and therapeutic efficacy.

Malignant Hematology-Laboratory (MHL) PP-MHL-15

Evaluating Minimal Residual Disease Monitoring in Acute Myeloid Leukemia Using Multiparametric Flow Cytometry: Insights and Applications

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Introduction

Minimal residual disease (MRD) monitoring plays a pivotal role in assessing treatment response and predicting relapse in acute myeloid leukemia (AML). Despite achieving complete remission, undetectable levels of leukemic cells can persist, leading to relapse. Multiparametric flow cytometry immunophenotyping (FCMI) offers a sensitive and accurate approach for detecting these residual leukemic cells. This study evaluates the effectiveness of FCMI in monitoring MRD and its prognostic value in AML patients.

Aims & Objectives

The primary aim of this study is to assess the sensitivity and prognostic value of FCMI in detecting MRD in AML patients. Specific objectives include:

1. Evaluating the correlation between MRD levels and relapse rates.
2. Assessing the impact of MRD status on overall survival (OS) and event-free survival (EFS).

Materials & Methods

We retrospectively analyzed de novo AML patients treated at our institution. Diagnosis of AML was made based on the morphology, cytochemistry, immunophenotype, cytogenetics, and/or molecular features as per the World Health Organization guidelines. Peripheral blood and/or bone marrow samples were collected at diagnosis and after induction chemotherapy. Post-induction MRD was assessed. MRD analysis was performed using a 13-color standardized multiparametric flow cytometry panel, incorporating leukemic-associated immunophenotypes (LAIPs). A threshold of 0.01% residual cells was used to define MRD positivity. MRD status was correlated with clinical outcomes, including OS and EFS.

Result

A total of 851 de-novo AML patients, including 315 pediatric and 536 adult cases, were analysed. The age range was from 2 months to 84 years. Median age was 26 years (Pediatric: 8 years, Adult: 38 years) with a M: F ratio of 1.5:1. There were 76 induction deaths (8.9%), and 138 patients (16.2%) were not in morphological remission. MRD negativity was achieved in 51.4% of patients post-induction. These MRD-negative patients demonstrated significantly better EFS compared to MRD-positive patients ($p<0.001$). MRD-negative patients also showed improved OS ($p<0.001$) compared to the MRD-positive group. Multivariate analysis confirmed MRD positivity as an independent predictor of poor outcomes.

Conclusion

FCMI is a highly sensitive and clinically valuable tool for MRD monitoring in AML, offering important prognostic insights, providing early identification of patients at high risk of relapse. Standardization of protocols, including gating strategies and sample preparation, is essential to enhance reproducibility and accuracy, making FCMI integral to personalized treatment strategies in AML.

Malignant Hematology-Laboratory (MHL) PP-MHL-16

An Unusual Case of Primary Plasma Cell Leukemia with Coexisting Fabry's Disease

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Background

Plasma cell leukemia is an uncommon plasma cell dyscrasia with a very poor prognosis. Fabry's disease is an X-linked genetic lysosomal disorder caused by alpha-galactosidase A deficiency. Their overlap has rarely been reported. Hereby presenting an extremely rare case of plasma cell leukemia with co-existing Fabry's disease.

Case Presentation

A 46 year-old male presented with an unremitting back pain and shortness of breath. On examination, he was pale with a moderately distended abdomen. Laboratory tests revealed Hb-7.5g/dl , TLC-10,300/cumm, Platelets- 60,000/cumm, Creatinine-11.3 mg/dl. Peripheral smear reveals 8% plasma cells. Bone marrow aspiration & biopsy shows replacement of hematopietic elements by sheets of plasmablasts. Flow cytometry findings of bone marrow aspirate showed positivity for CD38, CD138, kappa restriction and aberrant expression of CD117 and CD13. Further he underwent renal biopsy which showed myeloma cast nephropathy, which was the primary cause of acute kidney injury. Renal pathology also showed glomerulus with foamy podocyte cytoplasm, suggestive of a lysosomal storage disorder which was confirmed on Electron Microscopy. Echocardiogram shows hypertrophic cardiomyopathy.

Diagnosis

Patient was diagnosed as Fabry's disease with Primary plasma cell leukemia.

Treatment

Patient was administered with proteasome inhibitor bortezomib and the immuno-regulatory drugs lenalidomide and low-dose dexamethasone along with hemodialysis which was required biweekly.

Follow-up

We lost the patient within 3 months of diagnosis.

Conclusion

Co-existence of Fabry's disease and Plasma cell leukemia are rare and till now only two cases of coexisting Fabry's disease and Multiple myeloma or MGUS have been reported, with our patient being the third case reported. This is a serendipitous finding and hence being presented.

Malignant Hematology-Laboratory (MHL) PP-MHL-17

Ischemic Stroke in a Young Female: A Rare Presentation of A Common Hematological Malignancy

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Background

Acute promyelocytic leukemia (APL) is an aggressive hematologic malignancy with characteristic cytogenetic abnormality involving a reciprocal translocation between chromosomes 15 and 17, known as t (15;17) in more than 95% of cases. Coagulopathy in APL is a very complex disorder and is believed to result from interplay of various factors. Thrombotic events in APL are relatively rare, more so at initial presentation and often overshadowed by bleeding and infection-related issues that dominate the clinical presentation. We present an unusual case of APL presenting as ischemic stroke in a young woman.

Case Presentation

A 34-year female presented in emergency with acute onset right side hemiparesis and impairment of speech. Imaging studies revealed acute infarct in left middle cerebral artery involving caudate, posterior limb of internal capsule, insula and frontal region. Her cardiac evaluation was unremarkable. Subsequent to hospital admission within 2 days she developed fever with petechial rashes. Her hemogram revealed pancytopenia with 4% abnormal promyelocytes. Urgent bone marrow evaluation revealed 80% abnormal promyelocytes , microgranular variant.

Diagnosis

A diagnosis of acute promyelocytic leukemia with ischemic stroke was considered The diagnosis was subsequently confirmed on flow cytometric evaluation along with karyotyping and Fluorescent in situ hybridisation(FISH) being positive for PML-RARA translocation.

Treatment

She was started on Al Trans Retinoic Acid and Arsenic trioxide along with injection heparin.

Follow-up

At the end of 6 month of therapy, she was in complete remission with no neurological deficit or any fresh bleeding.

Conclusion

It is very rare for the thrombotic event to occur in APL prior to the initiation of all trans retinoic acid therapy and is one of the reasons that this case is unique. Differential diagnosis of underlying hematological malignancy especially APL should be kept in mind in acute presentation of stroke as the outcome can be adverse if therapy is not initiated early.

Malignant Hematology-Laboratory (MHL) PP-MHL-18

FANCD2 Western Blot Analysis for the Diagnosis of Fanconi Anaemia

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Introduction

Fanconi anemia (FA) is a rare inherited bone marrow failure (BMF) disorder, with an incidence of approximately 1 in 360,000 live births. The FA genes, collectively referred to as FANC, include several that are commonly mutated in FA patients, such as FANCA, FANCC, FANCG, and FANCD2. The FA pathway plays a crucial role in the repair of DNA damage, particularly interstrand cross-links that obstruct DNA replication. A critical process within this pathway is the monoubiquitination of FANCD2 and FANCI, which is mediated by the FA core complex, an E3 ubiquitin ligase. The FANCD2 monoubiquitination test, performed via Western blotting, allows the differentiation between monoubiquitinated and non-ubiquitinated FANCD2 isoforms.

Aims & Objectives

To correlate the results of FANCD2 monoubiquitination via Western blot with chromosomal breakage analysis (CBA) and validate its use as a diagnostic tool for Fanconi anemia.

Materials & Methods

Patients presenting with pancytopenia, with or without physical anomalies characteristic of FA, were included in the study between January 2020 and September 2024. Chromosomal breakage analysis was also performed as part of the diagnostic workup. Peripheral blood samples or skin biopsies were collected for Western blot analysis. Fibroblasts from skin biopsies were cultured and processed. A double band (FANCD2S and FANCD2L) on Western blot indicates a non-FA individual, while the absence of FANCD2L suggests a diagnosis of FA.

Result

A total of 182 cases were collected, with 153 cases reported. Of these, 87 samples were peripheral blood and 66 were fibroblasts derived from skin biopsies. Cases lacking the double band on Western blot were confirmed positive for FA, with 38 positive cases identified from blood samples and 37 from fibroblast samples. High CBA scores were observed in 25 cases from blood samples and 32 from skin biopsies, with a mean CBA score of 87 (range: 0–235.4). Among 11 cases with low CBA scores, the absence of FANCD2 monoubiquitination was also noted. Next-generation sequencing (NGS) was performed in 58 cases, corroborating the results.

Conclusion

The Western blot-based FANCD2 monoubiquitination test is a reliable diagnostic tool for Fanconi anemia, and when combined with chromosomal breakage analysis, offers a robust diagnostic approach.

Malignant Hematology-Laboratory (MHL) PP-MHL-19

Severe Osteopetrosis in a Pediatric Patient: A Case Report Highlighting Diagnosis, Management, and the Role of Hematopoietic Stem Cell Transplantation

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Background

Osteopetrosis, a rare genetic disorder characterized by defective osteoclast function and impaired bone resorption, leads to the progressive accumulation of bone and associated complications, such as bone marrow failure. This case highlights the critical role of early diagnosis, comprehensive supportive care, and the potential of HSCT in preventing life-threatening complications in pediatric patients with severe osteopetrosis. The importance of multidisciplinary management, including genetic counseling and long-term follow-up, is emphasized for improving patient outcomes.

Case Presentation

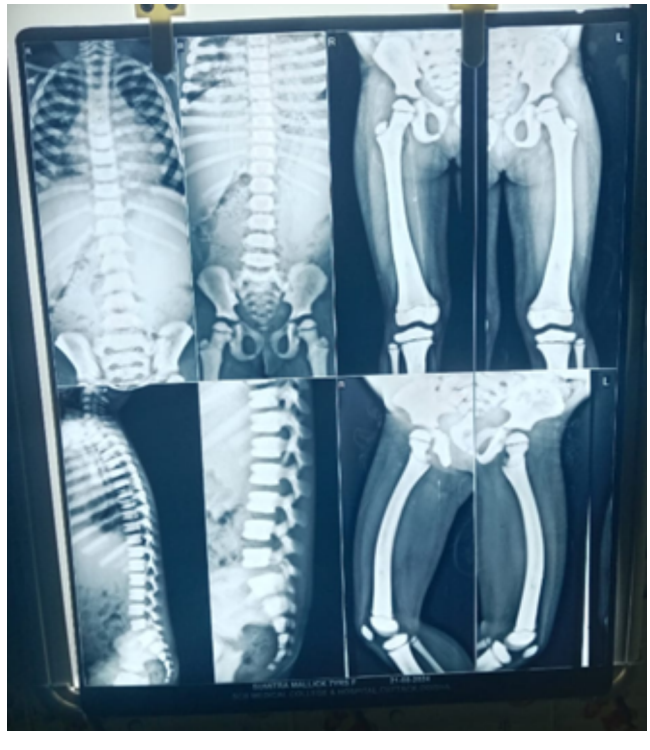
An 8-year-old female presented with a history of recurrent fractures, progressive bone pain, and delayed growth. She had features of severe osteopetrosis, including increased bone density, macrocephaly, and hepatosplenomegaly. Radiographic imaging revealed diffuse skeletal sclerosis, suggestive of osteopetrosis.

Diagnosis

Laboratory investigations showed pancytopenia with anemia, thrombocytopenia, and leukopenia. Bone marrow biopsy confirmed the diagnosis of osteopetrosis, revealing a hypocellular marrow with reduced hematopoietic cells. The hypocellularity was attributed to the excessive accumulation of abnormal, dense bone within the medullary cavities, impairing normal bone marrow function. NGS revealed no mutations.

Treatment

the medullary cavities, impairing norm Supportive treatment with blood transfusions, antimicrobial therapy for infections, and physical therapy for mobility were initiated. Due to the progressive nature of the disease and bone marrow failure, the patient was evaluated for hematopoietic stem cell transplantation (HSCT) as a potential curative treatment.



Follow-up

Patient is on follow up and evaluation of ASCT was going on.

Conclusion

Apart from regular Bone Marrow Failure Syndromes, Osteopetrosis can be a cause agent for inherited Bone Marrow Failure where ASCT can be a potential treatment options for the same.

Malignant Hematology-Laboratory (MHL) PP-MHL-20

Waldenstrom Macroglobulinemia – Enigmatic Series of 3 Cases!

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Background

Waldenstrom's macroglobulinemia (WM) is a rare lymphoma, characterised by clonal lymphoplasmacytic cells infiltrating bone marrow and producing IgM paraprotein. Common presentation is anaemia and organomegaly with L265P mutation in MYD88 gene.

Case Presentation

We hereby present 3 unusual cases of WM, highlighting the importance of a haematological work up with ancillary testing in making correct diagnosis of disease with various complications, facilitating proper management.

CASE 1: A 56-year-old male presented with complaints of recurrent epistaxis since one year. The patient had no lymphadenopathy or organomegaly. Test for cryoglobulin was positive in peripheral blood. Morphological and immunohistochemical examination of bone marrow revealed WM along with an elevated serum IgM level.

CASE 2: A 76-year-old male presented with complaints of high grade fever, generalized weakness, dry cough, haematuria since 4-5 days. CBC showed hyperleucocytosis. Bone marrow examination showed chronic lymphoproliferative disorder with plasmacytic differentiation. Clonal B cells were negative for CD5 and CD10 on flow cytometry.

CASE 3: A 82-year-old male presented with pedal oedema and hypertension since 10 years.

Renal biopsy showed Amyloidosis with IgM Lambda M band. Flow cytometry picked 0.6 % lambda restricted B cells.

Patient 2 and 3 tested positive for MY88 mutation whereas patient 1 tested negative.

WM is a rare B NHL.

3 cases discussed here had unusual presentation and even uncommon complications like cryoglobulinemia. These cases were managed with chemotherapy and symptomatic management.

Diagnosis

Patient 1: WM with cryoglobulinemia

Patient 2: WM with hyperleukocytosis

Patient 3: WM with Renal Amyloidosis

Treatment

Patient 1 received therapeutic plasma exchange and chemotherapy with Bendamustine-Rituximab.

Patient 2 succumbed to death after resuscitative measures.

Patient 3 received chemotherapy with Bendamustine-Rituximab.

Follow-up

Patient 1 is currently on follow-up and has no symptoms and has completed 4 cycles of chemotherapy.

Patient 3 is currently on follow-up, symptom-free and has completed 4 cycles of chemotherapy recently.

Conclusion

These 3 cases were indeed enigmatic as clinical features were unusual. Thus extensive work up including bone marrow examination, serum protein electrophoresis, immunofixation assay, serum free light chain assay, IHC and flow cytometric immunophenotyping helped to conform the diagnosis and start curative treatment.

Malignant Hematology-Laboratory (MHL) PP-MHL-21

Gelatinous Transformation of Bone Marrow- A Rare Finding

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Background

Gelatinous Transformation of Bone Marrow (GTBM) also known as serous atrophy is a degenerative change in the hematopoietic bone marrow. GTBM has been described in association of variety of clinical scenarios, chiefly in young malnourished. It is characterized by focal hypoplasia of fat cells, hematopoietic cells and accumulation of extracellular gelatinous substances. It is not a specific disease of bone marrow but a sign of generalized severe illness associated with weight loss and cachexia. In 1970, the gelatinous substances were identified as hyaluronic acid mucopolysaccharides. within last 3 decades, approximately only 20 papers have been published and they were mostly single case reports or marrow studies of patient with AIDS or anorexia nervosa. GTBM is a rare clinicopathological entity, involves bone marrow hypoplasia, fat atrophy and infiltration by gelatinous material.

Case Presentation

A 29 year old male presented with chief complaints of loss of weight since one year, loss of appetite since 3 months and generalised weakness since 10 days. He was incidentally diagnosed with HIV 2 months back and was started with ART. On physical examination, there was no organomegaly. On USG abdomen and pelvis, no abnormality was detected. Complete blood count revealed pancytopenia. Bone marrow examination was done in view of persistent pancytopenia despite multiple blood transfusions and it showed large areas of deposition of gelatinous substance along with adipose cell atrophy and loss of hematopoietic cells.

Diagnosis

On the basis of findings of bone marrow examination, diagnosis of Gelatinous Transformation of Bone Marrow (GTBM) was rendered.

Treatment

Patient was continued with ART along with symptomatic treatment.

Follow-up

Patient was lost to follow-up.

Conclusion

There is a lack of clinical suspicion for GTBM, which leads to an underdiagnosis of the disorder. GTBM should be taken into consideration as a differential diagnosis in all cases presenting with weight loss, malnutrition, and resistant peripheral cytopenia.

Malignant Hematology-Laboratory (MHL) PP-MHL-22

A Diagnostic Quandary: Differentiating AML With RUNX1::RUNX1t1 Fusion From Mixed Phenotype Acute Leukemia, B/myeloid

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Background

A 28-year-old woman with a history of acute myeloid leukemia (AML) and one previous relapse presented with fever, fatigue, and headaches lasting two weeks. Imaging revealed an intracranial bleed. Records from her prior treatment are unavailable.

Case Presentation

A 28-year-old woman with a history of acute myeloid leukemia (AML) and one previous relapse presented with fever, fatigue, and headaches lasting two weeks. Imaging revealed an intracranial bleed. Records from her prior treatment are unavailable.

Diagnosis

On further investigation, 86% of blasts were in the peripheral blood and 89% in the bone marrow. The bone marrow aspirate was subjected to immunophenotyping, which revealed 70.31% of all events under CD45 moderate and low side scatter region. These events were strongly positive for CD34, HLA-DR, cMPO, CD19, cCD79a, CD38, and CD58, with variable positivity for CD117, CD33 and CD81 and weak positive for CD11c. Hence, it was reported as Mixed phenotype acute leukemia, B/myeloid. However, further cytogenetic testing showed the t(8;21).

Treatment

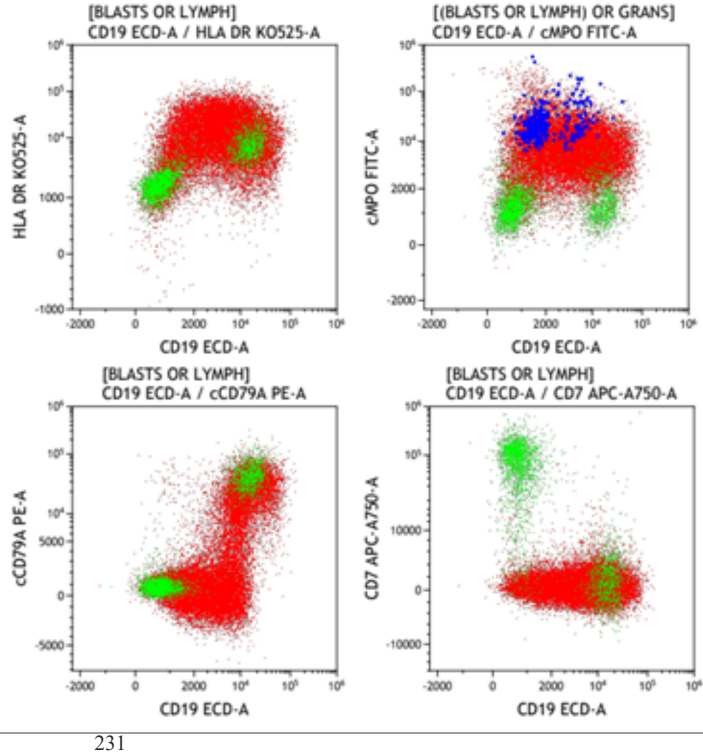
She was started on a FLAG plus venetoclax regimen.

Follow-up

Not available

Conclusion

It is not uncommon for AML with t(8;21) to exhibit B-marker expression. Incorporating additional cytogenetic and molecular studies is essential for accurate diagnosis and classification of AML. The t(8;21) translocation represents a distinct entity and is well-known for its favorable prognosis. In contrast, MPAL-B/M is generally considered high-risk acute leukemia, with outcomes that fall between those of acute myeloid leukemia (AML) and B-lymphoblastic leukemia despite intensive treatment. Whether this case must be labeled as MPAL or considered AML with a possible t(8:21) translocation remains a dilemma in a resource-limited setting. The possibility of t(8:21) AML progressing to MPAL also arises in such cases.



Malignant Hematology-Laboratory (MHL) PP-MHL-23

Delayed Diagnosis Dilemma : The HLH-hodgkin's Lymphoma Connection

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Background

Hemophagocytic lymphohistiocytosis (HLH) is a severe syndrome characterized by uncontrolled immune activation, leading to multi-organ damage and significant morbidity and mortality. HLH can be classified as primary or secondary, with the latter often triggered by malignancies, infections, or autoimmune disorders. This case report illustrates the diagnosing of HLH secondary to advanced Hodgkin's lymphoma due to a delay in histopathological assessment.

Case Presentation

A 28-year-old male presented with a five-month history of escalating fever, significant weight loss, and exertional dyspnea. Initial evaluations, including blood tests and a bone marrow biopsy, did not provide a definitive diagnosis. Despite recommendations for an excision biopsy of right cervical lymph node, the patient initially refused , leading to a deterioration of symptoms. Eventually, he underwent the procedure after 6 months of initial suspicion, which confirmed stage IV Hodgkin's lymphoma.

Diagnosis

Stage IV Hodgkin`s Lymphoma (Nodular Sclerosis) with secondary HLH

Treatment

Following the diagnosis, the patient was started on intravenous dexamethasone, resulting in a notable improvement in his symptoms. Immunohistochemical analysis confirmed the nodular sclerosis variant of Hodgkin's lymphoma. The patient subsequently was started on ABVD IA chemotherapy, leading to symptomatic improvement. Later he developed severe fungal pneumonia and succumbed to it.

Follow-up

patient succumbed to fungal pneumonia post ABVD IA

Conclusion

Hodgkins lymphoma may be the rare but important causes of HLH. Timely recognition of HLH can significantly improve patient outcomes. Clinicians should maintain a high level of suspicion for HLH in patients presenting with persistent systemic symptoms, especially in the context of suspected malignancies.

Malignant Hematology-Laboratory (MHL) PP-MHL-24

Acute Myeloid Leukemia with M-BCR Fusion Transcript: An Unusual Case

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Background

Acute myeloid leukemia (AML) is a heterogeneous group of hematological malignancies characterized by the clonal expansion of myeloid precursor cells with impaired differentiation. AML is classified by the World Health Organization (WHO HAEM-5) as AML with defining genetic abnormalities, AML with myelodysplasia related and AML defined by differentiation. Morphology, immunophenotyping and cytogenetics are the cornerstone of this classification. AML with BCR::ABL 1 fusion is one of the defining genetic abnormalities of AML requiring a blast percentage cut-off of >20%. This is a rare genetic abnormality present in 0.5–3% of AML cases. The BCR::ABL 1 fusion gene has three breakpoint cluster regions: M-bcr, m-bcr, and u-bcr with the M-BCR, resulting in a p210 (b2a2) transcript being the most common.

Case Presentation

We present an unusual case of a 62-year-old male who initially presented with hemorrhoids, fever,and easy fatiguability over two months, without hepatosplenomegaly. Laboratory tests revealed severe pancytopenia on peripheral blood. Bone marrow examination showed 83% blast population. Cytochemistry and flow cytometry confirmed a diagnosis of Acute Myeloid Leukaemia. Cytogenetic analysis identified a minor BCR::ABL (e1a2) translocation.

Diagnosis

Acute myeloid leukaemia with e1a2 BCR-ABL fusion gene

Treatment

The patient succumbed to sepsis before therapy could be started.

Follow-up

The patient succumbed to sepsis before therapy could be started.

Conclusion

Acute myeloid leukaemia with e1a2 BCR-ABL fusion gene is a rare aggressive acute leukaemia which requires early diagnosis and treatment.

Malignant Hematology-Laboratory (MHL) PP-MHL-25

Immunophenotypic Aberration of Myelomonocytic Markers and Expression of CD7 and CD56 in Chronic and Acute Leukaemia of Monocytic Differentiation and Comparison with Reactive Monocytosis-A Series of 10

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Background

Chronic myelomonocytic leukemia (CMML) is clonal MDS/MPN (myelodysplatic/myeloproliferative) overlap syndrome with absolute monocyte count of 500/cu.mm, relative monocytosis of >10%, blasts/promonocytes <20>94% classical monocytes (CD14+/CD16-) favour clonal monocytic population over reactive monocytes. Acute myeloid leukaemia with monocytic differentiation (AML-MD) is characterised by blast and promonocyte percentage of ? 20% and may be associated with AML with NPM mutation and KMT2A rearrangement. Immature monocytic population in AML-MD commonly shows downregulation of CD14, HLA-DR and aberrant expression of CD7 and CD56.

Case Presentation

A series of 10 cases which include three cases of CMML, five cases of AML-MD, and two reactive monocytosis.

Diagnosis

CD14 and CD16 pattern were analysed in CMML cases, expression of myelomonocytic markers (CD13, CD33, CD11b) and HLADR expression were analysed in AML-MD cases by flow cytometry, Aberrant expression CD7 and CD56 were also analysed in AML-MD cases. Classical monocyte percentage of >94% was observed in all CMML cases. CD14, HLA-DR downregulation were commonly seen and aberrant expression of CD7 and CD56 were seen in AML-MD cases.

Treatment

Not applicable

Follow-up

Not applicable

Conclusion

Although this series includes a limited number of cases, it did reveal common immunophenotypic abnormalities, which were compared to reactive monocytosis.

Malignant Hematology-Laboratory (MHL) PP-MHL-26

A Human-in-loop Model of Machine Learning Algorithm to Detect T-ALL MRD with Increased Confidence

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Introduction

Measurable Residual Disease (MRD) is an important biomarker in prognosticating T-cell acute Lymphoblastic leukaemia (T-ALL), as molecular or gene expression-based classification and prognostication are not frequently employed. MRD assessment in T-ALL is mainly by multiparameter flow cytometry (FCM). The lack of LAIPs and well-defined maturation patterns in T-cell precursors make the MRD assessment by FCM more challenging. This study aims to identify the normal precursor T cells and their maturation pattern and employ machine learning to differentiate these normal populations from the abnormal populations confidently.

Aims & Objectives

Our study aims to employ machine learning to differentiate normal T-cell precursor populations from the abnormal populations.

Materials & Methods

The ML model was trained using 5 normal controls, 4 cases with MRD negativity and 5 cases with MRD positivity using standard FCM assessment using a 12 colour MRD panel in each of the samples. This model was then validated on a validation cohort of 91 T-MRD samples that were processed between January and September of 2024.

Result

The ML model was trained on 10,46,400 events of cCD3+ and sCD3- population from 14 samples. Each event was labelled as normal or abnormal. Among Logistic Regression, Random Forests and XG Boost models, the XG Boost model performed the best with 99% accuracy and a 100% recall rate. This model was then validated with the validation cohort consisting of 91 samples. Concordance with standard FCM assessment was 82%, with discrepancies in 15 cases. These cases were positive by standard assessment but were negative by the ML model. 3 of these cases were with sCD3+ disease, which was excluded in the gating strategy of training the model. Another 7 cases had MRD values of less than the clinically significant cut-off. The ML model had a high PPV of 100%. Overall, the ML model had balanced precision and recall with an F1 score of 74%.

Conclusion

Incorporating ML algorithms in the general workflow imparts confidence and acts as a double-check in MRD assessments. Follow-up data of the validation cohort will be analysed to assess differences in the prognostic value of the ML algorithm and standard FCM assessment in identifying early relapse.

Malignant Hematology-Laboratory (MHL) PP-MHL-27

Cytogenetics profile of Philadelphia Chromosome-Positive B-cell Acute Lymphoblastic Leukemia and its impact on Measurable Residual Disease Outcome

Megala S
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Introduction

Philadelphia chromosome-positivity (Ph+) in B-cell acute lymphoblastic leukemia (B-ALL) is a high-risk cytogenetic abnormality. The co-existing high-risk additional cytogenetic abnormalities (ACAs) are linked to poor outcomes. However, the impact of ACAs on measurable residual disease (MRD) status and their potential as early markers for poor outcomes is unknown. This study aimed to determine the effects of ACAs on MRD outcomes in newly diagnosed Ph+ B-ALL.

Aims & Objectives

1. Determine the frequency of Ph+ B-ALL
2. Characterize the additional cytogenetic abnormalities in Ph+ B-ALL
3. Correlate the additional cytogenetic abnormalities with MRD outcomes

Materials & Methods

We retrospectively analyzed ALL patients seen at the Christian Medical College, Vellore, between 2014 and 2024, who underwent cytogenetic and flow cytometry-based analyses. The cytogenetic profiles were characterized into high-risk and low-risk based on additional cytogenetic abnormalities and correlated with flow cytometry-based MRD outcomes.

Result

In our cohort, 6.7% of cases (n=146/2166) were de-novo Ph+ B-ALL cases. The median age was 29.5 years (range: 1-70 years) with male to female ratio of 1.4:1. The median hemoglobin, WBC count, and platelet counts were 8.3 g/dl (range: 2.2-13.4), 18.3 x 109/L (range: 0.2-929.3), and 34.0 x 109/L (range: 1.0-1600.0), respectively (Table 1). Among these, 118 cases (80.8%) had Ph+ chromosomes with ACAs (ACAs+), while 28 cases (19.2%) had only Ph+ chromosomes (ACAs-). No statistically significant differences in hemoglobin, WBC, and platelet count were seen between these groups. The ACAs+ group was further divided into high-risk ACAs+ (HR-ACAs+) (n=74, 62.7%) and low-risk ACAs+ (LR-ACAs+) (n=44, 37.3%) cases. MRD data was available for 55 cases, showing MRD positivity in 12 (21.8%) HR-ACAs+, 7(12.7%) LR-ACAs+, and 8 (14.5%) ACAs- cases, with no statistically significant difference between groups.

Table 1: Clinico -demographic profile of De-novo Ph+ B-ALL

De-novo Ph+ B-ALL	Total (n=146)	No ACAs (n=28)	ACAs (n=118)	P-Value
Median Age (yrs)	29.5	29	29.5	0.75
Age Range (yrs)	1-70	2-70	1-63	
M:F ratio	1.4:1	2.1:1	1.3:1	
Female	60	9	51	
Male	86	19	67	
Age Group				
Children(≤15 Yrs)(%)	41 (28.1)	9 (32.2)	34 (28.8)	
Aya(16-39 Yrs) (%)	65 (44.5)	13 (46..4)	52 (44.0)	
Adult(≥40 Yrs) (%)	40 (27.4)	6 (21.4)	32 (27.1)	
CBC PARAMETERS				
Hb (g/dl), Median (range)	8.3 (range 2.2 – 13.4)	8.0 (range 3.1 – 12.9)	7.9 (range 2.2 – 13.4)	0.37
WBC x 10^9/L, Median (range)	18.3 (0.2 – 929.3)	18.9 (range 0.2 – 659.7)	18.3 (range 0.6 – 929.3)	0.78
Platelet count x 10^9/L, Median (range)	34.0 (1.0 – 1600)	36.0 (range 6.0 – 467.0)	34.5 (range 1000 – 1600000)	0.75
MRD STATUS (N=55)	55	16	39	0.93
MRD-POSITIVE	27	08	19	
MRD-NEGATIVE	28	08	20	

Conclusion

Additional cytogenetics abnormalities in Ph+B-ALL do not significantly alter the MRD outcome. However, the present study cannot comment upon its use as a predictor for overall and relapse-free survival.

Malignant Hematology-Laboratory (MHL) PP-MHL-28

Evaluating Relapse Patterns and Transcript Associations in Ph+ B-ALL Subtypes : A Comparative Study of Lymphoid and Multilineage Involvement

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Introduction

The new ICC divides "Ph+ B-ALL" into two subtypes: "B-ALL with t(9;22) with lymphoid only involvement" (Ph+ ALL-L) (L-type), and "B-ALL with t(9;22) with multilineage involvement" (Ph+ ALL-M) (M-type). The underlying difference between these subtypes reflects the target cell for the transformation event, with a multipotent progenitor serving as the target for M-type and committed lymphoid progenitor in L-type. L and M types may be distinguished, particularly after therapy, when the tumor burden estimated by assessing the BCR::ABL1 fusion transcripts is higher than flow cytometry.

Aims & Objectives

In this study, we aimed to compare the outcomes of these two subtypes.

Materials & Methods

All cases of Ph+ ALLs between March 2021 and July 2024 that were monitored for Measurable Residual Disease (MRD) at the Department of Haematology were included. MRD assessment was performed using multiparametric flow cytometry (FCM) and droplet digital PCR (ddPCR).

Result

A total of 116 cases of Ph+ B-ALL came for MRD monitoring at our centre. Of these, 56 had MRD assessment by both FCM and ddPCR and were included in this analysis. Cases that were positive by ddPCR and negative by FCM were defined as M-type (n=33/56), and those that were positive by both were defined as L-type (n=23/56). A further follow-up with at least one time point (~60 days) was present in 40 cases (M-type – 25; L-type – 15). No specific association with BCR::ABL1 transcript type was observed with the M and L types (M-type – p210-8/25, p190-17/25; L-type – p210-5/15, p190-10/15). HSCT was performed in 22/25 M-type cases and 7/15 L-type cases. M-type cases on follow-up showed plateaued ddPCR values with <0.01 <0.01% before and after transplant. Of the L-typecases, 4/15 showed relapse within a median of 5.5 months (2-18 months), and 1/15 showed refractory disease (p=0.0046). Of the relapse/refractory cases, 4/5 showed a p210 transcript.

Conclusion

M-type and L-type of Ph+ B-ALL did not show any association with BCR::ABL1 transcript types. Relapse was more common in the L-type than in the M-type and was higher in patients with the p210 transcript type.

Malignant Hematology-Laboratory (MHL) PP-MHL-29

Clinical, Hematological and Flowcytometric Immunophenotypical Findings of Atypical CLL: Our Experience

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Background

Chronic lymphoproliferative disorders are a heterogeneous category of neoplastic disorders with variable morphological and immunophenotypic characteristics. It is defined as the clonal proliferation of mature B, T, and NK lymphoid cells in the peripheral blood and bone marrow. Atypical CLL can be distinguished from typical CLL morphologically and immunophenotypically. Morphologically atypical CLL have large, atypical forms, prolymphocytes or cleaved cells. Immunophenotypically, atypical CLL differs from typical CLL in variable or lack of expression of CD5 and CD23, positive CD79b and the patient does not meet the criteria for any other B cell lymphoid malignancy.

Case Presentation

CASE REPORT 1: A 90/M presented with generalised weakness. Peripheral smear revealed leukocytosis along with smudge cells. Flow cytometric immunophenotyping does not reveal CD5 and CD23 expression.

CASE REPORT 2: A 45y/M presented with fever, weakness and hepatosplenomegaly showed moderate CD5 expression whereas negative CD23 expression.

CASE REPORT 3: An 80y/M was a known case of carcinoma sigmoid colon. Peripheral smear showed absolute lymphocytosis along with many smudge cells and prolymphocytes Flow cytometric immunophenotyping does not reveal CD5 and CD23 expression.

CASE REPORT 4: A 79y/ M with complaints of fever and weakness showed moderate to bright expression of CD5 and CD23 but with CD79b and CD20 positivity which groups it into atypical CLL.

CASE REPORT 5: A 52y/M with lymphocytosis on peripheral smear showed non restriction of kappa and lambda with negative CD5 and CD23, negative FMC7 and positive CD200

CASE REPORT 6: A 44y asymptomatic male patient, peripheral smear revealed absolute lymphocytosis, with cells having villous like cytoplasm, with CD5 negative, CD23 negative, CD11c bright positive on flowcytometric immunophenotyping.

Diagnosis

Atypical Chronic Lymphocytic Leukemia

Treatment

Ibrutinib

Follow-up

loss to follow up after 3 months

Conclusion

Atypical CLL (aCLL) is characterized by morphologic, phenotypic, and cytogenetic differences compared to classic CLL. However, following the recent introduction of targeted drugs designed on the basis of biological mechanisms, a better definition of aCLL is needed to provide the optimal treatment for each group of patients.

Malignant Hematology-Laboratory (MHL) PP-MHL-30

Uncovering the Rare Link: Increased Bone Marrow Mast Cells in Acute Lymphoblastic Leukemia

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Background

Acute lymphoblastic leukemia (ALL) is the second most common acute leukemia in adults, with incidence of 35 % of all haematological malignancies. In adults, 75% of cases develop from precursors of B-cell lineage, with the remainder consisting of T-cell precursors. Patients with T-lineage usually present with marked mediastinal lymph node enlargement and B-lineage usually presents with extensive bone marrow involvement. The presence of conspicuous bone marrow mast cells in the present case of ALL is intriguing and the antecedent diagnosis of Tuberculosis (TB) and deep vein thrombosis (DVT), pulmonary embolism (PE) could suggest a causal relationship between the conditions. DVT has been associated with TB at or after the diagnosis.

Case Presentation

A 55-year-old man came with complaints of fever, weakness of 2-3 days duration. Peripheral smear examination showed anaemia, leukopenia, lymphoblasts; bone marrow aspiration study revealed 80% lymphoblasts admixed with conspicuous mast cells.

Previously he came with complaints of fever ON and OFF and rashes all over the body of 20 days duration. He was diagnosed with mediastinal TB lymphadenitis and acute pulmonary artery thromboembolism along with DVT of left popliteal and small saphenous veins. Laboratory investigation showed anaemia, leukopenia (Hb:9.7gm/dl, TC:1260cells/cumm) and on evidence of abnormal cells. ESR was > 140mm/hr. Ferritin was increased.

Diagnosis

Immunophenotyping analysis by flowcytometry showed 80% blasts cell having dim CD45 low to intermediate side scatter, moderate expression of CD34, CD19, CD38, cCD79a, CD22, CD10(heterogenous), HLA-DR. Aberrant expression of CD13(Dim) and CD33(moderate) was noted and confirmed the diagnosis of CALLA positive precursor B-ALL.

Treatment

Patient received HRZE regimen for TB and Inj. Enoxaparin for DVT. He is now started on Berlin-Frankfurt-Munster 2002 chemotherapy for ALL.

Follow-up

Cytogenetics panel for risk stratification of ALL is awaited.

Conclusion

The presence of increased bone marrow mast cells in ALL is a rare occurrence. This could be attributed to the proinflammatory as well as the hypercoagulable state resulting in development of thromboembolism. The concurrence of TB and DVT with the subsequent development of ALL points to the thrombogenic potential of mast cells.

Malignant Hematology-Laboratory (MHL) PP-MHL-31

Genetic Profile of AML in Relation to Age, Gender and Immunophenotyping: A Study from Northwest India

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Nidhi Sharma, Ankur Kumar, Peeyush Kumar Saini, Sandhya Gulati

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Introduction

Molecular analysis continues to have an important role in the management of Acute Myeloid Leukemia(AML). It is necessary to diagnose specific molecular category of AML, to determine the most effective form of treatment and for prognostication

Aims & Objectives

1. To analyse the genetic profile of Acute Myeloid Leukemia cases presented to Advance Hematology Lab.

2. To analyse the relation of genotype to Age, gender and Immunophenotyping.

Materials & Methods

We performed a retrospective analysis of the molecular findings in AML. All cases of acute myeloid leukemia that presented to Advanced Haematology & HLA Lab from July 2023 to October 2024 were included in this study.

10 ml of EDTA blood sample collected. CBC was performed first then DNA extracted from the peripheral blood using phenol chloroform method.

We used the TRUPCR AML Kit which included 9 genes (PML-RARA, AML1-ETO, C- kit, NPM1, FLT3-TKD, FLT3-ITD, BCR-ABL1MajorandBCR-ABL1Minor, CBFB-MYH11). This kit is based on Real time PCR.

Result

GENE	TOTAL CASES	AGE (Yrs)	SEX	
			MALE	FEMALE
CBFB-MYH11	4	15-65	3	1
BCR-ABL MAJOR	9	15-65	6	3
BCR-ABL MINOR	-	-	-	-
PML-RARA	3	25-35	1	2
AML1-ETO	6	15-25	5	1
C-kit	3	15-25	2	1
NPM1	18	25-75	14	4
FLT3-TKD	4	5-65	1	3
FLT3-ITD	-	-	-	-

Among 101 acute myeloid leukemia patient analysed 59 were male and 42 were female giving a male to female ratio of 1.40:1. Mean age was 38.6yr. CBFB-MYH11 was detected in 4 cases (8.69%), BCR-ABL major was detected in 9 cases (19.56%), AML1-ETO in 6 cases (13.04%), NPM1 in 18 cases (39.13%), FLT3-TKD in 4 cases (8.69%), PML-RARA in 3 cases (6.52%) and C-kit in 3 case (6.52%). Among the 46 detected cases 67.3% were male and 32.6% were female. In rest of 55 cases none of the 9 mutation were detected. Flow cytometry was done in 33 cases, among them 96.9% were positive for CD33, 93.9% positive for MPO, 84.8% were positive for CD13, 78.78% positive for CD117,84.8% positive for HLA DR, 78.7% positive for CD34, 21.2% positive for CD7, 12.1% were positive for CD19, 24.2% positive for CD14 and 9% positive for CD38. Out of all AML subtypes 51.5% were male and 48.4%were female.

Conclusion

Our study had a limitation of less number of cases. More data is needed to establish any association.

Malignant Hematology-Laboratory (MHL) PP-MHL-32

Lynch Syndrome as a Cause of Daratumumab Reffractory Multiple Myeloma

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Background

Myeloma is a constellation of diseases with MGUS on one and plasma cell leukaemia at the other end of spectrum. The causal relationship has been attributed to age, gender, racial and ethnic background, underlying immunodeficiency, exposure to radiation & dioxin-related compounds. Few anecdotal reports in BRCA1/2, CDKN2A and mismatch repair deficiency have been published. Owing to the rarity of occurrence, exact disease biology, response to standard therapeutic regimen and outcomes are not clearly elucidated. This is attributed to less uptake of any genomic/genetic testing myeloma patients as the same is not mandated by international guidelines.

Case Presentation

A 53 year old male patient, presented with easy fatiguability, right shoulder pain and bilateral carpal tunnel syndrome and nephrotic range proteinuria.

Diagnosis

The diagnosis of MM was based on bone marrow findings, monoclonal M band and flowcytometry. Owing to primary refractoriness, a repeat bone marrow aspirate was subjected to NGS both on CD138 selected plasma cells as well as the CD138 negative cells. NGS revealed MSH6 p. Y397C which was predicted to be of conflicting interpretation to pathogenicity. To ascertain the nature of this mutation, IHC for MSH2 & MSH6 was employed on the biopsy which revealed a complete loss of MSH2 & MSH6 proteins. The mutation was present both in CD138+ &CD138- cells, confirming the ubiquitous presence and not only in tumor population.

Treatment

He was started on Dara-VRD induction regimen. However, he was refractory to treatment and there was disease progression after 2 cycles. He was switched to PAD regimen, in view of significant extramedullary disease.

Follow-up

There was improvement in his general condition and significant reduction in SFLC after 2 cycles. Currently he has received 4 cycles of PAD regimen and has achieved VGPR.

Conclusion

In a study on 26 myeloma patients, 54 cases showed instability in 5 different loci in 14q32 region This may plausibly mean that genomic instability in heavy-chain MM may be a common finding and probably plays a critical role in myelomagenesis.

This case underscores the importance of genomic/genetic testing especially in primary refractory cases of common malignancies like myeloma.

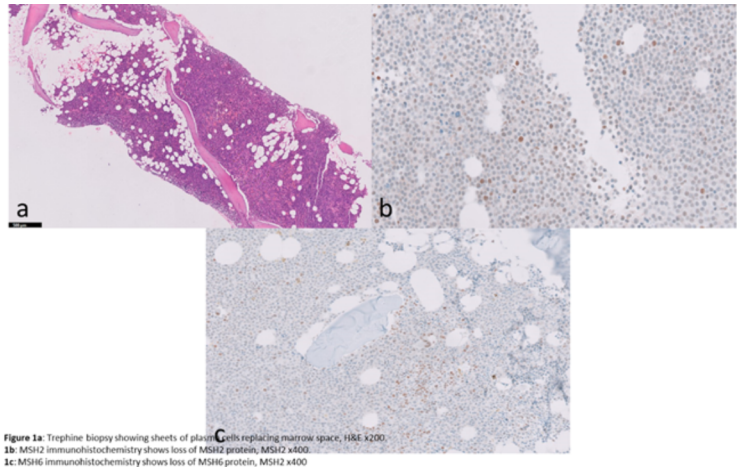

Figure 1a: Trephine biopsy showing sheets of plasma cells replacing marrow space, H&E x200.
1b: MSH2 immunohistochemistry shows loss of MSH2 protein, MSH2 x400.
1c: MSH6 immunohistochemistry shows loss of MSH6 protein, MSH2 x400

Malignant Hematology-Laboratory (MHL) PP-MHL-33

Genetic Profile of Acute Lymphoblastic Leukaemia in Relation to Age, Gender and Immunophenotype. A Study from North-West India

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Introduction

Molecular analysis continues to have an important role in the management of Acute Lymphoblastic Leukaemia (ALL). It is necessary to diagnose specific molecular category of ALL, to determine the most effective form of treatment and for prognostication.

Aims & Objectives

1. To analyse the genetic profile of Acute Lymphoblastic Leukaemia cases presented to Advance Haematology Lab.

2. To analyse the relation of genotype to Age, Gender and Immunophenotyping.

Materials & Methods

We performed a retrospective analysis of the molecular findings in ALL. All cases of acute lymphoblastic leukaemia that presented to Advanced Haematology HLA Lab from August 2023 to September 2024 were included in this study.

10ml of EDTA blood sample collected. CBC was performed first then DNA extracted from peripheral blood using phenol chloroform method.

We used the TRUPCR ALL Kit which included 7 genes (E2A-PBX1, TEL-AML1, MLL-ENL, MLL-AF9, BCR ABL1 Major Prime Probe Mix and BCR ABL1 Minor & Micro Primer Probe Mix). This kit is based on Real time PCR.

Result

Among 96 acute lymphoblastic leukaemia patient analysed 62 were male and 34 were female giving a male to female ratio of 1.82:1. Mean age was 28.8yr. BCR-ABL1 Major was detected in 14 cases(14.58%).BCR ABL1 Minor and Micro Prime Probe Mix was detected in 13 cases (13.54%), E2A-PBX1 in 3 case (3.12%) and TEL-AML in 1 case (1.04%). In rest of 65cases none of the 7 mutation were detected. Flow cytometry was done in 50 cases, among them 46 cases were positive for CD79a, CD10, CD19, HLADR, 43cases positive for CD34, 36cases positive for CD22, 27 cases positive for CD20 and 3 cases positive for CD38 which were in favour of B-ALL subtype. Out of all B-ALL subtypes 66.7% were male and 33.3% were female. 4 cases are positive for CD3, CD5, CD7, cCD3, which were in favor of T-ALL. Out of all T-ALL subtypes, all were male.

Conclusion

Our study had a limitation of less number of cases. More data is needed to establish any association.

GENE	TOTAL CASES	AGE(years)	SEX
E2A-PBX1	3	15-21	Male-1 Female-2
TEL-AML	1	3	Male
MLL-AF4	0	-	-
MLL-ENL	0	-	-
MLL-AF9	0	-	-
BCR ABL1 Major Primer Probe Mix	14	13-51	Male-6 Female-8
BCR ABL1 Minor & Micro Primer Probe Mix	13	22 - 53	Male – 4 Female - 9

Malignant Hematology-Laboratory (MHL) PP-MHL-34

From Mystery to Diagnosis "A VEXAS Case Report"

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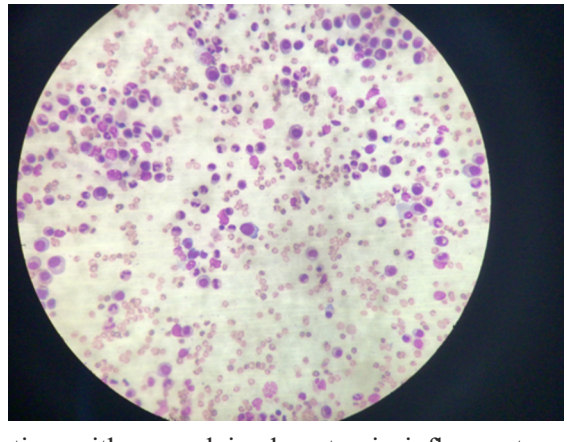
Background

50-year male with autoimmune symptoms

Case Presentation

A 50-year-old male presented with

1. recurrent erythematous skin lesions on extensor aspect of upper and lower limbs which would appear and disappear in 3 days, biopsy was suggestive septal panniculitis
2. Recurrent orbital swelling which would appear and disappear
3. K/c/o hyperthyroidism, thyroid scan showing diffuse uptake
4. Pancytopenia
5. Submandibular gland swelling
6. Bilateral parotid enlargement
7. Superficial thrombophlebitis
8. Pinna perichondritis
9. ACE level- normal, no hypercalcemia
10. Clinical features: Pallor: + Icterus:- , no organomegaly
11. History of transfusion: multiple PRBC/ Platelet
12. Family history: NIL
13. Treatment history: drastic improvement was seen with steroids
14. Latest CBC: HB- 4/ TLC- 2000/ PLT- 30k
15. ANA and ANCA by IF -negative
16. Viral Serology: negative



Diagnosis

Suggestive of VEXAS syndrome

Treatment

High dose steroids

Follow-up

High dose steroids

Conclusion

VEXAS syndrome should be considered in patients presenting with unexplained systemic inflammatory condition when associated with macrocytosis and other hematological disorder. Further, VEXAS syndrome has its genetic mosaicism arising in bone marrow and it involves all the systemic organs. VEXAS syndrome should be considered as a possible diagnosis when a history of recurrent fever, autoimmune symptoms is present in adult patients. A multidisciplinary approach is needed for diagnosing and management of this challenging entity. VEXAS syndrome will also be the area of intensive research to evaluate any co existing mutation in other genes and also to determine the clinical behaviour, outcome, appropriate therapy.

Malignant Hematology-Laboratory (MHL) PP-MHL-35

Cytomorphological and Immunohistochemical Assessment of Non-Hematopoietic Malignancies Metastasizing to Bone Marrow, Including Their Clinical and Hematological Features: A Case Series

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Introduction

Bone marrow is one of the rare but important site of metastasis of solid tumors. The key steps of metastasis include invasion, intravasation, circulation, extravasation and colonization. For tumor staging, therapy selection and prognosis risk stratification, the status of the bone marrow should be known for the presence or absence of metastasis.

Aims and Objectives

This study aimed to investigate the diagnostic significance of bone marrow biopsy in detecting bone marrow metastases from tumors of unknown primary origin and to analyze the clinical and hematological characteristics of patients with bone marrow metastases from non-hematopoietic malignancies

Material and methods

In this retrospective study, we reviewed bone marrow aspirates in our hospital. 6 cases of metastatic bone marrow tumors were diagnosed by light microscopy and the bone marrow samples from these cases with unknown primary tumors sites were examined by immunohistochemistry.

Results

Among all cases, the age of the patient ranged from 6-57 yrs (mean age of 28). 2 of the 6 were in paediatric age group. The common presenting sign and symptoms were fever, weight loss in 50% each and organomegaly in 33%. Anemia was the most common hematological finding found in all patients (100%) at the time of admission, while only 33% of patients simultaneously had thrombocytopenia. Abnormal liver function test and elevated urea were observed in 33.33% of patients, indicating potential renal impairment. All patients (100%) had high LDH, indicating significant tissue damage or metastasis. Small round cell tumor in children was the most common metastatic tumor in children.

Conclusion

Bone marrow metastasis can be presented as the initial presentation with hematological changes and may be misdiagnosed as a primary haematopoietic disorder. Morphology of metastatic cells is as per the primary site of tumor IHC can help to determine the primary tumor site in case of metastatic bone marrow with unknown primary tumor sites.

Malignant Hematology-Laboratory (MHL) PP-MHL-36

Correlation of CNS Involvement with Clinical Outcomes in Hematological Malignancies: A Single Centre Experience

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Introduction

Central nervous system (CNS) involvement is a serious complication of many hematologic malignancies and is associated with poor prognosis. Early detection of CNS disease in hematologic malignancies is important for treatment and can be accomplished through cerebrospinal fluid (CSF) analysis.

Aims & Objectives

To study the frequency of CNS involvement in various haematological malignancies and to find out their correlation with molecular spectrum, minimal residual disease status and survival outcomes.

Materials & Methods

It was a retrospective observational study involving consecutive patients of haematological malignancies who presented for CSF evaluation during last six months in Hematopathology laboratory. Information regarding demographics, presenting symptoms, imaging studies, flowcytometric and molecular analysis and survival outcome of the patients in both CSF-positive and negative groups were obtained from the EMR and compared.

Result

Out of a total of one-hundred and eighty-three patients, 74.86% were negative for malignant cells in CSF cytology, while 25.13% were CSF positive. B-Lymphoblastic leukemia (BALL) followed by CML-blast crisis were the commoner subtypes in CSF-positive group, while BALL and AML were commonly seen in CSF-negative group. There was no difference between the two groups in terms of age, CSF cell count, serum LDH levels and incidence of different molecular abnormalities except BCR-ABL ($p<0.001$). However, the CSF-positive group correlated significantly with >0.01% post-induction MRD status ($p=0.002$) and higher rates of relapse/death (0.03) in comparison to the CSF-negative group.

Conclusion

CNS involvement is a poor prognostic factor and mandates intensive treatment protocols for improving clinical outcomes.

Malignant Hematology-Laboratory (MHL) PP-MHL-37

Characterization of the T/NK-CLPDS by Flow Cytometry and Correlation with Clinical Spectrum: A Single Centre Experience

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Introduction

Multi-parametric flow cytometry (MFC) is a powerful tool for the diagnosis and classification of chronic lymphoproliferative disorders (CLPD). An abnormal CD4/CD8 ratio, aberrant gain or loss of antigens along with T-cell clonality using TRBC-1 by flow cytometry and/or TCR-gamma delta gene rearrangement by PCR-based assays help in clinching the diagnosis.

Aims & Objectives

To study the utility of flowcytometry in diagnosing T/ NK CLPDs and correlate with their clinical spectrum.

Materials & Methods

It was a retrospective observational study which included all patients of T/NK-CLPDs, diagnosed on the basis of peripheral blood 12-color flow cytometry and ancillary molecular studies during the last five years.

Result

Out of a total of eight-hundred patients diagnosed as CLPD, only twenty-five were T/NK-CLPDs (3.1%). T/NK-CLPDs mostly involved CD8+/CD4- (40%), followed by CD4+/CD8-(28%) subgroups. The commonest subtype detected were T-LGL, T-PLL, hepatosplenic-gamma delta TCL and ALCL, observed at a frequency of 32%, 16%, 16% and 12% respectively. Median age at presentation was 45 years with an M: F ratio of 2.5:1. 24% patients were aged >60years of age. 76% patients had extra-nodal disease and 4% had pleural effusion. Cutaneous lesions, generalised lymphadenopathy, hepatosplenomegaly were observed in 8%, 48% and 68% patients respectively. Constitutional symptoms were found in 56% patients in the form of fever, night sweats or weight loss. The most common FISH and NGS abnormalities were TCR-A/D rearrangement and ATM deletions respectively. All patients were alive at last follow-up with median follow up period of 12 months (Range 6-36 months).

Conclusion

T/NK-CLPDs are aggressive yet rare haematological malignancies, where precise diagnosis by flow cytometry, supported by clonality and imaging studies, helps in correct prognostication and optimal patient management.

Malignant Hematology-Laboratory (MHL) PP-MHL-38

The P53 Puzzle : Solving the Mystery of Pure Erythroid Leukemia

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Background

Pure erythroid leukemia (PEL) which is previously known as acute myeloid leukemia (AML) –M6b is a rare entity. It is a very aggressive subtype with an overall median survival of <6>80% erythroid lineage cells in the bone marrow (BM) and >30% proerythroblasts, with no significant increase in myeloblast component. Theoretically, PEL diagnosis might look straight forward, but in clinical practice it is quite challenging to differentiate from non-neoplastic erythroid proliferations, especially florid erythroid hyperplasia. As the literature mentions the importance of Tp53 role in arresting the maturation of erythroid lineage and Tp53 gene alterations (deletion/mutation) being considered as molecular hallmark, we considered doing p53 IHC to differentiate PEL from non-neoplastic erythroid hyperplasia by differential expression of p53.

Case Presentation

We performed immunohistochemistry on 3 cases of PEL and 5 cases of reactive erythroid hyperplasia due to variable other causes and then assessed positivity and intensity in pronormoblasts and basophilic normoblasts in a scale of 0-3+ (0 being completely absent and 3+being strong nuclear positivity). All the 3 PEL cases showed strong nuclear positivity (3+), whereas reactive erythroid hyperplasia showed heterogeneous positivity ranging from 0 to 2+.

Diagnosis

Pure erythroid leukemia

Treatment

Not applicable

Follow-up

Not applicable

Conclusion

P53 can be a useful marker in differentiating reactive erythroid hyperplasia's from PEL while waiting for results of cytogenetics.

Malignant Hematology-Laboratory (MHL) PP-MHL-39

When Rare Meets Rarer: Dyskeratosis Congenita and Disseminated Diffuse Large B Cell Lymphoma

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Background

Dyskeratosis congenita (DKC) is a rare, progressive bone marrow failure syndrome. It is characterized by the triad of reticulated skin hyperpigmentation, nail dystrophy, and oral leukoplakia. It is also a cancer predisposition syndrome caused by defects in telomere biology. It is most commonly associated with high risks of developing aplastic anemia, myelodysplastic syndrome, leukemia, and solid tumors. Non- Hodgkin's lymphoma is a rare malignancy in patients with DKC. We report a rare case of DKC with diffuse large B cell lymphoma involving lymph node, skin and bone marrow.

Case Presentation

A 38 years female, known case of DKC presented with new onset erythematous maculo-papular rashes over legs. The patient incidentally find to have increased uptake in lymph node and in bone marrow. Following which biopsy from skin, lymph node and bone marrow aspiration has been done. All three showed infiltration by atypical cells. These cells have abundant cytoplasm, pleomorphic nuclei, opened up chromatin, vesicular nuclei and prominent nucleoli. These cells were positive for CD20, CD19, MUM1 and negative for CD10, BCL-6, CD15 and ALK-1.

Diagnosis

A final diagnosis with diffuse large B cell lymphoma is made with multisystem involvement in a known case of dyskeratosis congenita.

Treatment

Chemotherapy regimen has been started.

Follow-up

Patient is responding to the therapy.

Conclusion

DKC is a rare disease occurring in one I one million people. It is mostly associated with solid organ malignancies and leukemia. In this report we present an unusual case of DLBCL involving lymph node, skin and bone marrow in a patient diagnosed with DKC. Usually patients diagnosed with DKC dies before 20 years of age due to bone marrow failure. In our case, the patient presented at 38 years with disseminated lymphoma. We believe that by reporting this presentation of the patient would add more information to the existing fund of knowledge.

Malignant Hematology-Laboratory (MHL) PP-MHL-40

Catch-22 in T/myeloid Mixed Phenotypic Acute Leukemia – Molecular Studies as a Conundrum of the Missing Link

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Background

Acute Leukemias with Ambiguous Lineage (ALAL) are a rare subset of acute leukemias characterized by a lack of clear lineage differentiation and include mixed phenotypic acute leukemia (MPAL) and acute undifferentiated leukemia (AUL). MPAL is an acute leukemia that features blasts with markers from more than one lineage, while AUL lacks distinct lineage commitment. We present a case of T/Myeloid MPAL (T/My MPAL) with an initially straightforward myeloid morphology but conflicting flow cytometric immunophenotyping (FC-IPT) findings and a puzzling molecular signature.

Case Presentation

16-year-old child presented with acute onset fever, body ache and generalized weakness. Clinical examination revealed bilateral cervical and axillary lymphadenopathy along with hepatosplenomegaly.

Diagnosis

Peripheral blood showed bicytopenia and leukocytosis with 79% granular blasts containing distinct Auer rods. Bone marrow (BM) was hypercellular and showed near total replacement by blasts which were cytochemically positive for myeloperoxidase (MPO) and non-specific esterase (NSE). Many blasts showed Auer rods. FCM-IPT showed 2 distinct sets of blast populations with a T and myeloid phenotype. The T lymphoid blast population showed an early T-precursor acute lymphoblastic leukemia (ETPALL) phenotype. Next Generation Sequencing (NGS) reported biallelic variants in WT1 (p.Glu212Ter in exon1 & p.Arg374ValfsTer12 in exon7) along with missense mutations in NRAS (p.Gly12Asp) and PTPN11 (p.Glu76Val) genes.

Treatment

The patient was put on Acute Myeloid Leukemia (AML) induction (3+7) regime. Day 21 BM showed 35% blasts and end of induction BM was not in morphological remission (MR) following which he was switched to ALL induction.

Follow-up

Presently, the end of 2nd induction BM is in MR, and he is being worked up for hematopoietic stem cell transplant (HSCT).

Conclusion

The case gives a therapeutic dilemma given the morphology supported AML, while the IPT findings favoured T/My MPAL and NGS detected variants like NRAS and PTPN11 commonly mutated in B/My MPAL & AML apart from the biallelic WT1 mutations, including a never previously described exon 1 nonsense mutation. Such overlap cases provide a bottleneck situation as they are under-recognized, and therapy is not well established. The current treatment recommendation in MPAL is an ALL-like induction regimen followed by allogeneic HSCT in first complete remission.

Malignant Hematology-Laboratory (MHL) PP-MHL-41

Hepatosplenic Gamma Delta T Cell Lymphoma Hiding in the Shadow of Hemophagocytic Lymphohistiocytosis

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Background

Hemophagocytic lymphohistiocytosis (HLH) is a common differential in fever of unknown origin with cytopenias and hepatospenomegaly. It can be primary or secondary to various autoimmune conditions, infections and malignancies. We herein present an interesting case who presented to us with fever of unknown origin and cytopenias.

Case Presentation

A 21-year-old male presented with 4 months history of unexplained fever and abdominal distension. On examination he had hepatosplenomegaly and icterus with yellowish discoloration of the skin and eyes.

He was extensively evaluated for fever and his work up was negative, viral markers were also negative. Laboratory parameters showed markedly increased ferritin, conjugated hyperbilirubinemia and reduced fibrinogen.

We received peripheral smear and bone marrow with a clinical suspicion of HLH.

CBC showed Hb 10.3 gm/dl, TLC 39 x 109/L and platelet count 98 x 109/L. Peripheral smear showed 9% blastoid cells. Bone marrow aspirate smears sowed 40% blastoid cells and hemophagocytosis.

Flow cytometry, lymphoma panel done on bone marrow aspirate revealed abnormal sCD3 bright + T cells positive for TCR gamma delta and showing loss of CD5. They showed CD2, CD7, moderate CD56, and variable CD16/CD26, and were CD4/CD8 double negative. Karyotyping/FISH for iso chromosome 7q was recommended but not performed. His radiology did not reveal any lymph nodes.

Diagnosis

Hepatosplenic Gamma Delta T-cell lymphoma (HSTCL) with secondary hemophagocytic lymphohistiocytosis (HLH).

Treatment

Patient was planned for chemotherapy he received ESHAP, GDP, bendamustine and venetoclax.

Follow-up

On follow up after 6 months he is refractory to chemotherapy and is currently admitted for alemtuzumab based therapy with plan to consolidate with Haploidentical bone marrow transplant.

Conclusion

In cases with HLH, pathologist should judiciously examine smears to diagnose underlying malignancy as a primary cause like in our case. Proper diagnostic approach including morphological examination of bone marrow and ancillary tests includes immunophenotyping is essential to reach at correct diagnosis. HSTCL is an aggressive disease and early diagnosis is crucial for timely management and salvaging the patient.

Malignant Hematology-Laboratory (MHL) PP-MHL-42

Case of Clinical Diagnostic Challenges: Autoimmune Disorder, Transfusion-Dependant Anemia and Myelodysplastic syndrome with SF3B1 mutation

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Introduction

Myelodysplastic neoplasm (MDS) encompass a diverse group of disorders defined by morphologies and genetic abnormalities. These can arise de-novo or as myeloid neoplasms post-cytotoxic therapy (MN-pCT).Diagnosing them, especially in the absence of elevated myeloblasts or cytogenetic anomalies, is challenging.This case illuminates the complexities faced when evaluating a patient with transfusion-dependent anemia undergoing treatment for autoimmune disorders.

Aims & Objectives

23 year old female patient, known case of juvenile idiopathic arthritis

Materials & Methods

We herein reported a 23-years old female patient who was a known case of juvenile idiopathic arthritis and autoimmune hepatitis with small duct primary sclerosing cholangitis overlap and later evaluated for right eye granulomatous uveitis, 7 years back, received methotrexate (MTX) as weekly regimen, along with Sulphasalazine and Wysolone for 5years. She now presented with transfusion-dependent anaemia. MTX administration was discontinued, and concentrated red blood cells were transfused, weekly Inj. Erythropoietin and Tab Danazol TDS since 7 months now yet patient continued to have anaemia. She was worked up for autoimmune hemolytic anemia which was unremarkable. Peripheral blood testing showed moderate anisopoikilocytosis, macrocytic to normocytic red cells and bone marrow analysis revealed hypercellular marrow with clusters of dyspoietic megakaryocytes and increased erythoid series cells showing dyspoiesis with 20% ring sideroblasts (RS) implying the diagnosis of MDS with Multilineage dysplasia and Ringed sideroblast (MDS-RS), now put in category of MDS with low blast with SF3B1 mutation according to WHO 2022 edition. She had a trisomy 8 diagnosed by FISH. Genomic DNA sanger sequencing of bone marrow aspirate specimens. revealed SF3B1 gene mutation (NM_012433: C. 2098A > G (P. K700E), usually accounts for 60% of the variants.

Result

In t- MDS, SF3B1 mutation have better prognosis

Conclusion

The 2022 WHO-classification recognizes the fact that MN-pCT can be sub-classified morphologically into Myelodysplastic neoplasm pCT, Myelodysplastic/ Myeloproliferative neoplasm pCT, AML-pCT. De novo MDS SF3B1-mutation had better outcomes compared to t-MDS SF3B1-mut although rate of AML transformation was similar. In patients with therapy related MDS, those with SF3B1-mut had better outcomes than those with SF3B1-WT. Complex cytogenetics, TP53 mutation, and transformation to AML occurred more with SF3B1-WT than with SF3B1-mut. Among t-MDS patients, SF3B1-mut may have a better prognosis. The present case is unique due to its rarity of subtype with many overlapping phenomenon and history of long term intake of low dose MTX. Besides that autoimmune phenomenon in MDS has been described in few case reports and case series. It is essential to consider methotrexate, a type of antimetabolite which may be implicated in t-MDS.

Malignant Hematology-Laboratory (MHL) PP-MHL-43

Hemophagocytic Lymphohistiocytosis with Myelodysplasia: A Case Report

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Background

Hemophagocytic lymphohistiocytosis (HLH) is a disease spectrum characterized by immune dysregulation causing systemic hemophagocytosis leading to severe cytopenias. The disease carries poor prognosis and patient management depends on timely diagnosis. HLH occurring in association with myelodysplasia is extremely rare. Timely diagnosis of HLH, especially when in association with myelodysplastic syndrome which itself leads to ineffective hemopoiesis, is essential for improved patient survival and outcome.

Case Presentation

Here, we describe a middle-aged female who developed rapid-onset severe anemia along with altered sensorium and generalized body swelling. The patient also had a history of 3 abortion during marriage and multiple previous episodes of severe pancytopenias requiring hospitalisation and multiple red cell concentrate transfusions.

Diagnosis

On examination, the patient was in altered sensorium and was agitated with a Glasgow coma score of 14. She had severe pallor, and generalized edema. An infero-laterally shifted cardiac apex and massive splenomegaly was noted on palpation and bilateral crepitations were noted on auscultation. Pericardial effusion was noted on ultrasound. The haemogram showed severe anemia (Hb = 2.6 g/dL) with pancytopenia. Liver function test, kidney function tests were normal whereas serum electrolytes showed mild derangement, and serum albumin was mildly reduced. Peripheral blood smear showed macrocytic anemia with polychromatophilia and pancytopenia. Neutrophils showed dysplastic changes in the form of cytoplasmic hypo-granulation, nuclear hypo-lobation, and pseudo-Pelger-Huet anomaly. Bone Marrow aspirate smear was particulate, hypercellular and showed trilineage hematopoiesis with frequent hemophagocytosis along with significant dysmyelopoiesis, significant dyserythropiesis (>30% precursors), and erythroid hyperplasia. Further workup showed elevated triglyceride levels and serum ferritin levels. Vitamin B12 and folate levels were normal. Based on these findings a diagnosis of Hemophagocytic lymphohistiocytosis (HLH) with Myelodysplastic syndrome(MDS) was made.

Treatment

The patient was managed with multiple red cell concentrate (RCC) transfusions to stabilize sever anemia and pancytopenia, which were started as soon as patient was admitted.

Follow-up

Patient expired within 24 hour of diagnosis. Follow-up was not possible.

Conclusion

This case highlights the severity and seriousness of pancytopenias in cases of HLH-MDS as a combination of both pathological processes contribute to reduced peripheral blood cell counts, and also highlights the importance of timely diagnosis and start of treatment.

Malignant Hematology-Laboratory (MHL) PP-MHL-44

Bone Marrow Involvement in Lymphomatoid Granulomatosis – Flow Cytometry Confirming This Extremely Rare Occurrence

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Background

Lymphomatoid granulomatosis is a rare Epstein-Barr virus associated B-cell lymphoproliferative disorder primarily affecting the lungs. Bone marrow involvement in extremely rare, and warrants a search for an alternate diagnosis. Here we present a bona fide case of lymphomatoid granulomatosis with morphology and flow cytometry proven bone marrow involvement.

Case Presentation

A 54-year-old lady presented with shortness of breath, intermittent low-grade fever, and productive cough. A diagnosis of granulomatous inflammation was provided on transbronchial lung biopsy. She was lost to follow-up, but returned after two months with worsening symptoms and bilateral lung consolidation. This time, a wedge biopsy was performed, which showed multiple lymphoid nodules, with presence of scattered large cells showing positivity for CD30, CD20, PAX5 and EBER-ISH, and a diagnosis of lymphomatoid granulomatosis, grade 1 was offered. EBV viral load was negative. Peripheral blood showed normal complete blood count, while the bone marrow biopsy revealed multiple interstitial as well as paratrabecular lymphoid aggregates, which were CD20 positive and CD3 negative. Flow cytometry was performed on the bone marrow aspirate, which showed 3.1% kappa restricted B-cells (CD5 and CD10 negative), confirming bone marrow infiltration by a mature B-cell neoplasm.

Diagnosis

Lymphomatoid granulomatosis grade-1, with bone marrow involvement

Treatment

In view of her poor general condition, the patient was started on R-mini-CHOP chemotherapy regimen. She showed some initial improvement and was discharged after one cycle. She was given three more cycles, but her condition slowly worsened and she started developing mouth ulcers and severe nausea. A further dose reduction was planned, but she succumbed to her illness.

Follow-up

Patient passed away after four cycles of R-mini-CHOP.

Conclusion

Although extremely uncommon, bone marrow involvement may occur in lympomatoid granulomatosis. To the best of our knowledge, this is the first case with flow cytometry- confirmed bone marrow infiltration in lymphomtoid granulomatosis. Additionally, we also highlight the poor outcome of this rare lymphoma, even with grade 1 disease

Malignant Hematology-Laboratory (MHL) PP-MHL-45

Intravascular Large B-cell Lymphoma: The Silent Intruder

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Background

Intravascular large B-cell lymphoma (IVLBCL) is a rare and aggressive extranodal lymphoma characterized by the proliferation of large malignant B-cells confined to the lumina of blood vessels. Unlike typical lymphomas, IVLBCL does not primarily involve lymph nodes and can impact almost any organ, including the central nervous system (CNS) and skin, affecting 30-40% of patients.

Case Presentation

We report a series of five patients diagnosed with IVLBCL on bone marrow biopsy at our institution over the past decade. The mean age of the patients was 54 years (range: 51-86 years). Among these patients, three (60.0%) presented with B-symptoms, one (20.0%) exhibited lymphadenopathy, and three (60.0%) had hepatosplenomegaly. One patient (20.0%) each had skin rash, pyelonephritis and altered mental status respectively. One patient had pancytopenia and all patients had thrombocytopenia. The mean hemoglobin (Hb) level was 7.9 g/dL (range:4.8-12.9), the mean total leukocyte count (TLC) was 7.3x109/L (range: 3.3-16.3 x109/L), and the mean platelet count was 51.4 x109/L (range: 15-90 x109/L). Bone marrow aspiration and biopsy was performed on all patients. Bone marrow aspirate revealed large atypical cells with cytoplasmic vacuoles ranging from 2-50% (mean-26%). Hemophagocytosis and bone marrow necrosis were seen in one patient each.

Diagnosis

Four patients underwent flow cytometry, which revealed a CD5-positive mature B-cell neoplasm with kappa restriction. Immunohistochemistry (IHC) for CD20 was performed on all the cases and it highlighted the presence of CD20-positive abnormal B-lymphoid cells within the lumina of blood vessels.

Treatment

One patient is surviving and has received 6 cycles of R-CHOP regimen.

Follow-up

Three patients died within a year after diagnosis. One patient is surviving and has received 6 cycles of R-CHOP regimen, following which his MRD (measurable residual disease) is nil.

Conclusion

IVLBCL is a rare neoplasm with a notably poor prognosis. The morphology of the atypical cells along with their localization on biopsy and the characteristic immunophenotype helps in early detection.

Malignant Hematology-Laboratory (MHL) PP-MHL-46

Tp53 Deletion Should Be Suspected in B Lineage Acute Lymphoblastic Leukemia with Hypodiploid/near-triploid Clones by Flow Cytometric Ploidy Analysis: Insights from a Case Series of Cases

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Introduction

TP53 deletions in B-cell Acute Lymphoblastic Leukemia (B-ALL) are rare but associated with aggressive disease and treatment resistance. This case series presents five patients with TP53-deleted B-ALL

Aims & Objectives

The aim of this study is to conduct a retrospective analysis of five B-ALL patients with FISH-confirmed TP53 deletions, focusing on their clinical presentations, cytogenetic profiles, and treatment outcomes

Materials & Methods

Retrospective analysis of five B-ALL patients with FISH-confirmed TP53 deletions, reviewing clinical presentations, cytogenetics, and outcomes

Result

The cohort (2 males, 3 females) had a median age of 23 years (range: 16-54). Median leukocyte count was 10.5 x 10^9/L (range: 3.8-98.7 x 10^9/L) with median bone marrow blast count of 90% (76-91%). DNA index analysis revealed diverse ploidy patterns: one case showed high hypodiploidy (0.95), another exhibited diploidy (1.03). A third case presented a major diploid population (0.98) with a near-triploid population (1.57). The fourth case displayed 15% low hypodiploid blasts (DI 0.86) and 85% near-triploid blasts (DI 1.45), suggesting possible endoreduplication. The final case showed 30% near-triploid (DI 1.6) and 70% high hypodiploid (DI 0.95) populations. Three of 5 cases showed near-triploid populations. One case exhibited IGH::CRLF2 rearrangement. All cases were CD10 positive except one with partial positivity.

Conclusion

Three patients expired with a median overall survival of only 11 months and two patients are alive including one case who relapsed after CAR-T therapy. Our series highlights the aggressive nature of TP53-deleted B-ALL. A suspicion of TP53-deletion is required in patients with hypodiploid or near-triploid clones and underscores the need for advanced therapeutic approaches.

Malignant Hematology-Laboratory (MHL) PP-MHL-47

Myelodysplasia-related Acute Myeloid Leukaemia as Per the Who-haem5 Classification: A Tertiary Care Centre Experience

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Introduction

Myelodysplasia-related acute myeloid leukaemia (AML-MR) is a distinct entity characterized by specific cytogenetic and molecular abnormalities associated with myelodysplastic neoplasm. We aimed to analyse the cytogenetic and molecular profile of AML-MR patients at our centre.

Aims & Objectives

To determine the frequency and spectrum of cytogenetic and molecular abnormalities in AML-MR patients.

Materials & Methods

A retrospective analysis of 272 AML patients diagnosed between April 2018 and April 2024 was conducted. 38 AML-MR patients diagnosed as per WHO-HAEM5 were included in the study. Karyotyping and NGS-based molecular studies (Myeloid Panel by NGS) data were collected.

Result

38 patients with the age range of 17 to 87 years with Slight male preponderance was seen. Complex karyotype was the most common cytogenetic abnormality, observed in 42% (16/38) cases. Monosomy 7 and del(5q) were frequent findings occurring in combination with other abnormalities in 50% and 23 cases respectively. Isolated monosomy 7 18.4% (7/38) and Isolated deletion 7q in 13.1% (5/38). Three cases had a normal karyotype (7.8%). Molecular analysis by NGS identified NPM1 mutations in 2 cases, TP53 in 3 cases, ASXL1 in 2 cases, and mutations in SRSF2, BCOR, and U2AF1 in one case each. Three cases were classified as AML-MR based solely on molecular findings.

Conclusion

Incidence of WHO HAEM5-defined AML-MR was 13.9% in our study with cytogenetic abnormalities identified in 92 cases. Complex karyotype was the most common abnormality followed by monosomy 7 and del 5q. TP53 was the single most common molecular mutation. Our study demonstrates the heterogeneous cytogenetic and molecular landscape of AML-MR. The combination of cytogenetic and molecular analyses is crucial for accurate diagnosis of AML-MR patients.

Malignant Hematology-Laboratory (MHL) PP-MHL-48

Splenic Infarction in the wake of Acute Promyelocytic Leukemia

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Background

Splenic infarction occurs due to the blockage of splenic vessels, leading to tissue ischemia and necrosis. While uncommon, it has been reported in patients with acute myelogenous leukemia (AML). This case report presents a rare instance of acute promyelocytic leukemia (APL) (AML-M3) manifesting with splenic infarction.

Case Presentation

A previously healthy 35-year-old man developed abdominal pain and dizziness following hemia surgery. Physical examination revealed pallor, and splenomegaly. Laboratory results showed a WBC count of 54× 10^9/L, hemoglobin of 7 g/dl, platelet count of 16×10^9/L, LDH at 3300 IU/L, prolonged PT, elevated INR, and D-dimer >2000 ng/mL... Bone marrow biopsy confirmed APL (AML-M3) with over 95% abnormal promyelocytes. Flow cytometry indicated blasts positive for CD33, CD117, and negative for HLA-DR, while molecular testing confirmed PML-RARA positivity. Imaging (ultrasound and CT) revealed splenic infarction and splenomegaly.

Diagnosis

Imaging studies showed peripheral hypodensity and lack of contrast enhancement in the spleen, confirming splenic infarction. API. was confirmed through bone marrow biopsy and flow cytometry.

Treatment

Chemotherapy was initiated with daunorubicin, all-trans retinoic acid (ATRA), and arsenic trioxide, along with supportive care including fresh frozen plasma (FIP) and platelet transfusions. Despite the recommendation for a splenectomy on day 28 post-remission, it was not performed due to thrombocytopenia.

Follow-up

The patient was monitored with regular imaging, showing persistent splenic lesions. Thrombocytopenia continued to prevent splenectomy, and supportive care was ongoing with close follow-up.

Conclusion

This case underscores the difficulty in managing splenic infarction in APL. patients, where thrombotic complications and disseminated intravascular coagulation play a critical role. Careful monitoring and individualized treatment are vital, along with regular follow-up to manage complications and reduce the risk of relapse.

Malignant Hematology-Laboratory (MHL) PP-MHL-49

PRCA, AIHA and Paraneoplastic Cranial Nerve Palsy: A Unique Presentation of Angioimmunoblastic T-cell Lymphoma

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Background

Angioimmunoblastic T-cell lymphoma (AITL, currently called Nodal T follicular helper cell lymphoma, angioimmunoblastic type), is a commonly under/mis-diagnosed form of T-cell lymphoma, especially because it shows a wide range of presenting features.

Case Presentation

A 56 years gentleman presented with diplopia, facial deviation to one side and inability to close the left eye, suggestive of cranial nerve palsies. However, the CE-MRI and CSF work-up was normal. His CBC showed bicytopenia (Hb – 55g/L, platelets – 20 x109/L) with leucocytosis (TLC – 18.63 x109/L). Direct Coombs test was positive (anti-IgG 3+), but the reticulocyte count was low (absolute reticulocyte count – 7.1 x109/L). Peripheral blood smear showed 4% circulating plasma cells. Bone marrow examination was done, and the aspirate revealed 22% plasma cells and marked erythroblastopenia (1% erythroid precursors). The bone marrow biopsy was hypercellular, with an interstitial increase in plasma cells and lymphocytes. There was an increase in eosinophils, and vascular prominence. On flow cytometry, the plasma cells were found to be polyclonal, but 35% of the T-cells showed downregulation of CD3 and CD7, CD4positive/CD8 negative profile, and expression of CD10 and CD279 (PD-1). Possibility of marrow infiltration by AITL was suggested. Clinical examination and radiological examination revealed hepatosplenomegaly along with bilateral cervical and inguinal lymphadenopathy. FNAC from lymph nodes showed atypical cells in a polymorphous background, suggesting lymphoma. Flow cytometry was done from the FNA, and showed a similar population of abnormal T-cells as seen in bone marrow aspirate.

Diagnosis

Nodal T follicular helper cell lymphoma, angioimmunoblastic type, stage 4, with autoimmune hemolytic anemia, pure red cell aplasia and paraneoplastic cranial nerve palsies.

Treatment

Patient was initially given IVIg. Once diagnosis of AITL was established, he was given prephase chemotherapy to which there was an initial response, and was followed by 3 cycles of CHOP. Cyclosporine was added for PRCA.

Follow-up

His condition deteriorated rapidly after 3 cycles of CHOP, and he succumbed to refractory septic shock.

Conclusion

Diagnosing AITL is challenging due to its myriad presenting features, with flowcytometry playing an important role. PRCA and AIHA may occur simultaneously in AITL. Managing such patients is very tricky, with high risk of mortality.

Malignant Hematology-Laboratory (MHL) PP-MHL-50

Challenges in treatment of a rare association of Angioimmunoblastic T cell Lymphoma and Autoimmune haemolytic anaemia

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Background

Angioimmunoblastic T-cell lymphoma (AITL) is an aggressive form of T-cell lymphoma characterized by a complex interplay of immune dysregulation and neoplastic transformation. It typically presents in older adults and is rarely associated with autoimmune diseases and Epstein-Barr virus infection.

Case Presentation

44 yr old male presented with complains of low grade fever, which was insidious in onset, intermittent nature, and generalized weakness and easy fatiguability since 2 months. On examination, he had severe pallor, icterus. Patient also had generalised lymphadenopathy with firm, rounded, discrete, non-tender and non-matted lymph nodes and Enlarged bilateral parotid and mandibular gland with no hepatosplenomegaly.

Diagnosis

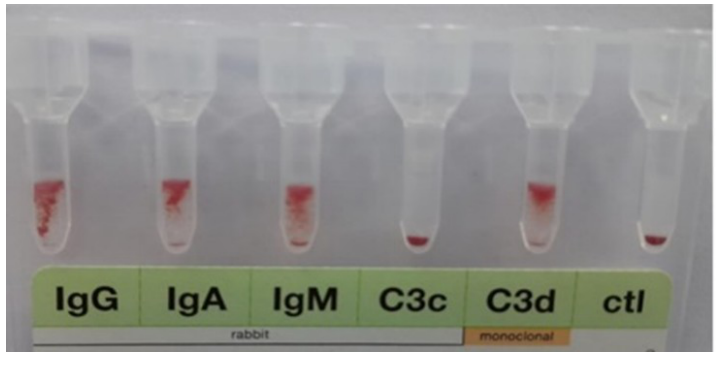
His hemogram revealed Haemoglobin of 6.6 gm/dL and on peripheral smear nucleated RBCs, polychromatophils, spherocytes, rouleaux formation with 2% corrected reticulocyte count were detected. With Indirect hyperbilirubinemia and LDH of 798 U/L; DCT showed grade 4 positivity and monospecific DAT was positive for IgG, IgM, C3d and IgA altogether suggestive of a mixed AIHA. Protein Electrophoresis showed polyclonal hypergammaglobulinemia. Bone marrow smear and biopsy showed hypercellular marrow with erythroid hyperplasia without any infiltration by atypical lymphoid cells suggestive of autoimmune haemolytic anaemia(AIHA) Excisional lymph node biopsy and Immunohistochemistry demonstrated CD45/3/5/10/30/EMA positivity, in scattered large cells with CD4>CD8. CD20 was Positive (Membranous) in background B cells. CD21 & 23 were positive, and highlight expanded and distorted follicular dendritic cell meshwork. ALK was negative and Ki67 was 20-30%, altogether favouring Angioimmunoblastic T- cell lymphoma with secondary AIHA.

Treatment

Despite a T-cell Neoplasm, Rituximab is considered in some centres with limited data based on B cell infiltration in background. He is currently post third cycle of CHOP chemotherapy regimen and his constitutional symptoms have resolved and bulk of lymphadenopathy has been reduced, but his haemoglobin persists to be around 5.5 gm/dL. So weekly Rituximab has been added to CHOP to target AIHA causing B cell clone.

Conclusion

AITL remains a challenging diagnosis due to its clinical presentation and histological similarities to other lymphoproliferative disorders. Early diagnosis and a tailored treatment approach can significantly improve outcomes. We need to tease out outcomes in AITL with secondary AIHA with RCHOP based therapy.



Poster Presentations (PP) Benign Hematology-Clinical (BHC) PP-BHC-1

Sideroblastic Anemia - The Mystery of Blue Granules

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Background

Sideroblastic anemia is a heterogeneous group of disorders with abnormal accumulation of iron in the mitochondria of erythroid precursors and presence of ring sideroblasts in the bone marrow. The frequency of acquired sideroblastic anemia far exceeds that of the hereditary varieties. Drugs and toxins lead this category, propelled largely by the high frequency of alcohol abuse in many societies . Here we present a case of drug induced acquired sideroblastic anemia to highlight the associated diagnostic difficulties.

Case Presentation

21 year old male, newly diagnosed retroviral disease and on anti -retroviral therapy (TDL –Tanofovir/Dolutegravir/Lanuvudine regimen) for last 3 months presented with generalised weakness for 15 days and vomiting for 4 days. Laboratory evaluation revealed Hb value of 5.8 gm/dL & RBC count of 2.11x106/µL with normal Total leucocyte count and Platelet count, normal CD4 and CD8 counts and negative HIV viral load. Reticulocyte count was 1.74%. Bone marrow examination showed normocellular marrow with mild dyspoesis in all the 3 lineages and increase in iron stores with presence of ring sideroblasts (37%). Serum ferritin level was mildly elevated (574 ng/ml),Serum vitamin B12 and folate levels were normal. Cytogenetics to rule out Myelodysplastic Syndrome was advised.

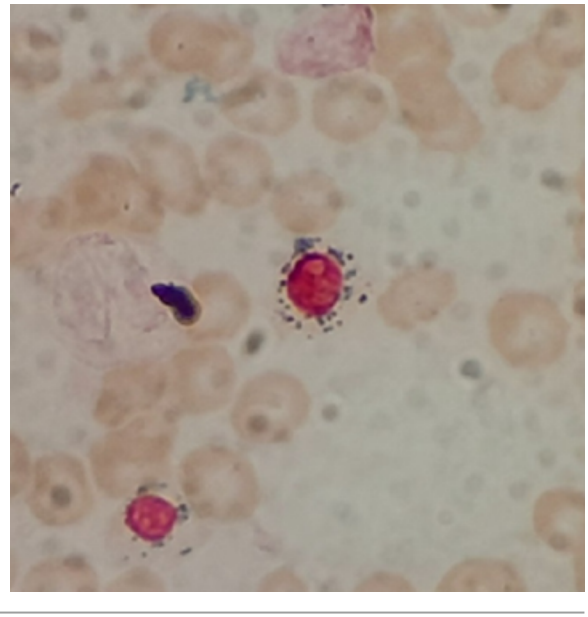
Diagnosis

Drug (Dolutegravir) induced Sideroblastic anemia .Literature mentions a case report of Dolutegravir induced acquired sideroblastic anemia in a case of HIV positive patient where the Hb value improved drastically after replacing Dolutegravir with Raltegravir.

Myelodysplatic Syndrome needs to be ruled out by molecular studies and follow up counts .

Treatment

The patient's family denied further investigations and treatment due to financial constraints. Patient was lost for follow up.



Follow-up

NA

Conclusion

Dolutegravir is a new antiretroviral drug with effective virologic suppression, good tolerability and infrequent drug–drug interactions, but patient may develop rare side effect like sideroblastic anemia. Anemia can be multifactorial in a HIV patient but clinicians must be aware of the potential for drug induced sideroblastic anemia as removal of the offending agent becomes the first step of management.

Benign Hematology-Clinical (BHC) PP-BHC-2

Understanding the Epigenetic Blueprint of Venous Thrombosis: Pathways to Future Therapeutics

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Introduction

Venous Thromboembolism (VTE) is shaped by a confluence of genetic, environmental, and epigenetic determinants. Epigenetic processes, encompassing non-coding RNAs, DNA methylation and histone modifications, present promising opportunities for the advancement of diagnostic methodologies and therapeutic interventions. In the context of the emergence of precision medicine, the strategic targeting of the epigenome has become essential for the effective management of multifaceted diseases such as VTE through its impact on gene expression and therapeutic efficacy.

Aims & Objectives

This study intends to examine the epigenetic framework of VTE, focusing on the significance of microRNAs (miRNAs) and mutations in DNA methyltransferases (DNMTs). The objective was to identify potential biomarkers that could formulate early diagnosis and therapeutic approaches for the management of VTE.

Materials & Methods

We undertook a meta-analysis in accordance with PRISMA guidelines to evaluate the influence of microRNAs in the etiology of venous thromboembolism (VTE). Relevant studies were discerned based on stringent inclusion and exclusion criteria. With regard to DNA methylation, experiments are underway to conduct genotyping of DNMT mutations through the application of real-time polymerase chain reaction (RT-PCR). This approach specifically targets single nucleotide polymorphisms (SNPs) through allelic discrimination assay to elucidate the relationship between DNMT mutations and the susceptibility to VTE.

Result

The meta-analysis identified three microRNAs—hsa-miR-1233-3p, hsa-miR-103a-3p, and hsa-miR-200c—that may be integral to the pathogenesis of VTE. These microRNAs exhibit considerable promise to serve as robust diagnostic or therapeutic biomarkers for VTE. The current SNP genotyping of DNMT mutations will provide findings that will subsequently undergo analysis to establish their relevance concerning DNA methylation and susceptibility to VTE.

Conclusion

This on-going investigation underscores the critical role of epigenetic determinants, specifically microRNAs (miRNAs) and DNA methyltransferase (DNMT) mutations, in the pathophysiology of VTE. The identified miRNAs indicate their considerable potential for both diagnostic and therapeutic applications. Findings on DNMT mutations will further elucidate the role of DNA methylation in VTE susceptibility. These insights contribute to the evolving landscape of precision medicine, where epigenetic targeting may lead to more effective, personalized interventions for VTE management.

Benign Hematology-Clinical (BHC) PP-BHC-3

CE Population Data from Automated Hematology Analyzers: Does it End Our Search for the 'ideal Biomarker' for Sepsis?

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Introduction

Sepsis remains a leading cause of morbidity and mortality among critically ill patients, despite significant advancements in understanding its complex pathophysiology. Cell Population Data (CPD), derived from parameters such as fluorescence, cell size, and internal complexity of leukocytes using next-generation automated cell counters, has emerged as a potential diagnostic tool for sepsis.

Aims & Objectives

This study aimed to assess the diagnostic utility of CPD and its association with the Sequential Organ Failure Assessment (SOFA) score and serum procalcitonin levels in sepsis patients.

Materials & Methods

This is a cross-sectional study carried out in the intensive care unit of a tertiary care center over a period of six months from October 2023 to March 2024. All consecutive patients > 18 years of age diagnosed with sepsis as per Sepsis -3 guidelines were included in this study. Patients with severe renal or liver disease, hematological or advanced solid malignancies and patients on myelosuppressive agents, chemotherapy or steroids, neutropenia and autoimmune diseases were excluded from the study. Specimens were run for complete blood counts including cell population data on Sysmex XN 1000 hematology analyzer, serum procalcitonin levels assayed and SOFA score calculated on day 1 of admission apart from routine hematological and biochemical investigations. Univariate and multivariate analyses were conducted on CPD dataset, with Receiver Operating Characteristic (ROC) curves used to determine sensitivity and specificity. Spearman's rank correlation was used to assess the correlation of CPD parameters with SOFA score and serum procalcitonin levels.

Result

A total of 72 patients with sepsis and specimens from 72 controls were evaluated. CPD parameters such as HFLC%, NE-WY, IG%, NE-SSC, MO-WZ, MO-X, MO-WY, LY-X, and LY-Z were significantly elevated in sepsis patients. Orthogonal Partial Least-Squares Discriminant Analysis (O-PLSDA) identified MO-X, MO-WY, LY-X, and LY-Z as key discriminators for sepsis. MO-X showed a sensitivity of 95.83% and a specificity of 73.61%, while IG% had a sensitivity of 83.3% and specificity of 80.5%. Positive correlations were observed between procalcitonin and MO-X, as well as between LY-X, LY-Z, MO-X, and the SOFA score.

Conclusion

CPD is a promising, cost-effective biomarker for diagnosis of sepsis. Its correlation with SOFA score and procalcitonin suggests its potential role in assessing severity of sepsis and guiding clinical management.

Benign Hematology-Clinical (BHC) PP-BHC-4

Quality Analysis of Haematological Parameters of Whole Blood, Packed Red Blood Cells and Platelet Concentrate: A Study from a Tertiary Care Hospital

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Introduction

The ultimate goal of blood transfusion services is to provide whole blood and blood components that are safe, efficacious and potent to the recipients. Building blocks of quality include- quality control, quality assurance and quality audit. Quality control is a process by which product standards are established and met without mistake.

Aims & Objectives

To establish the quality of standards of haematological parameters of whole blood, Packed Red Blood Cells (PRBCs) and platelet concentrate in a blood bank of tertiary care with reference to standard guidelines was prepared and were tested for haematological parameters of quality control for the period of 1stJanuary 2023 to 31st December 2023.

Materials & Methods

This was a retrospective study of 6004 samples in which 2.08 % of total whole blood collection (48/2306), 1.29 % of PRBCs (48/3698), and 5.8 % of platelet concentrate (48/826) was analysed.

Result

The quality analysis of haematological parameters for whole blood, PRBCs and platelet concentrate were done. All the whole blood and PRBCs samples tested had hematocrit above 30% and 65% respectively. 94 % platelet concentrate samples yield of >3.5×1010/U and WBC and RBC contamination was well within the normal range.

Conclusion

Continuous quality improvement is of utmost importance for safe and potent blood transfusion services. Thus, care should be taken to use standard criteria for quality assessment and adherence to standard values should be periodically ensured by objective analysis.

Benign Hematology-Clinical (BHC) PP-BHC-5

Prevalence of ABO Rh Blood Group Among Donors

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Paras HMRI Hospital, Patna

Introduction

Distribution pattern of Blood Group at our centre

Aims & Objectives

To study prevalence of blood groups

Materials & Methods

Retrospective data collection

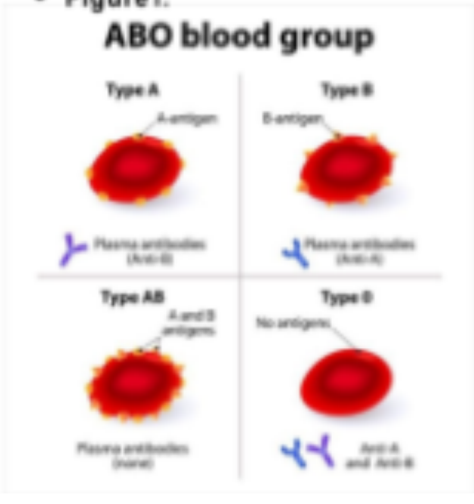
Result

Most prevalent blood group among donors is B+

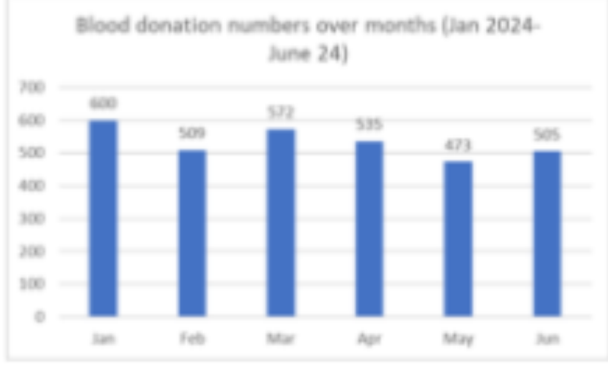
Conclusion

Blood group prevalence differs in different regions. Availability pattern can help in finding donors.

- **Figure1:**



- **Figure2:**



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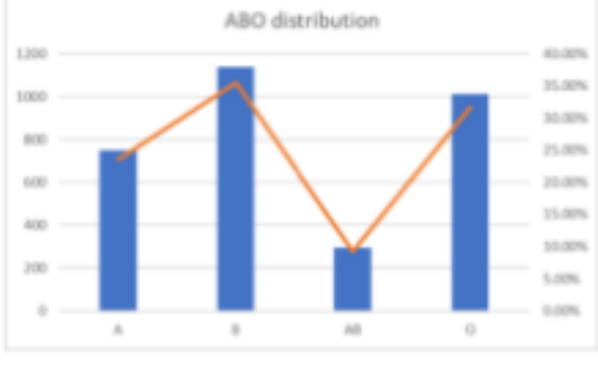
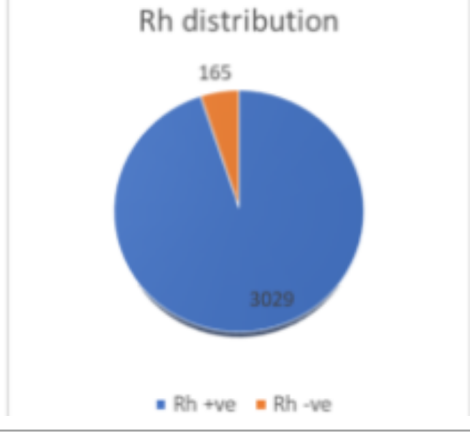


- **Figure4:**



Benign Hematology-Clinical (BHC) PP-BHC-6

Single Dose Dexamethasone with Tab Netupitant and Tab Palonosetron for CINV Prophylaxis in Multiday Highly Emetogenic Chemotherapy Regimens for Lymphoma Patients

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Introduction

RCHOP and ABVD regimen are Highly Emetogenic multiday Chemotherapy regimens for treatment of cHL (Classical Hodgkin Lymphoma) and NHL (Non-Hodgkin lymphoma) respectively.

Aims & Objectives

This study investigates the efficacy of Generic Netupitant and Palonosetron tablets with Dexamethasone single dose (dexamethasone-sparing antiemetic regimen) for the prophylaxis of chemotherapy-induced nausea and vomiting (CINV) in lymphoma patients receiving multiday Chemotherapy.

Materials & Methods

This multicentre, retrospective study evaluates the data of 129 patients who received HEC (RCHOP or ABVD regimen) and were administered Generic Netupitant 300 mg, Palonosetron 0.5 mg tablets (Nykron combi-pack) with a single dose of 8 mg/12mg dexamethasone, prior one hour chemotherapy on Day 1 of multi day chemotherapy for every cycle. The data was collected from September 2022 till September 2023. Outcomes measures included complete response (no vomiting and no need for rescue medications), complete protection (no significant nausea (<2.5 cm on VAS), no vomiting, and no use of rescue medication) and complete control [no emetic episodes, no rescue therapy, and no nausea (0 cm on VAS)] during the acute phase (0-24 hours) & delayed phase (24-120 hours) post-chemotherapy.

Result

The data of 129 patients were evaluated in which 75 NHL patients with mean age 44.05 years, received highly emetogenic chemotherapy R-CHOP, a chemotherapy regimen consisting of rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone. While remaining 54 Hodgkin's Lymphoma patients with mean age 33.18 years received high emetogenic ABVD (doxorubicin, bleomycin, vinblastine, dacarbazine) chemotherapy. The Dexamethasone-sparing regimen with Tablet Netupitant & Palonosetron demonstrated good efficacy with 100% complete response rate & complete protection rate across all cycles. Few patients did present with mild nausea (VAS nausea scale score <3) hence complete control varies between 53 - 65%. (Fig. 1.)

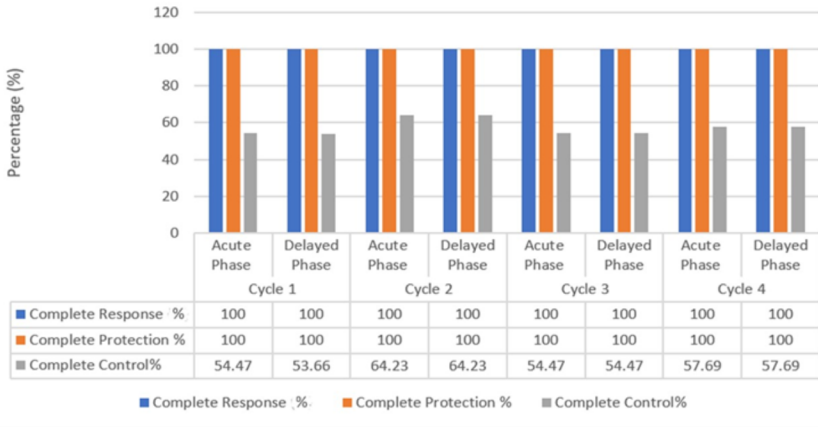

Figure 1: Complete Response (CR), Complete Protection (CP) & Complete Control (CC) of Dexamethasone sparing CINV prophylaxis regimen for Highly chemotherapy Regimens

Conclusion

Dexamethasone-sparing NEPA regimen was highly effective for preventing nausea and vomiting in difficult setting of multiday chemotherapy regimens (ABVD and RCHOP) for Lymphoma patients.

Benign Hematology-Clinical (BHC) PP-BHC-7

Eltrombopag in Chronic ITP with Hepatic Venous Outflow Obstruction

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Background

Case Report

Case Presentation

22 years old male a k/c/o chronic ITP on eltrombopag with complaints of abdominal discomfort, weakness and nausea.

Diagnosis

Hepatic venous outflow obstruction

Treatment

Conservative management

Follow-up

Went referral

Conclusion

To be cautious while prescribing eltrombopag suspecting rare side effects.

Lab investigations	
Bilirubin direct	4mg %
Bilirubin total	5.9 mg%
Bilirubin indirect	1.9 mg%
SGOT	6837U/L
SGPT	1939U/L
PT	62 sec
Urea	70mg%

Benign Hematology-Clinical (BHC) PP-BHC-8

Evans Syndrome: A case study

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Background

Case Study

Case Presentation

3 years old female presented with complaints of exchymotic rashes and sub conjunctival haemorrhage.

Diagnosis

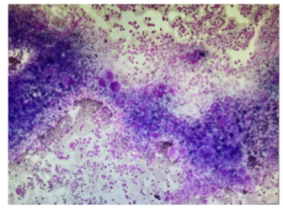
Evan's syndrome

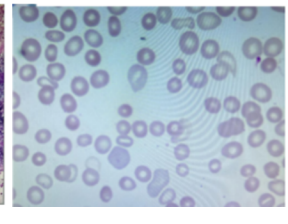
Treatment

Steroid+Romiplostim+Rituximab

Follow-up

Lost patient due to respiratory distress.





Conclusion

Evan's syndrome treatment mostly requires more than single line of treatment and long treatment has also various risk associated.

Benign Hematology-Clinical (BHC) PP-BHC-9

Clinical Spectrum of Rare Coagulation Factor Deficiency

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Introduction

The term 'Rare Coagulation Factor Deficiency' represents 3 to 5% of all factor deficiency and refers to disorder of Thrombin and fibrin formation which includes Factor I, II, V, VII, X, XI, XII, and XIII deficiency. Most of these conditions are inherited as Autosomal recessive, so explain the rarity of these disorder.

Aims & Objectives

Our aim is to study the prevalence, spectrum of rare bleeding disorder (RBDs), characterize the severity of deficiency, severity of clinical manifestations and to relate them with factor level.

Materials & Methods

This is retrospective analysis conducted in the Department of Hematology, sahayadri superspeciality Hospitals and Laboratory, Pune from year 2000 to September 2024. A detailed history, sign and symptoms were noted and diagnosis on the basis of coagulation profile done. The disease Severity assessed by using factor assays. Clinical bleeding episodes were classified into four categories according to severity.

Result

Data of total 48 patients with RBDs were retrieved.The means age of patients was 32.2 yrs (range from 1 day to 75 yr) with 6.25% aged <1 yr and 2.08% >70 year. Female represents 53.17% (26 participants), this indicates relative balanced gender ratio with slight female predominance. The most common deficiency was Factor VII (29.17%,11 patient)and Factor XII (22.92%,11 patient) followed by Factor V,XIII ,IX and fibrinogen. Only 2 case of combined factor deficiency with one case revealing LMAN1 mutation. Most common symptoms include bruising and muscle haematoma (20.83%,10 participants each) followed by menorrhagia in females and post surgical bleed. Also there was strong association between factor level and bleeding severity for Fibrinogen and Factor XIII and weak for V, VII, X and XI

Conclusion

Factor VII deficiency was the most prevalent deficiency identified. There is variable association between coagulation factor level and clinical bleeding Severity in different RBDs with strong association observed only in Fibrinogen and FXIII deficiency.

Benign Hematology-Clinical (BHC) PP-BHC-10

Surveillance of Hemoglobin Variants in Routine Antenatal Screening, A Single Center Experience: Information for an Informed Decision

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Introduction

The hemoglobinopathies are genetic disorders which are common worldwide with variation in different regions of the world and classified into two main groups of thalassemia syndromes and structural haemoglobin variants.7% of the entire world population is carrier for various haemoglobin variants. Antenatal screening of primigravida women, is hence important to detect pregnancies posing a high risk of clinically significant hemoglobinopathy in the foetus.

Aims & Objectives

To study the spectrum of hemoglobinopathies during routine antenatal screening at a tertiary care centre in North India

Materials & Methods

A retrospective analysis was performed of high-performance liquid chromatography (HPLC) values of women and their partners who underwent antenatal hemoglobinopathy screening over a period of two years at our institute.

Result

Out of the total 3552 patients who were routinely screened,128 women had a haemoglobin variant detected on HPLC. Spouse screening was advised in all these women which revealed,10 of them to be positive for a hemoglobinopathy. The majority of them (74.63%) were offered a diagnosis of beta thalassemia trait, followed by HbD Punjab (12.3%). Other variants detected included Hb E trait (6.5%) delta beta-thalassaemia trait (3.6%) sickle cell trait(2.1%),HbJ and HbQ.

Conclusion

Hemoglobinopathies pose a major burden to the public healthcare system in India and robust antenatal screening of women helps in early detection of such high-risk pregnancies, so that they are provided with timely genetic counselling and necessary intervention. However, widespread implementation of such screening is tough and other ways need to be explored to identify at-risk pregnancies at an early stage.

Benign Hematology-Clinical (BHC) PP-BHC-11

Assessment of the Cost and Apheresis Time Associated with Mobilization Approach for Lymphoma Patients Undergoing Autologous Stem Cell Transplantation

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Introduction

Apheresis centres aim higher CD34+ cell yields for BMT in lymphoid malignancies as products are cryo-preserved. Apheresis and cryopreservation significantly contributes to the overall costs, which can escalate further in the event of mobilization failure or inadequate yields.

Aims & Objectives

The objectives were to

1. Estimate the frequency of patients requiring plerixafor and second apheresis at our centre.
2. To estimate the cost and apheresis time involved.
3. To determine peripheral blood CD34 cut off for optimal CD34 yield and to determine a model for optimal cost and apheresis time at our setting.

Materials & Methods

Retrospective cross-sectional study on patients underwent stem cell apheresis and cryopreservation. Optimal CD34 yield defined as >3×106 CD34+cells/kg in single apheresis collection. Inclusion: Patients mobilized with G-CSF for 5 days. G-CSF+ Plerixafor (P) administered when Day-5 Peripheral Blood (PB) CD34 <20/µL or Apheresis Yield <3x106/kg. Exclusions: Mobilization failure and patients with interruptions between collection sessions. Mobilization costs (G-CSF, Plerixafor), daily apheresis, cryopreservation and flow cytometry expenses based on institution rates were added for estimating patient's total costs.

Result

Out of 49 patients, three had mobilization failure and excluded from analysis. 30 patients received only G-CSF before apheresis and 16 (35%) patients' utilized plerixafor. Table 1 shows distribution and cost estimation. 15 (32%) patients underwent two apheresis sessions (4 with G-CSF alone on D6 and 11 patients with G-CSF + P on D6.) With ROC, PB CD34 count >52 cells/µl predicted yield >3x10^6/kg with adequate sensitivity of 72% and higher specificity 86%. Cost and apheresis time was better in patients with low CD34 counts on D5 underwent first apheresis on D6 after G-CSF+P.

Variables	Unit	G-CSF (n=30)		G-CSF+P (n=16)	
		One Apheresis	Two Apheresis	One Apheresis	Two Apheresis
Number	N	26	4	5	11
Mobilization Regime D5		5d x G-CSF	5d x G-CSF	5d x G-CSF	5d x G-CSF
D5 CD34 Count (Median)	Cells/µl	84	45	9	34
D5 Apheresis yield (Median)	x10^6/kg	6.4	2.8	No collection	2.6
Mobilization Regime D6		Not applicable	6d x G-CSF	6d x G-CSF +P	6d x G-CSF + P
D6 CD34 Count (Median)	Cells/µl	Not applicable	40	17	56
D6 Apheresis yield (Median)	x10^6/kg	Not applicable	2.8	3.0	4.9
G-CSF Doses (INR160/dose)	No	9	11	11	11
Plerixafor Doses (INR17000/dose)	No	0	0	1	1
Apheresis (INR15000/session)	No	1	2	1	2
Cryopreserved (INR 10000/bag)	Bag	3	6	3	6
Flow CD34 on Peripheral Blood	No	1	2	2	2
Flow CD34 on Apheresis Product	No	1	2	1	2
Cost Involved	INR	57,440	113,760	79,760	130,760

Conclusion

One third of patients required plerixafor and two apheresis session in our setting. Deferring apheresis for patients with a D5 PB CD34 count <52 cells/µl and performing single apheresis on D6 with the G-CSF +P regimen may help reduce overall costs related to stem cell apheresis and cryopreservation in lymphoma patients.

Benign Hematology-Clinical (BHC) PP-BHC-12

Immune Hemolytic Anemia as Paraneoplastic Syndrome in Hodgkin's Lymphoma

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Background

Autoimmune hemolytic anemias (AIHA) are usually associated with non-Hodgkins lymphoma but rarely with Hodgkin's lymphoma (HL). The initial clinicoradiological presentation as disseminated tuberculosis with AIHA can further complicate the diagnosis of HL as both Disseminated TB and HL are very close clinical mimickers and even have known associations with AIHA. Moreover, predominantly necrotic lymph nodes in rare cases of HL can further delay the diagnosis.

Case Presentation

A 42- year- old male presented with a history of on and off fever, cough with expectoration from last 4 months, also shortness of breath and jaundice from 15 days. He was transfused with 6 units of blood but was still anaemic. Multiple necrotic bilateral cervical and axillary lymph nodes were noted on ultrasound which on FNAC showed only lymphocytes and histiocytes in a necrotic background. Acid fast bacilli could not be demonstrated on smear or CBNAAT. The ultrasound and CECT of liver and spleen showed multiple heteroechoic lesions suspicious of granulomas. A clinicoradiological diagnosis of disseminated tuberculosis was made.

We received post transfusion blood for hematological examination which revealed severe normocytic normochromic anemia (hemoglobin -5.2gm/dl) and spherocytes on peripheral smear. The reticulocyte count was 1.92. There was indirect hyperbilirubinemia and the Direct Coombs test was positive. Given the rapid fall in hemoglonbin, DCT positivity, and indirect hyperbilirubinemia possibility of immune hemolytic anemia was suggested. Simultaneously, a third time FNAC was attempted which revealed some large atypical cells with prominent nucleoli, granulomas in a necrotic background. Subsequent biopsy from the lymph node showed histopathological features suggestive of Hodgkins lymphoma, mixed cellularity. The tumor cells were CD15 and CD30 positive.

Diagnosis

Hodgkin's lymphoma, lymph node biopsy with autoimmune hemolytic anemia

Treatment

The patient was empirically started on ATT, however, no symptomatic relief noted. The patient expired before receiving HL treatment.

Follow-up

follow up could not be done as patient expired.

Conclusion

This case highlights the diagnostic dilemma posed in diagnosing hodgkins lymphoma due to concurrent immune hemolytic anemia and clinicoradiological overlap with disseminated tuberculosis leding to a fatal outcome. So, AIHA should be considered as a paraneoplastic condition hence prompt and thorough search for underlying cause should be made.

Benign Hematology-Clinical (BHC) PP-BHC-13

Iron Overload Associated Myelodysplasia Like Bone Marrow Changes in Cytopenic Beta Thalassemia Major

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Introduction

Beta thalassemia major (BTM) is a transfusion dependant anemia (TDA) characterized by severe hemolysis, hepatosplenomegaly and increased risk of long-term complications such as iron overload associated organ dysfunction, infections, and growth abnormalities. Bone marrow (BM) examination is rarely indicated in such subjects to rule out hypersplenism.

Aims & Objectives

To describe the clinico-hematological characteristics of a series of adult cytopenic subjects with TD-BTM

Materials & Methods

Clinicohematological and iron overload associated BM morphological changes of five adult subjects with TD-BTM is presented.

Result

The cases included are five males (18 to 31 years) who presented with TDA on irregular iron chelation therapy. Complete blood count showed pancytopenia with prominent target and tear drop cells along with hepatosplenomegaly. Two had cardiac manifestations in the form of cardiomyopathy with co-existent pericardial effusion, two had stunted growth, and one had neurological manifestation in the form of status epilepticus secondary to brain abscess in association with hepatic abscess. BM aspirate and trephine biopsy, performed to evaluate hypersplenism, showed scantly particulate and difficult aspirate in four along with variable cellularity (40-90%) with erythroid prominence, prominent dyserythropoiesis in the form of megaloblast like changes, nuclear budding, irregular outline, and abnormal chromatin. Myelopoiesis was suppressed with prominent dysplastic (pseudo Pelger-Huet like) neutrophils. Megakaryocytes showed significant myelodysplasia like morphology in the form of micromegakaryocytes, nuclear hypolobation, and abnormal chromatin. Reticulin stain revealed MF Grade 1/2 fibrosis (WHO), and Perls stain performed, both on BMA and BMBx, revealed extensive hemosiderosis (6+) with nodular aggregates of hemosiderin laden macrophages. Marrow morphological changes called for aggressive iron chelation therapy.

Conclusion

Bone marrow examination needs to be considered to rule out the possibility of iron overload associated secondary myelodysplasia among adult TD-BTM subjects who present with persistent cytopenia (s) for monitoring of iron chelation therapy.

Benign Hematology-Clinical (BHC) PP-BHC-14

Drug Utilization Study of Generic Eltrombopag in Immune Thrombocytopenia Patients

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Introduction

Immune thrombocytopenia (ITP) is an autoimmune disorder characterized by a decrease in circulating platelets due to spleen destruction and the inability of megakaryocytes to restore normal counts. The first line of treatment involves immunosuppressive therapy with glucocorticoid drugs. Eltrombopag, a thrombopoietin receptor agonist, has been widely used to manage ITP by stimulating platelet production. However, data on the utilization and outcomes of Generic Eltrombopag in India remain sparse.

Aims & Objectives

To provide comprehensive insights into the real-world application and efficacy of Generic Eltrombopag in Immune thrombocytopenia (ITP) patients.

Materials & Methods

Single-centre retrospective, in patients diagnosed with ITP, who recieved Generic Eltrombopag 50 mg (Elromo). Data of 102 ITP patients were collected from Jan 2024 to Sept 2024. This registry encompasses data, documenting treatment and haematological response associated with Generic Eltrombopag.

Result

Preliminary findings indicate that Generic Eltrombopag is effective in achieving a significant increase in platelet counts in most patients. The response rate, defined as a platelet count increase to at least 50,000/µL, which at baseline under influence of prior treatment (dexamethasone etc) was 51.5%, which in 4 weeks improved to 83.33%, and at 8 weeks follow-up was 81.57% and at 12 weeks follow-up was 77.78%. Additionally, no patients had any bleeding episodes and does not require any rescue medicines.

Follow Up	Variables	MEAN
Baseline (n=102)	Platelet count	54675.49
4 weeks (n=86)	Haemoglobin	12.24
	TLC	8600.75
	Platelet count	143555.56
8 weeks (n=38)	Haemoglobin	12.47
	TLC	8994.1
	Platelet count	203315.79
12 weeks (n=22)	Haemoglobin	12.73
	TLC	7734.76
	Platelet count	193333.33
16 weeks (n=10)	Haemoglobin	12.5
	TLC	5373.32
	Platelet count	140700.13
20 weeks (n=6)	Haemoglobin	12.08
	TLC	6569.67
	Platelet count	102666.67
24 weeks (n=3)	Haemoglobin	11.92
	TLC	9420
	Platelet count	114000

Conclusion

The Indian Drug Utilization Registry provides valuable real-world evidence supporting the use of Generic Eltrombopag in managing ITP. The findings underscore the drug's efficacy and safety, offering a cost-effective alternative to branded versions. Continued data collection and analysis will further elucidate long-term outcomes and optimize treatment strategies for ITP patients in India.

Benign Hematology-Clinical (BHC) PP-BHC-15

Retrospective Analysis of Drug Utilization and Safety of Iron Isomaltoside 1000 (FERUNO) in Cancer Patients with Iron Deficiency Anemia

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Introduction

Anemia is prevalent among oncology patients, impacting 39.3% to 63.4% of patients, and Iron deficiency anemia (IDA) being the most common cause. Iron Isomaltoside 1000 (Feruno) is a novel intravenous iron formulation designed to replenish iron stores efficiently and safely.

Aims & Objectives

This retrospective study aims to evaluate the drug utilization and safety profile of Iron Isomaltoside 1000 in the treatment of IDA among cancer patients.

Materials & Methods

This study is a single-center retrospective, drug utilization registry, in 98 cancer patients diagnosed with iron deficiency anemia, who were prescribed, Iron Isomaltoside 1000 (Feruno). Data on patient demographics, dosage, frequency of administration, haemoglobin levels, and adverse events were collected and analysed.

Result

The mean (±SD) age of cancer patients was 56.64±13.40 years, with Breast, ovarian, colon, gastrointestinal, and kidney cancer representing 23%, 14%, 14%, 12%, 11% of IDA cases respectively. Mean (±SD) Hemoglobin prior to treatment was 8.93±1.71 mg/dl (Figure 1). The average iron need was 1396.9 mg, and the most frequent dose administered was 1000 mg. The treatment was effective and well-tolerated, with minimal adverse reactions. 2 Patients had mild rash at injection site and 1 patient had mild Rash (site not specified). The adverse event was non serious and did not require discontinuation or dose change.

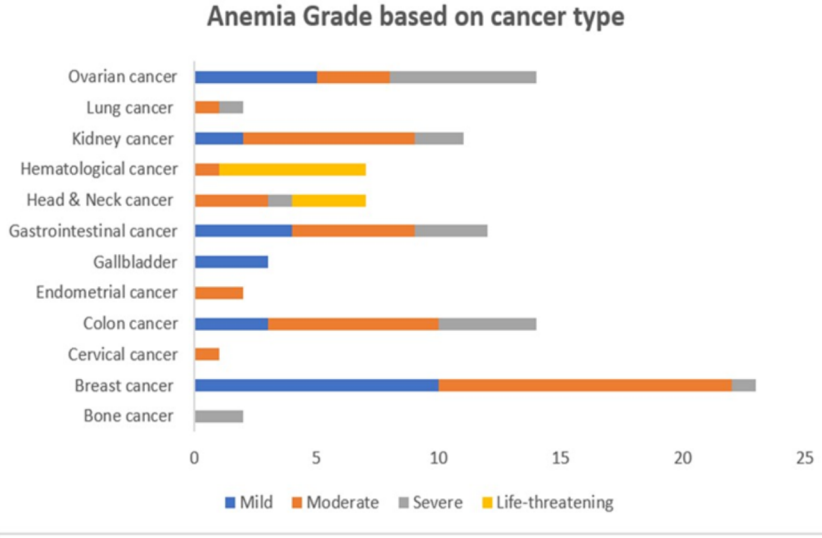

Figure 1: Different grades of Iron deficiency anaemia based on different Cancer types in patients

Conclusion

Safety profile of Iron Isomaltoside was favourable, with minimal adverse events. Given that the iron need of cancer patients is usually above 1 gram, and the most frequent dose prescribed was 1000 mg, administering the recommended dose (20 mg/kg body weight) in a single infusion can improve patient compliance and ensure most patients receive the total dose infusion.

Benign Hematology-Clinical (BHC) PP-BHC-16

Epstein Barr Viremia: The Many Avatars in Hematology

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Introduction

Epstein-Barr Virus (EBV) has a high seroprevalence rate of 95% among humans. Although most primary infections (PI) are asymptomatic, up to 35-50% develop infectious mononucleosis, with only a select few developing further complications during the Pl. Post PI, EBV enters into latency but can undergo lytic replication and cause manifestations like chronic active EBV, autoimmune diseases, and even tumorigenesis.

Aims & Objectives

The primary aim of the study is to highlight the unique and varied hematological presentations of Epstein-Barr Virus (EBV) infections in the community and further discuss the current literature on the management of EB Viremia.

Materials & Methods

The study is a case series of five adults (> 20 years) with a confirmed EBV infection by quantitative polymerase chain reaction in the peripheral blood and its varied hematological scenarios. Information was collected from an electronic hospital database.

Result

Case one was a delayed presentation of primary infection with EBV, causing generalized lymphadenopathy in a 37-year-old adult female, with spontaneous resolution. Case two showed a unique complication of infectious mononucleosis in the form of severe nasal obstruction due to lymphadenopathy. Although this resolved with a short course of steroids, it caused a diagnostic dilemma as it mimicked a lymphoma. Case three was an EBV-induced Natural killer / T cell lymphoma with an excellent response to modified SMILE therapy. Cases four and five demonstrate post-hematopoietic stem cell transplant (HSCT) scenarios of EBV viremia and the role of rituximab and the reduction of immunosuppression as part of pre-emptive therapy.

Conclusion

EBV remains a significant cause of fever and lymphadenopathy in younger adults, even beyond adolescence, and can mimic lymphoma. It has a self-limiting course, except in some rare situations of secondary complications, which may need a short course of steroids. Early monitoring of the EBV serology and quantitative virology using real-time PCR can help avoid unnecessary interventions. It can also help in prognostication and assess disease responses in EBV-related tumorigenesis. Post-HSCT EB viremia remains a significant cause of morbidity and mortality. It needs stringent monitoring beginning at least four weeks post-HSCT to at least a year or beyond with ongoing immunosuppression for graft versus host disease.

Benign Hematology-Clinical (BHC) PP-BHC-17

HBH Disease : A Missed Cause of Haemolytic Anemia in Adults

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Background

One of the clinically significant forms of Alpha Thalessemia is HbH disease which is caused by deletion of three alpha genes. HbH usually presents in the first years of life, however in some cases it may not present till adulthood due to unknown confounders. Herein, we present a case of late presentation of HBH disease in an adult male.

Case Presentation

A 28-year-old male presented with history of fever, abdominal distension, progressive paleness for 3 months. On clinical examination, palor and hepatosplenomegaly was observed. There were previous similar complaints in the past. The patient received first transfusion at the age of 16 years and received 2-3 transfusions thereafter. Peripheral smear showed moderate anisopoikilocytosis, dimorphic red cells, spherocytes with 2% reticulocyte count. LDH, DCT/ICT, HPLC, G-6 PD assay and OFT was advised. BM aspirate revealed cellular reactive marrow with mild erythroid hyperplasia. Meanwhile, OFT, DCT/ICT was found to be normal. The HPLC revealed a preintegration peak, and examination of reticulocyte smear showed presence of golf ball inclusions confirming the HBH disease.

Diagnosis

Hbh disease

Treatment

Patient is being treated for chronic anemia

Follow-up

Molecular studies are being done for genetic phenotyping

Conclusion

HBH – alpha thalassemia is a known clinical entity; however, the clinical picture varies and is often underdiagnosed. Careful examination of routine blood smear is helpful to pick up the disease.

Benign Hematology-Clinical (BHC) PP-BHC-18

Standardizing a Method of Preparation of Platelet Lysate for Tissue Regeneration

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Introduction

Platelets represent a natural reservoir of mediators such as growth factors and cytokines that make it a potential candidate in regenerative medicine. Due to the myriad composition of bioactive molecules present in platelets, platelet-derived biomaterial, like human platelet lysate (HPL) has been used in wide range of clinical applications. An important step in HPL production is the lysis or activation of platelets to release stored active substances such as growth factors, cytokines, and chemokines into the plasma or platelet additive solution plasma. The various preparation methods and non-standardized protocols of platelet lysate preparation complicate the interpretation of both experimental and clinical results.

Aims & Objectives

In an attempt to standardize the method for preparing platelet lysate, we aimed to compare between different methods of platelet lysate preparation and to study the effect of platelet lysate prepared from these methods on cell viability, proliferation, and migration in fibroblast cells.

Materials & Methods

The platelet count was fixed and the lysate was prepared using different methods like freeze-thawing, homogenization, sonication, and a combination of these methods. Platelet lysate prepared from the above methods was lyophilized and stored at 4°C. The total protein concentration in these was quantified. L929 cells were treated with PL prepared from various methods and its effect on cell viability, proliferation and migration was evaluated. All quantitative data were expressed as mean ± SD(n=3). Results were analyzed using two-way ANOVA.

Result

The results indicated that the process of homogenization is more effective compared to the other methods in terms of ease of handling, short processing time, and a significant increase in cellular viability, proliferation, and migration upon treatment to the cells.

Conclusion

In conclusion, homogenization can be an ideal and effective method for preparing platelet lysate from platelet concentrates. This type of systematic study in the preparation of platelet lysate will be useful in obtaining a standardized preparation protocol that can be followed worldwide.

Benign Hematology-Clinical (BHC) PP-BHC-19

Interim Results from a Non-interventional, Post Authorisation Safety Study of Nonacog Beta Pegol as Routine Prophylaxis in Patients With Haemophilia B

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Introduction

Ongoing global post-authorisation safety study (requested by the European Medicines Agency, sponsored by Novo Nordisk) interim analysis, investigating nonacog beta pegol (N9-GP) prophylaxis in patients with haemophilia B

Aims & Objectives

Evaluate the safety and efficacy of N9-GP prescribed by physicians in routine practice

Materials & Methods

International, multi-centre study aiming to enroll 60 any-age males with haemophilia B who received N9-GP prophylaxis at physicians' discretion. Study approved by independent ethics committee. Informed consent obtained. Patients with N9-GP hypersensitivity and pre existing factor IX (FIX) inhibitors excluded. First visit: 01/04/2019; last visit expected: Q4 2027. Primary endpoint: adverse drug reaction (ADR) occurrence; additional endpoints: serious adverse event (SAE) frequency, bleed count, haemostatic effect, polyethylene glycol (PEG) plasma levels, neurological examinations

Result

At interim cut-off (31/03/2022), 41 patients were enrolled; mean (range) age: 34 years (9–74); disease severities: 2% mild, 27% moderate, 66% severe, 5% missing. Four patients withdrew (one withdrawal of consent; three on physician decision [one moved from centre, two due to bleedings]). Cumulative N9 GP exposure time: 40 patient-years.

During a median (range) treatment period of 1.1 years (0–2.4), no ADRs, allergic reactions, thromboembolic events or FIX inhibitors were reported. Six patients reported AEs (Table 1). Two SAEs (gastric ulcer, cholecystitis) and one AE of special interest (headache) were reported. No AEs were considered treatment related.

Mean (median) annualised bleeding rate was 0.49 bleeds/year (0.00); 73% of patients reported no bleeds (Table 2). No bleeds resulted in re-bleeds. Although mean PEG plasma levels were stable, three patients had levels ≥8.0 µg/mL: two attributed to higher/more frequent dosing, one to high body weight. Of the four patients with abnormal neurological examination findings at baseline, one experienced symptomatic deterioration (abnormal gait) attributed to ankle complications

Table 1: Adverse events overview

	Patients (n)	Events (n)
All adverse events	6	10
Serious adverse events	2	2
Adverse events by relationship to nonacog beta pegol		
Probably or possibly related	-	-
Unlikely related	6	10
Severity		
Mild	4	5
Moderate	3	4
Severe	1	1
Outcome		
Recovered/resolved	5	8
Recovering/resolving	1	1
Recovered/resolved with sequelae	1	1
Not recovered/not resolved	-	-

Table 2: Bleeds overview

	N = 41
Bleeds, n	24
Patients with bleeds, n (%)	11 (26.8)
Site	
Joint, n	15
Muscular, n	4
Gastrointestinal, n	4
Mouth/gums/nose, n	1
Spontaneous bleeds, n	15
Traumatic bleeds, n	9
Treatment-requiring bleeds, n	13
Patients with treatment-requiring bleeds, n (%)	6 (14.6)
Haemostatic response	
Excellent, n	6
Good, n	4
Moderate, n	0
Poor, n	1
Missing, n	2

Conclusion

In real-world practice, N9-GP prophylaxis in patients with haemophilia B was efficacious, with no safety concerns identified. These findings confirm clinical trial observations.

Benign Hematology-Clinical (BHC) PP-BHC-20

Characterization of Anti-m Antibodies : A 12-year Retrospective Study at a Tertiary Care Hospital in South India

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Introduction

Though considered, a common naturally occurring and clinically insignificant, anti-M can lead to both hemolytic transfusion reaction and hemolytic disease of fetus and newborn.

Aims & Objectives

To assess the frequency and characteristics of anti-M antibody at our tertiary care facility.

Materials & Methods

A retrospective observational study was conducted by reviewing the immunohematology register of our centre to identify cases with anti-M antibodies detected between Jan 2012 to August 2024. Demographic, lab parameters and clinical details were obtained from the registers, hospital and laboratory software.

Result

A total of 157 cases were identified with anti-M antibody during the study period of which, 135 (85.9%) were patients and 22 (14.1%) were in donors. Males comprised of 56.7% (89) and the age range was 1 year to 94 years. In more than half of the cases (57.3%, 90) the antibody was reacting at room temperature and at 37◦C. The antibody was naturally occurring in 50.96% (85) of the cases. Sensitizing events of pregnancy, transfusion and both were present in 22.3% (35), 21.01% (33) and 5.7% (9) of cases respectively. In 9.5% (15) cases the antibody was present in co-existence with other antibodies. Anti-M showed dosage in majority of the cases 100(63.7%). The turn around time for identifying M antigen negative, crossmatch compatible units was higher when the antibody was showing dosage effect. The frequency of detecting anti-M was highest in the second quarter (May-Aug; 38.9%) of the year followed by last (Sep-Dec; 33.1%) and first quarter (Jan-Apr; 26.1%).

Conclusion

Anti-M detected was mainly characterized by having a wide thermal amplitude and was primarily of natural occurrence. Establishing a registry of M antigen negative individuals will reduce the turnaround time for delivering safer transfusions to patients with anti-M antibodies especially when they demonstrate a dosage effect.

Benign Hematology-Clinical (BHC) PP-BHC-21

Empowering Sickle Cell Disease Management in Indian Tribal Communities: Evaluating a Digital Ecosystem for Enhanced Quality of Life and Healthcare Access

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Introduction

Sickle Cell Disease (SCD) remains a significant public health challenge in India, particularly within tribal communities – 10-15

Aims & Objectives

To explore the feasibility of a digital ecosystem in remotely monitoring QoL for individuals with SCD in tribal communities through a wearable device and patient-reported outcomes (PRO)-app – improving outcomes/access to care, while increasing patient/public/provider education.

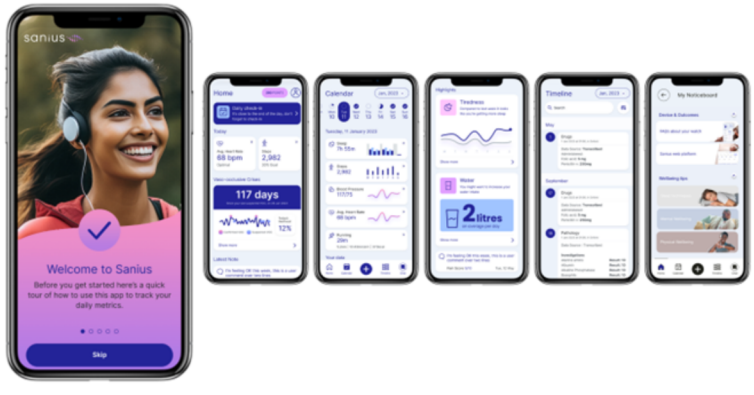
Materials & Methods

This work extends an established UK ecosystem, wherein individuals with SCD utilised a wearable device and specialised PRO-app (EQ-5D-5L, pain/mood/fatigue scores, symptoms, and vaso-occlusive crises (VOCs)). Previous abstracts indicated significant improvements in EQ-5D-5L, enhancing QoL and health management.

The ecosystem was adapted for Indian tribal communities, guided by local clinicians and enrolling an initial pilot of 270 patients. Patient engagement strategies included community education/materials and in-person health camps. Feedback from 4 highly engaged participants was assessed for initial impacts in this cohort.

Result

Among participants, 75% (3/4) reported that the app helped them track their hydration, which was critical in self-management. Daily pain monitoring was mentioned by all participants, with 100% noting this improved their symptom awareness/management. 50% mentioned the role of the app in managing VOCs, highlighting how regular monitoring contributed to better control during crises. Additionally, 50% mentioned its support in adhering to their medication schedule through reminders.



Mental health tracking, specifically for anxiety/depression, was noted by 50%, with 1 participant expressing that it contributed to a more positive outlook. Participants also reported greater visibility into their health data, which enabled more effective home management of their condition.

Conclusion

This approach has proven a vital tool in empowering patients with health visibility; feedback revealing a significant impact on improving disease management and enhancing QoL. With remote VOC detection, health tracking, tailored educational resources, and metric baseline establishment capabilities for future monitoring and expansion, the approach shows feasibility in bridging current gaps in healthcare delivery for patients in India. Future work will explore the real-world impact on patient outcomes longitudinally.

Benign Hematology-Clinical (BHC) PP-BHC-22

Series of 3 Cases Divided by Unique Etiologies - United by Anemia & Jaundice

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Background

Hemolytic anemias are a common cause of anemia and jaundice. Finding the underlying etiology of hemolytic anemias is essential for proper management. We herein present three diagnostically challenging cases of hemolysis which had unusual underlying cause.

Case Presentation

Case 1: A 26-day-old infant presented with persistent mixed jaundice, anemia, and hepatosplenomegaly following early-onset sepsis and phototherapy.

Case 2: A 27-year-old female with leprosy on dapsone therapy developed a drop in hemoglobin from 11 to 9 g/dl, peripheral smear revealed signs of hemolysis such as polychromatophils and bite cells. But screen for G 6PD deficiency was negative.

Case 3: A 22-year-old male presented with history of multiple hospital admissions for easy fatiguability, decreased appetite and fever without splenomegaly. Lab work up revealed severe macrocytic anemia and hemolysis.

Diagnosis

Case 1: Gestational alloimmune liver disease with coexisting Hb H disease confirmed by NGS testing.

Case 2: Dapsone-induced hemolytic anemia confirmed through a clinical correlation between dapsone use and hemolysis, with negative G6PD deficiency and direct Coomb's test.

Case 3: Bone marrow revealed 6% blast with auer rod amidst dysplastic erythroid hyperplasia. Myelodysplastic neoplasm with increased blasts 2, with WT1 gene mutations was final diagnosis in this young male.

Treatment

Case 1: Patient responded well to treatment with IVIG.

Case 2: Discontinuation of dapsone resulted in resolution of hemolysis.

Case 3: Offered hypomethylating therapy and an allogenic bone marrow transplant; however, the patient opted for alternative therapies.

Follow-up

Case 1: Regular monitoring of hemoglobin levels and liver function was undertaken. Hb is maintained at 9 g/dl after active management of GALD.

Case 2: Hemoglobin levels normalized following discontinuation of dapsone, and anemia resolved on follow-up.

Case 3: Despite multiple episodes of hemolysis and hospital admissions, the patient refused curative treatments. The disease progressed to acute myeloid leukemia after eight months.

Conclusion

This case series demonstrates hemolysis can be manifestation of a wide spectrum of underlying causes ranging from genetic hematological disorders to drug-induced hemolysis and malignancies. In the current era where we have multiple diagnostic tests we need to have a proper approach which includes critically reviewing the smear, clinical correlation thorough history taking, and the selection of appropriate advance diagnostic tests to guide treatment.

Benign Hematology-Clinical (BHC) PP-BHC-23

Platelet Parameters and Acute Coronary Syndrome: Uncovering the Hidden Link

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Introduction

Acute coronary syndrome (ACS) is a multifactorial condition influenced by various risk factors. Abnormal platelet parameters may serve as early indicators for coronary artery disease (CAD), potentially allowing for timely intervention to reduce morbidity and mortality associated with ACS.

Aims & Objectives

This study aims to investigate the relationship between platelet parameters and CAD, identifying abnormal platelet parameters as a risk factor for the disease.

Materials & Methods

This was a retrospective study conducted on a 110 diagnosed cases of ACS patients, admitted to the hospital from January 2024 to May 2024. Among the ACS cases, 30 patients had myocardial infarction (MI), and 80 had CAD. 103 normal healthy individuals, who were selected from blood donors taken as control. EDTA blood samples were collected upon admission for complete blood count and platelet parameter analysis including platelet count (PC), mean platelet volume (MPV), plateletcrit (PCT), platelet distribution width (PDW), and platelet large cell ratio (P-LCR) using the Sysmex XN 1000 automated analyser. Comparative analyses were conducted between ACS patients and the healthy control group. Statistical analyses were performed using SPSS software, with p-values <0.05 considered significant.

Result

The platelet count in ACS patients was significantly lower as compared to controls (229.88±91.7 x 109/L for ACS vs. 264±66.71 x 109/Lfor controls, p=0.00019). MPV (11.822±1.403 fL for ACS vs. 11.127±1.041 fL for controls, p=0.0001), PDW (15.602±3.742 fL for ACS vs. 13.423±2.615 fL for controls, p=0.0001), and P-LCR (39.3645±10.817 for ACS vs. 33.7922±8.5393 for controls, p=0.0001) were significantly higher in the ACS group. However, PCT showed no significant difference between the two groups (0.3007±0.2742% for ACS vs. 0.2910±0.6222 % for controls, p=0.7247).

Conclusion

Platelet parameters, particularly MPV, PDW, and P-LCR, are significantly elevated in patients with acute coronary syndrome. Routine haematological tests can readily identify these parameters, enabling early detection and preventive treatment strategies for at-risk individuals.

Benign Hematology-Clinical (BHC) PP-BHC-24

Acquired Hemophilia - A Haematologist's Nightmare

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Background

Acquired hemophilia A (AHA) is a rare bleeding disorder occurring equally in both genders in the elderly age and commonly presents as skin & subcutaneous bleeding rather than deep site-bleed. Nearly, half of patients will have underlying malignancy/autoimmune disease. In few proportion of patients, it can present as isolated aPTT prolongation without bleed. Mortality due to AHA estimated to be ? 20?ove > 65 years. Treatment includes combined hemostatic bypassing agents and immunosuppressive agents. Early Factor VIII recovery is a good predictor of survival. AHA has a high rate of recurrence despite IST, hence close monitoring of FVIII activity is required for follow up.

Case Presentation

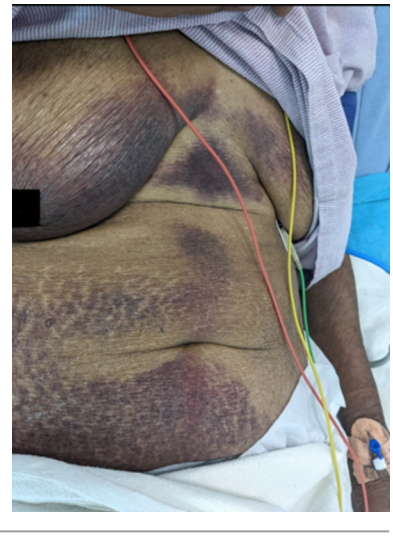
An 82 year female, known case of hypertension, presented in the emergency with complaints of spontaneous reddish - purplish patches over right shoulder, extending to some part of the back and chest, right flank and abdomen over 3 days.On general examination, she had pallor, along with swelling over the right shoulder, with discolouration and extension as mentioned above. The swelling had minimal fluctuation. HRCT Thorax was suggestive of large hematoma in right lateral chest wall. Patient was initially reviewed by the Department of general surgery and was planned for exploration in view of a large Hematoma.

Diagnosis

Hemogram showed severe anaemia Hb 5g/dl with normal total count and platelet count of 1.5 lakh with aPTT of 55sec (28 s), PT 10 s (10.3 s) and fibrinogen 208 mg/dl, thrombin time 18s. Acquired haemophilia was suspected and aPTT based mixing study was done and it didn't show correction after 2 hours of incubation and factor VIII activity turned as 2.8% and F IX activity was 71.8%.Factor VIII inhibitor by Bethesda assay was 32 a high-titre inhibitor.

Treatment

Patient was started on bypassing hemostatic agents (Novoseven 90 mcg/kg every 4 hourly) with immunosuppressants (steroids, ritu I ab, cyclophosphamide). Workup for hematolymphoid malignancy was negative.



Follow-up

Patient had transient improvement with the employed measures but later developed pneumonia secondary to IST and succumbed to AHA.

Conclusion

Acquired Hemophilia should be suspected in patients presenting with isolated APTT prolongation with no significant family history of bleeding disorder in the absence of any pre-existing malignancy, autoimmune condition and infections. Prompt action and suspicion is vital for management of this condition, using Immunosuppressive agents, hemostatic measures and by-passing agents. Patients can attain partial to complete response within a month. Acquired Hemophilia requires regular follow up and monitoring as it may recur.

Benign Hematology-Clinical (BHC) PP-BHC-25

Megakaryocytic Aplasia in Vitamin B12-deficient Megaloblastic Anemia

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Background

Megakaryocytic aplasia in B12-deficient megaloblastic anemia is rare. Its pathogenesis is not well understood.

Case Presentation

We report the cases of two patients with vitamin B12-deficient megaloblastic anemia in whom marrow megakaryocytes were absent (Table). Both patients were vegetarian and showed palpable splenomegaly; patient 2 (Table) had marked scleral icterus and bilateral retinal hemorrhages. Immunohistochemical staining for CD-61 megakaryocyte antigen showed absence of megakaryocytes in the marrow core biopsy in patient 2 (Table). Both patients received packed red cell transfusions; patient 2 received three units of random donor platelets.

Diagnosis

Vitamin B12-deficient megaloblastic anemia with megakaryocytic aplasia responsive to replacement therapy.

Treatment

Patients received transfusion support and treatment with parenteral vitamin B12 led to brisk reticulocytosis and a rise in the platelet count to 167 x109/L and 97 x109/L in ten and seven days respectively in patient 1 and 2.

Follow-up

At 3-month follow-up both patients were well and results of complete blood count were normal

Conclusion

A study of bone marrow megakaryocyte number, its hematologic correlates, and response to replacement therapy may help in furthering our understanding of megakaryopoiesis in megaloblastic anemia.

Laboratory findings in two patients with megaloblastic anemia and megakaryocytic aplasia

*Serum total bilirubin/Direct bilirubin

** patient to be tested for UGT1A1 mutation

† Intrinsic factor antibody

No.	Age/Sex	Hb g/dL	WBC $x10^9$/L	Platelets $x10^9$/L	MCV fL	LDH U/L	TB/DB* mg/dL	Serum B_{12} pg/mL	Serum Folate ng/mL	IFAb†
1	75 y/M	3.8	3.2	18	114	2148	1.6/0.4	<150	-	Absent
2	22 y/M	2.3	1.9	1	123	2700	9.4/0.4**	123	<0.5	Absent

Benign Hematology-Clinical (BHC) PP-BHC-26

Infantile Pure Red Cell Aplasia Secondary to Deficiency of ADA2 (Adenosine Deaminase 2) - Time to Think Beyond Diamond Blackfan Anemia

Amiya Ranjan Nayak
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Introduction

Deficiency of Adenosine Deaminase 2 (DADA2) syndrome is a rare autosomal recessive disorder caused by mutations in the ADA2 (CECR1) gene, located on chromosome 22q11. DADA2 manifests predominantly in two phenotypes: vasculitic and hematologic. The ADA2 protein plays a crucial role in purine metabolism and immune regulation, and its deficiency results in chronic inflammation and vascular damage.

Aims & Objectives

Clinical and laboratory profile of patients with pure red cell aplasia secondary to ADA2 mutation

Materials & Methods

A retrospective observational study was conducted on nine patients diagnosed with infantile PRCA secondary to DADA2. Clinical profiles, laboratory parameters, and genetic analysis were reviewed. The study included data on patient demographics, phenotypic classification, genetic mutations, and laboratory findings, including hemoglobin levels and absolute reticulocyte count (ARC).

Result

Eight out of nine patients presented with infantile onset of PRCA, with a median age of presentation at three months. The mean hemoglobin level was 5.78 g/dL, with a mean ARC of 7733/μL. One patient developed vasculopathy, a hallmark of the vasculitic phenotype. Genetic analysis revealed that two patients had nonsense mutations, and the most common ADA2 mutation identified was p.Ile93Thr. None of the patients responded to steroid therapy.

Conclusion

This case series opens up a new horizon in the differential diagnosis of infantile and childhood PRCA. The study emphasizes the importance of distinguishing DADA2 from DBA, particularly given the overlapping hematologic features.

Benign Hematology-Clinical (BHC) PP-BHC-27

Factors Driving Participation in Clinical Trials Among People with Sickle Cell Disease Differ in Importance Across Geographic Regions: Findings From the Global Listen Survey

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Introduction

Recruiting and retaining a large and diverse group of participants is crucial to the success of global clinical trials (CTs) of new therapies for sickle cell disease (SCD). Learnings and Insights into Sickle Cell Trial Experiences (LISTEN) Survey identified a need to communicate the potential benefits of CT participation for individuals and the wider SCD community, as well as the anticipated safety profile, to improve access to and recruitment into CTs.

Aims & Objectives

To investigate potential geographic differences in the importance of factors affecting the ability and willingness of people with SCD (PwSCD) to participate in CTs

Materials & Methods

PwSCD (≥18 years) in 17 countries completed a quantitative survey (Oct 2022 and Jun 2023) assessing factors that drive the decision to participate in a CT across five categories. Respondents rated the importance of factors on a 7-point scale. Responses are reported by Middle East and North Africa (MENA), Sub-Saharan Africa (SSA), South America (SA), North America (NA), Europe (EUR), and India (IND). Differences between the mean were assessed using two-proportion Z-tests.

Result

Overall, 1,145 PwSCD across six regions completed the survey (Table 1). The proportion of respondents not aware of CTs was large in IND (88%), MENA and SSA (39%) (Table 2). Prior participation in SCD CT was reported low 16% in SSA, 11% in MENA, and 0% in IND (Table 3). The potential to better manage symptoms was rated extremely/very important by smaller proportion of respondents in IND than in other regions (Figure 1A). When considering wider trial impact, fewer respondents in SSA and IND rated supporting new treatment developments for the benefit of other PwSCD extremely/very important. Among factors related to CT information, understanding planned safety measures was most often ranked first or second in importance across regions, except in IND where who is leading the trial ranked in the top two. (Figure 1B).

Conclusion

Geographic differences in the importance of factors motivating or discouraging PwSCD to participate in CTs may reflect differences in education needs, local culture, or confidence in the healthcare system. These geographical differences should be considered when designing trial protocols to enhance recruitment and diversity in global CTs.

Table 1: Region wise break Up - 1,145 PwSCD completed the survey.

Region	MENA	SSA	SA	NA	EUR	INDIA	Total
No. of Responders	142	307	122	254	242	87	1145

Table 2: The proportion of respondents not aware of CTs.

Region	MENA	SSA	SA	NA	EUR	INDIA
% Not Aware	39	39	12	5	5	88

Table 3: Prior participation in an SCD CT

Region	MENA	SSA	SA	NA	EUR	INDIA
Prior Participation In SDC (%)	11	16	33	37	25	0

Benign Hematology-Clinical (BHC) PP-BHC-28

EB Thalassemia with Autoimmune Hemolytic Anemia

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Background

Haemoglobin E-beta thalassaemia is the genotype that accounts for about 50% of severe beta-thalassaemia cases globally and shows significant clinical variability. Although uncommon, autoimmune hemolytic anemia (AIHA) can occur as a serious and potentially life-threatening complication of congenital anemias. Factors that have been linked to the onset of anti-RBC autoimmunity include prior splenectomy, recent blood transfusions, infections, and pregnancy.

Case Presentation

A 23-year-old woman with h/o abortion at four months of pregnancy and severe anemia presented with difficulty in cross matching . Previously she receive eight units of PRBC without any difficulty. Clinical examination showed significant splenomegaly, raising suspicion of hemolytic anemia. High-performance liquid chromatography (HPLC), direct and indirect Coombs tests, and lactate dehydrogenase (LDH) tests were ordered alongside routine investigations, ultimately leading to a diagnosis of E-beta thalassemia with autoimmune hemolytic anemia (AIHA).

Diagnosis

EB Thalassemia With Autoimmune Hemolytic Anemia

Treatment

She was started on steroid (predinisolone 1mg/kg) along with low dose rituximab weekly protocol. After cross match she received 1 unit M and c negative PRBC without any problem. Her Hb improved partially from 3.6 to 6g/dl. She was discharged with a hemoglobin of 6g/dl folic acid and b12 supplementation.

Follow-up

Steroid was tapered and stopped on follow up and she maintained Hb of 6g/dl over 8 months.

Conclusion

Autoimmune hemolytic anemia (AIHA) in the context of congenital anemia is a rare and difficult to diagnose entity. AIHA should be considered when there is a sudden drop in hemoglobin levels or a notable worsening of hemolytic markers. A key indicator is a decrease in pretransfusion hemoglobin or an increased need for transfusions. In this case, our patient has moderate anemia and has not received transfusions since childhood. Her pregnancy may have triggered the onset of AIHA and alloimmunization secondary to multiple PRBC transfusion lead to increase in severity of anemia which lead to work up of the condition there by diagnosing the entity.

Benign Hematology-Clinical (BHC) PP-BHC-29

Combined Coagulation Factor Deficiency, A Study of 2 Cases – A Prodigious Find

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Background

A rare spectrum of inherited disorders known as familial multiple coagulation factor deficits are characterized by concordant decline in the levels of two or more coagulation factors. This condition is common in areas with high proportion of consanguineous marriages & in gated communities. Most common type of combined coagulation factor deficiency is of factor V& VIII. The common clinical features are epistaxis, menorrhagia, profuse bleeding during or following trauma, surgery, or childbirth.

Case Presentation

Case report 1:

A 56-year-old male (known case of hemophilia A with hypertension, bilateral renal calculi and hydronephrosis) reported to the ENT department with a large diffuse anterior neck swelling with ecchymotic patches (soft & tender) was felt (preceded by a fall, 4 hours ago). On examination, Patient had a hot potato voice and a blood pressure of 157/84 mm/Hg. An emergency tracheostomy was performed with incision & drainage of retropharyngeal hematoma.

The coagulation parameters were deranged PT/INR (17.7 secs/1.84) & APTT (70 secs). Additionally, the patient was found to have deficiency of factors VIII (42.0%) & IX (4.5%)(normal range for VIII & IX: 50-150 %). Deficiency of Factor IX was an incidental finding (Hemophilia B).

Case report 2:

A 19-year-old female reported to the Gynecology dept. with complaints of menorrhagia, dysmenorrhea, & irregular periods for the past 2 months. She had a past history of gum bleeding and epistaxis. Her clinical & radiological findings were normal except deranged PT/INR (17.7/1.8) and Hb= 6.7 g/dl. She was transfused 4 units of Fresh Frozen Plasma. She had an episode of epistaxis and gum bleeding for which coagulation factor assay was done, where she was found to be factor V (50%) (normal: 62-139%) & factor X (57%)(normal: 77-131%) deficient. She was managed symptomatically with Fresh frozen plasma and had a complete recovery, is currently on follow up.

Diagnosis

Combined factor deficiency (VIII & IX) & (V & X) respectively.

Treatment

Treatment: Fresh Frozen plasma

Follow-up

Both the patients are currently on follow up and are doing well.

Conclusion

Since combined deficiency of factor VIII & IX, as well as V & X (1 in 1,000,000, for both) is very rare and has consequences, which makes our cases worthy of reporting.

Benign Hematology-Clinical (BHC) PP-BHC-30

Spectrum of Fetal Hemoglobin and/or Hemoglobin A2 Levels on HPLC in Central India

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Introduction

Quantification of fetal hemoglobin (HbF) is clinically useful and crucial to diagnose some important globin gene disorders where HbF levels vary. This spectrum includes mainly, β- and δβ-thalassemia, HPFH, Sickle cell anemia, HbE, and several acquired conditions viz pregnancy, anemias, and drugs- hydroxyurea. Therefore, a correct interpretation of HbF is mandatory. In all these conditions HbA2 plays a pivotal role in differentiating them. β- Thalassemia carriers are identified by an HbA2 value ≥4% albeit some may present with borderline levels of HbA2 (3.5-4%). The spurious increase in HbA2 level is due to co-elution with glycated HbS, Hb Lepore, and HbE along with hyperthyroidism and megaloblastic anemia. On the contrary, iron deficiency anemia and alpha thalassemia reduce HbA2 levels. Therefore, a careful determination of the HbA2 level with RBC indices, iron status, and familial studies is necessary to avoid diagnostic pitfalls.

Aims & Objectives

Significance of spectrum of HbA2 and/or HbF in screening of hemoglobinopathies by HPLC in Central India.

Materials & Methods

HPLC done in a routine hematological investigation in hospitalized and outpatients. Also done in screening program for community-based population and in ANC patients. All the samples were run on BIO-RAD HPLC VARIANT II machine irrespective of the results of the solubility test for the last one year. A total of 2200 samples were run and classified according to the percentage levels of HbA2, HbF, HbA and presence of any additional window. All the diagnoses were made taking into consideration the RBC indices, clinical presentation, transfusion, and family history.

Result

The results obtained are shown in the table submitted.

RESULTS:

Diagnosis	No of cases
Normal AA2	1368
AS Pattern	572
SS Pattern	137
HbE trait	02
Possibility of α thalassemia	01
β Thalassemia Major	02
β Thalassemia Minor	60
Heterozygous for HbS with possibility of α thalassemia	43
Heterozygous for HbJ	01
Double heterozygous for HbS & β thalassemia	10
Double heterozygous for HbS & Hb E	01
Double heterozygous for HbS & HPFH	02
Heterozygous for HbQ with IDA	01

Conclusion

The RBC indices viz Hb, MCV, MCH, and RDW along with RBC count played pivotal roles in interpreting HPLC findings. Depending on the deletion/ mutation of the number of β, and α chains the levels of HbA2, HbA, and HbF vary. As there are wide range of causes of increased levels of HbF, its spectrum with HbA2 on HPLC is full of surprises which when correctly interpreted help in accurate diagnosis.

Benign Hematology-Clinical (BHC) PP-BHC-31

Mucormycosis in Allogenic Hematopoietic Stem Cell Transplant Recipients: A Case Series from a Large Volume Bone Marrow Transplant Center

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Background

Mucormycosis has a predicted incidence of around 5% in hematopoietic stem cell transplant recipients. The disease-related mortality rate is 75%, with a median survival duration of fewer than 2 months.

Case Presentation

In a 14-year consecutive series of 451 allogeneic bone marrow transplant recipients, we identified three cases (0.66%) of invasive mucormycosis. Only one infection occurred within the first 100 days after transplantation, while the remainder complicated the late post-transplant course (median day of diagnosis from transplant: 124). Corticosteroid-treated graft-versus-host disease or severe neutropenia were present in all cases. Sites of infection included rhino-cerebral, pulmonary, hepato-splenic and renal with one case showing dissemination.

Diagnosis

In all cases diagnosis was confirmed by histopathology with Grocott-Gomori's Methenamine Silver and Periodic Acid Schiff stain, KOH mount and fungal culture from tissue after strong suspicion by CT scan. In two cases culture was verified by DNA sequencing. The causative organism was Rhizopus microsporus in two cases and Rhizopus arrhizus in the other one.

Treatment

All the cases were treated with 50 mg per day dose of Amphotericin B (Liposomal form at 150 mg per day was used in one case) for a median duration of 35 days. In one patient Isavuconazole 200 mg per day is being used for 4 months after 30 days of Amphotericin B. Surgical intervention was done in two cases with nephrectomy in once case and DRAFFIII procedure and craniotomy with abscess drainage in the other one.

Follow-up

By radiological response assessment, partial response or progression was observed in all the cases after a median of 21 days. In a median follow up of 139 days, one patient is surviving where Isavuconazole is being used. Mucormycosis was the primary cause of death in one patient. In the other patient death was due to bacterial and non-mucor fungal pneumonia.

Conclusion

Mucormycosis is a fatal infective complication in allogenic hematopoietic stem cell transplant recipients. This may have a better prognosis if diagnosed early and treated aggressively.

Benign Hematology-Clinical (BHC) PP-BHC-32

A Rare and Unique Case of Post Infective Hemophagocytic Lymphohistiocytosis

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Background

Hemophagocytic Lymphohistiocytosis (HLH) is a life-threatening condition caused by uncontrolled activation of cytotoxic T cells, natural killer (NK) cells, and macrophages leading to hypercytokinemia resulting in organ damage. HLH can be primary (genetic) or secondary (triggered by infections, malignancies, autoimmune diseases, etc.). Post-infective HLH is rare, only few reported cases are available in literature.

Case Presentation

A young female without any comorbidities, presented with high-grade fever, shortness of breath, and chest discomfort. Initially she was admitted to an outside hospital, referred to our centre in view of worsening health status. On examination, she was tachypnoeic and hypoxic requiring NIV support. She was admitted in Medicine ICU for further evaluation and management. Her chest X-ray showed bilateral infiltrates, tropical fever panel revealed Scrub IgM positive. In view of worsening respiratory status, she required intubation and mechanical ventilation. She was managed with appropriate antibiotics, and other organ supportive measures. Gradually her condition improved, weaned off from ventilator, extubated, shifted to ward, and eventually discharged after 30 days of hospital stay. After a week of her discharge, she presented with new-onset fever. On evaluation, she was found to have bicytopenia, transaminitis, hepatosplenomegaly. HLH was suspected based on her clinical presentation, and on further evaluation there was elevated lactate dehydrogenase and hyperferritinemia. A bone marrow biopsy showed lymphoplasma histiocytosis with focal hemophagocytosis. Her H score was 246 (99% probability of HLH). All the infection work-up and autoimmune profile was negative. PCR tests for Epstein-Barr virus and cytomegalovirus were negative.

Diagnosis

Post infective Hemophagocytic Lymphohistiocytosis.

Treatment

She was treated with dexamethasone as per the HLH protocol. Intravenous immunoglobulin was given in view of persistent high H score, and no significant clinical improvement in spite optimal steroid dosing. She improved gradually, and discharged on tapering dose of steroid.

Follow-up

The patient was followed on weekly basis, she is clinically better and her H score showing declining trend.

Conclusion

Post infective Hemophagocytic Lymphohistiocytosis though rare, it's a life-threatening condition. Timely recognition and appropriate management are key to better outcome.

Benign Hematology-Clinical (BHC) PP-BHC-33

Association of Serum Ferritin and Liver Fibrosis Detected by Fibroscan (Transient Elastography) in Children with Transfusion Dependent Beta Thalassemia (TDT)

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Introduction

Iron overload (IO) is a major complication in TDT patients. Multiple blood transfusions lead to iron overload in various organs particularly in the liver and heart significant liver fibrosis and ultimately cirrhosis. Therefore, monitoring of LIC (Liver Iron Concentration) is of utmost importance to prevent life-threatening complications. Liver biopsy although considered as the gold standard for estimating LIC but it has its own limitations such as invasiveness, sample variability because of uneven iron distribution, and interobserver variability. Magnetic resonance imaging (MRI) transverse relaxation time (T2*) is preferred method for detecting IO in the liver in recent times, but it is expensive, requires an expert radiologist for interpretation and not widely available. There is an unmet need for a non-invasive, reliable, reproducible and affordable tool for early detection for liver fibrosis and timely intervention to prevent cirrhosis.

Aims & Objectives

The present study aims to evaluate the role of TE in the assessment of liver fibrosis and its correlation with serum ferritin in transfusion dependent thalassemia patients.

Materials & Methods

Cross-sectional study. Total of 47 transfusion dependent Thalassemia between age group 5 to 15 years were enrolled for the study. Detailed history, clinical examination and baseline investigations including complete haemogram, liver function tests, hepatitis B and hepatitis C serology as well as serum ferritin were estimated in every patient at the time of enrolment. (TE) was done to assess the degree of hepatic fibrosis by an expert radiologist in all the patients. Children with any chronic liver pathology e.g. hepatitis B, hepatitis C, HIV, Wilson's disease, autoimmune hepatitis) were excluded from the study.

Result

A total Of 47 patients,35(74.5%) male and 12(25.5%) female were enrolled. Patients were stratified according to serum ferritin values as mild (<1000 ng/ml), moderate (1000-4000 ng/ml) and severe (> 4000 ng/ml) iron overload. The respective mean Liver Stiffness Measurement (LSM) values analysed in mild category of iron overload is 7.14 kPa (3.9 kPa-8.9 kPa), moderate is 7.452 kPa (4.55 kPa-17.13 kPa) and severe IO is 9.242 kPa(4.9 kPa-18.4 kPa). The ferritin level was (1124.2 ± 176.2 ng/ml)) in patients with stages (0, 1) compared to stages 2, 3, 4 (2873.4 ± 977.8 ng/ml), p value <0.05.

Conclusion

We observed a strong positive correlation between serum ferritin level and severity of liver fibrosis. Transient elastography (TE) is a valuable non-invasive technique of measuring liver stiffness due to hepatic fibrosis and a reliable tool for predicting iron overload in these patients.

Benign Hematology-Clinical (BHC) PP-BHC-34

Chronic Lymphocytic Leukemia with Hansens Disease

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Background

Chronic Lymphocytic Leukaemia (CLL) frequently presents with skin manifestations, varying from non-specific eruptions to leukaemia cutis. However, this case aims to explore the journey of managing a patient with concurrent CLL and Hansen's disease.

Case Presentation

The patient, known with a history of CLL since 2007, had been managed with 6 cycles of FCR and later Ibrutinib after a relapse in 2021. In January 2023, the patient developed atypical erythematous patches and sensory loss on the legs, which later progressed to multiple papules on the back. A biopsy was suggestive of borderline tuberculoid Hansen's disease.

Diagnosis

Initial findings in January indicated Hansen's disease, which led to the initiation of Multi-Bacillary Multi-Drug Therapy (MBMDT). By June, further investigations were warranted due to the emergence of new symptoms, including swelling of the left foot and persistent fever. Over subsequent months, several CBCs consistently revealed lymphocytosis. These findings corroborated the diagnosis cellulitis, which were seen alongside the persistence of CLL as evidenced by a bone marrow study revealing lymphocytosis. Additional tests, including karyotyping and cytogenetics in July, revealed normal karyotype and chromosome 13q deletions. A PET CT scan also indicated potential inflammatory or infiltration processes occurring in various regions of the body, emphasizing the complexity of the case.

Treatment

Considering the complex diagnostic findings, the treatment was multi-faceted. While the patient continued the CLL management with Ibrutinib, the newly diagnosed Hansen's disease was addressed with MBMDT. In light of the emergence of cellulitis and the persistence of CLL, patient was withdrawn from Ibrutinib and a shift in treatment strategy was considered, planning for a chemotherapy regimen of Rituximab + Bendamustine for 6 cycles.

Follow-up

The patient's clinical journey is characterized by regular monitoring and adjustments in treatment strategy, reflecting the multifaceted nature of the disease manifestations encountered.

Conclusion

This case underscores the need for a multidisciplinary approach in managing rare coexisting conditions like CLL and Hansen's disease. It highlights the importance of vigilant follow-up and further research into such rare associations, especially in patients with evolving skin lesions.

Benign Hematology-Clinical (BHC) PP-BHC-35

Assessment of Safety and Effectiveness of Extended Half-life (EHL) Treatments in Patients at an Indian Tertiary Care Center: A Retrospective Observational Study

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Introduction

Extended half-life (EHL) recombinant factor VIII (rFVIII) promises optimal prophylaxis by decreasing the dose frequency, increasing the compliance, and improving the quality of life without compromising safety and efficacy in Hemophilia A.

Aims & Objectives

This study aims to analyze the effectiveness and safety of glycopegylated extended half-life (EHL) factor, N8GP in Indian patients with Hemophilia A [HA].

Materials & Methods

Data were collected from 15 HA patients who were switched to glycopegylated N8GP from standard half-life factors. Variables such as age, weight, family history, past dosage, frequency of past dosage, target joints, annualized bleeding rate (ABR) were collected at baseline. EHL dose, frequency of EHL dose, duration of treatment, ABR after switching to EHLs were collected at the end of the observation period. Factor consumption before and after switch to EHLs were calculated, patient's general comments on change in quality of life were recorded. The results are expressed using descriptive statistics.

Result

Mean age of patients was 26.8 years, with ages ranging from 7 to 42 years. A majority, 80%, had a positive family history. At baseline, most patients were administered a dose of 29 IU/kg of standard half-life factors two to three times per week (Table 1). The mean ABR at baseline was 15.1, and patients reported having 2 to 4 target joints. The mean dose of N8GP administered was 26 IU/kg on a weekly basis, with an average treatment duration of 8.4 months. Following the switch to N8GP, none of the patients reported spontaneous bleeding. One patient experienced traumatic bleeding, which was managed with a single dose of 40 IU/kg of N8GP. Patients noted an increase in their level of physical activity and a reduction in absenteeism. No adverse drug reactions were reported during the study period.

Table1: Summary of Patient Data: SHL and EHL Treatment Details

Variable	Mean (SD)
Age	26.8 (10.89)
Weight (kg)	56.1 (10.89)
SHL Dose (IU/Kg)	28.67 (2.58)
SHL Frequency	Twice a week to thrice a week
ABR Baseline	15.1 (3.16)
N8GP Dose (IU/Kg)	25.67 (3.77)
N8GP Frequency	Once a week
ABR After Switch	1 (Traumatic)
Duration (months)	8.4 (3.8)

Conclusion

The study shows that weekly administration of 26 IU/Kg N8GP is effective in reducing the annualized bleed rate in patients with haemophilia. Further research with a larger sample size is recommended to validate these findings and explore additional factors influencing treatment outcomes.

Benign Hematology-Clinical (BHC) PP-BHC-36

Evaluation of Indigenous Competitive Immunochromatography Based Rapid Test "sickle Check" for Point of Care Testing for Sickle Cell Disease in Hospital Setting

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Introduction

Sickle cell anemia (SCA) is a public health problem in central India with a prevalence of 9.4-22 %. Diagnostic test like HPLC require laboratories equipped with specialized instruments and highly trained pathologists and technicians which are unavailable in resource-limited settings. The crucial need for the development of a low cost point of care testing devices for sickle (POCT) has been elucidated by the World Health Organization as a priority. Initial Kits and device like sickle scan were developed in USA. Now many indigenous kits are also available. We intend to share our experience of validating indigenous POCT SICKLE CHECK ™ kit from Tulip Diagnostics against HPLC at our center.

Aims & Objectives

1. To assess the validity of competitive immunochromatography based rapid test for POCT for sickle cell disease in hospital setting.
2. To compare the diagnostic accuracy for detection of sickle cell disease against a gold standard Hb HPLC test

Materials & Methods

Study was conducted at AIIMS Nagpur, 550 unknown samples were analyzed from October 2023 to February 2024. Both the investigations HPLC Biorads variant II and SICKLE CHECK ™ from tulip diagnostics kit results were compared simultaneously considering HPLC as gold standard. Sensitivity and specificity of the Sickle Check test were calculated.

Result

For the sensitivity and specificity calculation, only 500 cases detected as Normal, sickle cell trait (AS) and sickle cell anemia (SS) by HPLC were considered.

Sensitivity for sickle check ™ to detect sickle cell trait was 96 .5% and specificity was 99.5% while

sensitivity to detect SCA was 100% and specificity was 99.7%

Out of remaining 50 cases, 3 cases of compound heterozygous sickle with beta thalassemia and 1 case of HBS with HPFH were diagnosed as SCA.All heterozygous hemoglobinopathies other than sickle were detected as normal by this POCT test.

Conclusion

Sickle check and other POCT devices give rapid results and is easy to interpret. The patient data sheet provided with each test card makes interpretation easy for health care worker and avoids any errors in interpretation across POCT devices working on different principles. Hence, it is a good device for community screening for sickle cell disorder. However, other hemoglobinopathies like beta thalassemia will be missed. Cases with faint band should be confirmed by HPLC. Patients testing positive with POCT device should be confirmed by HPLC or CZE to avoid mislabeling of compound heterozygous states.

Benign Hematology-Clinical (BHC) PP-BHC-37

A Twist on the Classic Presentation from Skin to Marrow. A Rare Progression

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Background

Pancytopenia is one of the most common indications for bone marrow (BM) examination. The etiology ranges from malignancy to infective and benign diseases. The involvement of BM by infections often presents as pyrexia of unknown origin. The most common infections involving the BM are leishmaniasis, HIV, tuberculosis, fungal infections, scrub typhus, parvovirus, malaria, filarial, and rarely leprosy. Here we present a case of a common disease rarely found in BM.

Case Presentation

Case: A 24-year-old male presented to medicine OPD with fever, per rectum bleeding, and red rashes all over his body. On investigations, he had pancytopenia and tested positive for dengue. He was also given platelet transfusion for the same but his general condition didn't improve. BM aspiration and biopsy were performed along with a biopsy from red rashes. Both showed an increased number of foamy histiocytes along with infection-related changes. Significant history was revealed later leading to a rare presentation of a common disease.

Diagnosis

1) Infected related changes
2) Peripheral Destruction of platelets
3) Hemophagocytosis secondary to Hansen's disease

Treatment

Treatment with Multi Drug Therapy which include Dapsone, Rifampicin and Clofazimine and also Thalidomide resulted in normalization of blood counts and healing of skin lesions.

Follow-up

Follow up with CBC, Peripheral smear and pancytopenia improved with intensive Chemotherapy and hematinics.

Conclusion

BM aspiration and biopsyalong with a high index of suspicion is an important investigation in the diagnosticworkup of cases of pancytopenia due to infective pathology which has therapeutic significance.It should be performed in all cases of persistent pancytopenia and should be evaluated in light of clinical details and supportive investigations.

Benign Hematology-Clinical (BHC) PP-BHC-38

Case Series of Thrombotic Thrombocytopenic Purpura- Tertiary Care Hospital Study

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Background

Thrombotic thrombocytopenia purpura is a rare life threatening condition which belongs to a group of RBC fragmentation syndromes characterized by Pentad of symptoms which include anemia, thrombocytopenia, fever, acute kidney injury and neurological manifestations. Early detection and prompt treatment is necessary for a good quality of life. Therapeutic plasma exchange is the gold standard treatment of choice. Here we present the case series of TTP patients at our institute, their presentation, diagnosis , treatment and outcome.

Case Presentation

This is a retrospective and prospective case series for 2 years which included 6 patients, of which all the reported cases were only females with median age of 38 years. Most cases had fever and bleeding manifestations. 83% (5) of patients had fever, 66% (4) had neurological manifestations and 50% (3) presented with bleeding manifestations. One case had multiple ecchymotic patches with bleeding PR with pregnancy loss.

Diagnosis

For all patients, routine blood investigations done which included were Blood counts, Renal function tests, Liver function tests, LDH, DCT, Bone marrow aspiration and biopsy and ADAMTS 13 profile. Complete blood counts showed bicytopenia with leucocytosis, Renal function showed altered creatinine and LFT showed indirect hyperbilirubinemia. LDH was elevated in all cases and Five cases showed low ADAMTS 13 activity with high ADAMTS antibody levels confirming Immune TTP.

One case showed complete absence of ADAMTS 13 activity and antibody. So molecular work up done which showed homozygous mutation in ADAMTS 13 gene in region of intron 26 suggesting congenital TTP.

Treatment

All patients received combined therapy with PLEX, pulse dose steroids for 3 days followed by 1mg/kg with a slow tapering of corticosteroids and totally 4 doses of rituximab. All patients tolerated the procedure well. During the PLEX procedure LDH and complete blood counts were monitored. Congenital TTP required FFP support.

Follow-up

All patients after completion of PLEX, LDH showed decreasing trend and normalization of blood counts. On follow up they are doing better both clinically and laboratory parameters.

Conclusion

Without treatment, TTP is almost universally fatal with mortality rate approaching 90%. With a timely institution of therapeutic plasma exchange mortality decreased and all patients survived.

A disintegrin and metalloprotease with thrombospondin Type 1 motif, member 13 (ADAMTS 13) is important in diagnosing and initiating treatment.

Benign Hematology-Clinical (BHC) PP-BHC-39

The Spectrum of Anemia: The Impact of Different Types on HbA2 Levels

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Introduction

The β-thalassemia trait is primarily diagnosed through elevated levels of hemoglobin A2 (HbA2 > 4.0%). However, nutritional anemias can alter HbA2 levels and create a diagnostic challenge in patients with borderline HbA2 levels (3.3–3.9%) when molecular testing for β-thalassemia is unavailable.

Aim and Objective

This study aims to investigate the effect of different types of nutritional anemia on HbA2 levels to better understand their implications for diagnosing β-thalassemia trait.

Materials and Methods

This retrospective observational study included 215 anemic patients who presented to a tertiary care hospital over a 15-month period (March 2023 to June 2024). Routine blood investigations, including complete blood count (CBC), high-performance liquid chromatography (HPLC), and biochemical investigations, were performed. Demographic profiles, CBC, HPLC, and biochemical parameters (serum iron, vitamin B12) were recorded from the hospital information system. Statistical analysis was conducted to compare HbA2 levels across the different anemia groups.

Results

Of the 215 patients, 145 were female, and 70 were male, with a median age of 25 years and a mean hemoglobin level of 7.7 g/dL. Among the patients:110 were case of iron deficiency anemia with microcytic hypochromic (MCHC) blood picture (mean serum iron = 42.4 mcg/dL, mean MCV = 67.5 fL) and a mean HbA2 level of 2.5%. 12 were β-thalassemia trait cases with an MCHC blood picture (mean MCV = 74.19 fL) and a mean HbA2 level of 7.86%. 29 were vitamin B12 deficiency anemia case with a macrocytic blood picture (mean vitamin B12 = 150 pg/mL, mean MCV = 118.92 fL) and a mean HbA2 level of 3.4%. 64 patients had a normocytic normochromic blood picture (mean MCV = 82.8 fL) with mean HbA2 level of 2.9%.

Conclusion

The diagnosis of β-thalassemia trait is not typically complicated by mild iron deficiency anemia. However, megaloblastic anemia can result in elevated HbA2 levels, creating diagnostic uncertainty. It is recommended to repeat HPLC testing after adequate supplementation of vitamin B12 and folic acid in cases of megaloblastic anemia before proceeding to molecular diagnostics.

Benign Hematology-Clinical (BHC) PP-BHC-40

Correlation of CD-4 Counts with Ocular Manifestations in HIV Positive Paediatric Patients

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Introduction

Acquired Immunodeficiency Syndrome (AIDS), the final stage of HIV infection, is characterized by a marked decrease in CD4 counts. In paediatric patients with AIDS, a wide range of ocular manifestations can occur, varying from dry eyes to Herpes zoster ophthalmicus. Understanding these manifestations in relation to CD4 counts is crucial for managing the ocular health of affected children

Aims & Objectives

This study aims to investigate the correlation between CD4 counts and ocular manifestations in HIV-positive paediatric patients.

Materials & Methods

We conducted a cross-sectional observational study at a tertiary care hospital, involving paediatric patients undergoing antiretroviral therapy (ART). Participants underwent a comprehensive ophthalmic examination, including visual acuity assessment and fundoscopy. CD4 counts were measured alongside other relevant clinical parameters.

Result

The study included participants with a mean age of 4.6 ± 3.5 years and a mean duration of HIV illness of 8.85 ± 3.72 years. The mean CD4 count among the participants was 807.36 ± 380.4 cells/mm^3. In the cohort with CD4 counts greater than 500 cells/mm^3, the majority exhibited no ophthalmic manifestations. Conversely, all participants with CD4 counts below 500 cells/mm^3 displayed some form of ocular involvement. Statistical analysis revealed a significant association between the presence of ocular manifestations and CD4 counts ($p = 0.001$)

Conclusion

Our findings indicate a strong correlation between CD4 counts and ocular manifestations in HIV-positive pediatric patients. Higher CD4 counts are associated with a lower incidence of ocular issues, highlighting the importance of regular monitoring of CD4 levels to prevent and manage ocular complications in this vulnerable population. Early intervention and appropriate ART adherence are essential for preserving eye health and overall quality of life in children living with HIV.

Benign Hematology-Clinical (BHC) PP-BHC-41

Unusual Presentation of a Rare Case-Congenital Bile Acid Synthesis Defect 1

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Background

Congenital Bile Acid Synthesis Defect 1 is a rare autosomal recessive inborn error of bile acid synthesis producing defective bile acids.

Case Presentation

10 month male child, born of non-consanguineous marriage, presented with multiple episodes of epistaxis and spontaneous knee joint bleed from 7 months of life. No hepatosplenomegaly, jaundice, radiological evidence of cholestasis. Notably, the family history is significant: the first sibling died shortly after birth due to suspected intracranial bleeding, while the second sibling experienced intrauterine demise (IUD) attributed to suspected neonatal cholestasis.

Diagnosis

Congenital Bile Acid Synthesis defect 1

Treatment

Vitamin K monthly

Follow-up

Not available

Conclusion

Early disease diagnosis is critical for early treatment with bile acid replacement therapy, with an excellent chance for recovery. In contrast, protracted diagnosis and treatment leads to poor outcome even death.

Benign Hematology-Clinical (BHC) PP-BHC-42

Factor VII Deficiency with Varied Clinical Spectrum: An Eye Opener

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Background

VII (FVII) deficiency is an uncommon autosomal recessive bleeding disorder characterized by isolated prolongation of prothrombin time with normal activated partial thromboplastin time. FVII is a vitamin K dependent coagulation factor synthesized in the liver and its deficiency may present mainly as inherited and rarely as acquired forms. FVII deficiency is caused by diminution or absence of blood coagulation FVII.

Case Presentation

We have 2 reported cases of factor VII deficiency, first case 65 yr old male who reported for cardiac surgery with no h/o any coagulation disorder and during PAC evaluation he was diagnosed to have Factor VII deficiency. He was operated and supported with rFVIIa. Second case a 16 yr old male presented with gum bleeding, associated with past history of cephalohematoma and prolonged umbilical bleeding. On through GI evaluation, he was supplemented with inj Vit K along with FFP and rFVIIa after which he responded well.

Diagnosis

Discussion : The age of the patient at the clinical onset may differ depending on severity of the deficiency. Patients with FVII deficiency have an increased risk of intraoperative and postoperative bleeding. Definitive diagnosis is confirmed by specific FVII assay in plasma. As a consequence of their rarity, clinical data, characteristic bleeding symptoms, pathophysiology and treatment remain limited.

Treatment

Administration of recombinant activated FVII (rFVIIa) is widely accepted in therapeutic management.

Follow-up

Regular follow up was been advised for both the cases.

Conclusion

Conclusion: FVII is an uncommon but important findings which should be considered in the general medical finding in the general medical setting when an isolated prolonged prothrombin time is detected. FVII coagulation activity did not correlate with clinical bleeding symptoms. Here we are reporting two diverse forms of FVII deficiency, which enable us to better understand the presentation of disorders at variable ages.

Benign Hematology-Clinical (BHC) PP-BHC-43

Impact of Volume Reduced Over Full Volume Platelet Transfusions in Tertiary Care Oncology Centre in Western India

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Introduction

Platelet transfusions are crucial for patients with thrombocytopenia. However, in oncology setup the frequent transfusion of platelet is often needed for supportive care of patients.

Aims & Objectives

This study aimed to retrospectively evaluate the impact of transfusions of full volume over volume-reduced platelet and ABO compatibility on platelet increments in patients undergoing platelet transfusions.

Materials & Methods

A retrospective analysis of apheresis platelet transfusions(n=159) in our tertiary care oncologist centre was conducted. Total 55 were full volume apheresis platelet(FVAP) was un-manipulated whereas 104 transfusions were volume reduced apheresis platelet(VRAP) was prepared by centrifugation of FVAP at g x 2000 for 10 minutes followed by reducing supernatant plasma and re-suspending the platelet. In addition Platelet increment were measured based on ABO compatible transfusions, age and CCI calculated to confirm refractory cases. Adverse transfusion reactions(ATR) are analyzed. The t test and spearman's rank correlation coefficient(rs) was analyzed and P value < 0>.

Result

Among 159 transfusion, 104 with VRAP and 55 with FVAP including 4 transfusions to refractory patients. Mean platelet increments were significantly higher in the FVAP(Mean±SD:31.2±21.9) than VRAP(Mean±SD:21.9±17.4). In FVAP transfusions, ABO-compatible platelets yielded higher increments(Mean=43.8) than ABO-incompatible(Mean=29.6) but in VRAP increment didn't significantly influenced(Mean=23 vs Mean=21). Refractory patient's observed mean CCI was 450. FVAP transfusions

incremented high in adults(Mean=44.1) than paediatric(Mean=34) comparing similar in adults and paediatric by both FVAP & VRAP. The comparative result of increment by FVAP & VRAP is statistically significant(p=0.029) and negative relationship by Spearman's coefficient(p=0.47). ATR wasn't reported for studied transfusions.

Conclusion

Our findings suggest that full-volume platelet transfusions generally result in higher platelet increments compared to volume-reduced transfusions. ABO compatibility appears to be more influential in FVAP transfusions. Even though the VRAP transfusions is indicated to reduce ATR like HTR, TACO, Allergy, etc. in patients. Adverse Transfusion Reactions may reduced significantly, since all transfused platelets are leuco-reduced and gamma-irradiated.

Benign Hematology-Clinical (BHC) PP-BHC-44

Atypical Presentation of Vitamin B12 Deficiency in Pregnancy: A Diagnostic Challenge with Overlapping Preeclampsia Features

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Background

Severe vitamin B12 deficiency can lead to hematologic abnormalities that resemble thrombotic microangiopathy disorders, such as hemolysis, elevated liver enzymes, and low platelet count (HELLP) syndrome. This overlap complicates the differentiation between preeclampsia and severe vitamin B12 deficiency, particularly in patients with unexplained anemia or thrombocytopenia.

Case Presentation

A 33-year-old female (G3P1L1A1) at 35 weeks gestation presented with severe anemia and thrombocytopenia. Laboratory results revealed a hemoglobin level of 4.5 g/dL and a platelet count of 30,000/μL. Coagulation profile and liver and renal function tests were normal. Although serum ferritin and iron profiles were within normal ranges, lactate dehydrogenase (LDH) levels were markedly elevated at 13,260 U/L, raising clinical suspicion of HELLP syndrome. A peripheral blood smear displayed moderate anisocytosis and normocytic to macrocytic red cells, including macroovalocytes, polychromatophils, fragmented RBCs, and nucleated RBCs (15-18 per 100 WBCs). The white blood cells showed a mild left shift and hypersegmented neutrophils, with occasional circulating megaloblasts. Further serological evaluation indicated low serum vitamin B12 levels (126 pg/mL). Based on the peripheral blood picture, complete blood count parameters, and serological findings, a diagnosis of severe vitamin B12 deficiency was established, likely contributing to megaloblastic anemia. This diagnosis clarified the pancytopenia and hemolytic profile due to ineffective erythropoiesis linked to severe vitamin B12 deficiency.

Diagnosis

Diagnosis of severe vitamin B12 deficiency was made postpartum.

Treatment

On postoperative day 1 (POD 1), the patient received 2 units of platelets, and intravenous magnesium sulfate (MgSO4) was continued for 24 hours. The antibiotics administered were intravenous monocef and metrogyl. Additionally, the patient was started on intravenous elderveit (2 ml) for 5 days to address her underlying deficiencies

Follow-up

The patient was started on injectable vitamin B12 and monitored with reticulocyte counts every other day. After treatment, the reticulocyte count improved from 0.75% to 1.75%, and vitamin B12 levels rose from 126 pg/mL to over 1000 pg/mL. Concurrently, hemoglobin increased from 6.1 g/dL to 8.7 g/dL, platelet count rose from 30,000/µL to 120,000/µL, and total leukocyte count improved from 3600/µL to 4900/µL.

Conclusion

This case, initially suspected as preeclampsia or HELLP syndrome, underscores the significance of recognizing undiagnosed vitamin B12 deficiency. Despite the lack of typical neurological symptoms, severe hematologic abnormalities were evident. Prompt identification and treatment of vitamin B12 deficiency led to substantial short-term improvements in laboratory results and better long-term outcomes for the patient.

Benign Hematology-Clinical (BHC) PP-BHC-45

ABO Antibody Titration Study: A Comparative Evaluation of Reproducibility of Haemagglutinin Titres in Automated Solid Phase Red Cell Adherence Versus Column Agglutination Technology

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Introduction

Determining platelet ABO Haemagglutinin titres is crucial for ensuring the safety and efficacy of blood transfusions Nonetheless, inconsistent outcomes across several platforms may provide challenges for clinical decision-making.

Aims & Objectives

This study aimed at comparing the ranges and equivalency of ABO Haemagglutinin titers across two distinct platforms: a fully automated blood bank analyzer with solid phase red cell adherence technology(SPRCA) to semi-automated gel based Column Agglutination Technology(CAT).

Materials & Methods

A total of 134 platelet donors blood samples were tested for ABO antibody titre for equivalency and range study for both IgM and IgG on both SPRCA and semi-automated CAT platforms. In addition 20 random samples were tested in triplicates for precision calculation. Pearson Correlation Coefficient Analysis were used. P value< 0.05 was regarded statistical significant.

Result

Equivalency among SPRCA and CAT platforms, for each isotype was 63.4% for IgM, 44.8% for IgG. IgM titers correlated well with SPRCA platform. The average titer ranges (in doubling dilutions) for the automated and semi-automated methods, respectively, were 5.6±2.4 and 5.6±2.4 for IgM and 4.3±3.7 and 4.5±3.5 for IgG.

In precision comparison of 20 samples, Mean of standard deviation in IgM results observed is 0.05 for SPRCA & 0.52 for CAT whereas in IgG, 0.12 for SPRCA & 0.52 for CAT.

Conclusion

The study evaluates that both automated SPRCA and semi-automated CAT platforms have shown strong positive correlation for IgM and moderate correlation for IgG antibody titre measurement. Study indicating higher precision in automated SPRCA platform compared to the semi-automated CAT platform. The SPRCA based fully automated platform offers improved efficiency, reproducibility and standardization compared to the semi-automated CAT platform.

Benign Hematology-Clinical (BHC) PP-BHC-46

Winds of Change: Unveiling a Neutrophilic Shift in Evans Syndrome

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Background

Evans syndrome, characterized by autoimmune haemolytic anaemia (AIHA) and immune thrombocytopenia (ITP), often presents diagnostic and therapeutic conundrums. It is associated with non-cross-reacting autoantibodies directed against antigens specific to red blood cells, platelets, or neutrophils. Although lymphocytosis is frequently described, this case highlights a unique post-rituximab neutrophilic response, adding complexity to disease management.

Case Presentation

A 21-year-old male presented with severe anaemia (Hb 5 g/dL), marked neutrophilic leucocytosis (TLC 70,000/mm^3), and indirect hyperbilirubinemia post-rituximab therapy.

Diagnosis

Direct Coombs Test was 4+ positive, confirming haemolysis.

Bone marrow aspirate demonstrated reactive granulocytic hyperplasia.

Treatment

Inj. Rituximab once weekly

Inj. Trenexa 1 gm thrice a day

Follow-up

Detailed autoimmune workup for co-existing comorbidities.

Conclusion

This case highlights the complexity of Evans syndrome with a neutrophilic shift post-rituximab. Understanding these unexpected haematological shifts and vigilant monitoring are critical for successful management.

Benign Hematology-Clinical (BHC) PP-BHC-47

Assessing the Effectiveness of Granulocyte Transfusions in the Management of Febrile Neutropenia Patients with Hematological Malignancies - A Single-centre Retrospective Study

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Introduction

The primary cause of non-relapse mortality in patients undergoing intense treatment for hematological malignancies is febrile neutropenia due to bacterial and fungal infections. GT could be an important adjunctive treatment option for severely neutropenic patients with infections unresponsive to adequate antimicrobial therapy due to increasing incidence of MDR in Inpatient setting. The main difficulties with GTX technique are donors procedural anxiety & safety issues with administration of dexamethasone and pre-harvest G-CSF

Aims & Objectives

To describe efficacy and survival rates with GT in FN episodes in a hemato-oncology unit. All patients who received GTX had grade 4 neutropenia (< 500 x 109/L) & FN/sepsis unresponsive to adequate doses of antimicrobial therapy

Materials & Methods

Retrospective study in patients of acute leukemia & other hematological malignancies who received GTX for management of FN as per standard criteria. Donors for GTX harvest received combination of G-CSF & dexa prior to granulocyte apheresis. Granulocyte was collected with automated spectra optia after entering the donor particular details. Yield to be collected based on pre count of donor (WBC & DC). The kit was primed with ACD-A & target inlet to anticoagulant ratio was kept as 13:1 with an infusion rate of 0.8ml/min/L of the TBV. Gamma irradiation (≥25 Gy) of granulocyte concentrates was done in all patients to prevent TA-GVHD

Result

Retrospective data of total 42 FN episodes in 22 patients receiving intensive CTX. Of these,16 patients were AML cases treated with 9-3+7 induction, 2 – HIDAC, 2-FLAG-IDA + Venetoclax & 3 - AIE induction.1 patient cml in myeloid blast crisis 1 case of DLBCL 1 case of refractory B ALL 1 case of AUL & 2 case of very severe aplastic anemia. 1 received BEAM conditioning regimen as part of ASCT for relapsed HL,. 11 patients on norepinephrine support for septic shock & 4 patients on mechanical ventilation. The mean GTX yield per harvest was 2.51 x 1010 cells/bag & mean dose of GTX administered was 3.96 x 108 cells/kg. Mean increase in TLC & ANC post-GTX were 488/µl and 447/µl respectively. There was 87% survival & no significant adverse events observed in donors & recipients.

Conclusion

GT administered at appropriate time & adequate dosage for managing FN episodes in profoundly neutropenic patients can be life-saving. Adequate motivation of GTX donors through proper counselling to minimize donor inconvenience to increase the number of GT is utmost.

Benign Hematology-Clinical (BHC) PP-BHC-48

A Study to Evaluate Microcytic to Hypochromic Ratio as a Discriminant Index in Patients with Hypochromic Anaemia and its Correlation With Thalassemia Trait

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Introduction

Differentiating iron deficiency anemia from thalassemia trait in patients with hypochromic anemia poses a challenge for both pathologists and clinicians, as this distinction affects the selection of further confirmatory tests. Accurately distinguishing between iron deficiency and thalassemia in individuals with hypochromic anemia is crucial for minimizing unnecessary investigations.

Aims & Objectives

In this study, we aimed to evaluate the performance of microcytic to hypochromic ratio (MicroR/Hypo-He, M/H ratio) as a discriminant index in hypochromic anaemia.

Materials & Methods

In this prospective study, we have examined 22 cases of hypochromic anemia, including instances of iron deficiency anemia, thalassemia, and other hemoglobinopathies. We utilized Receiver Operating Characteristic (ROC) analysis to determine the optimal cut-off value, sensitivity, and specificity of the M/H ratio for distinguishing thalassemia trait.

Result

We are continuing to collect additional cases, and the results will be analyzed and presented during the poster session following the final analysis and determination of the total number of cases.

Conclusion

The M/H ratio serves as a valuable discriminative index for differentiating thalassemia trait from iron deficiency anemia (IDA) in cases of hypochromic anemia, prior to diagnostic testing for thalassemia confirmation. A high M/H ratio is more indicative of thalassemia trait than IDA. Nevertheless, further studies are needed to solidify the M/H ratio's role as a screening tool for distinguishing thalassemia in hypochromic anemia.

Benign Hematology-Clinical (BHC) PP-BHC-49

Spectrum of Hemoglobinopathies at a Tertiary Care Centre in Northern India

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Introduction

Genetic disorders of hemoglobin are the commonest inherited red cell disorders worldwide and its prevalence varies with geographic distribution. These disorders are an important cause of morbidity and mortality imposing significant burden on health resources in our country. Hence, screening and early detection can help in proper management and prevention of more severe hemoglobinopathies in future generations.

Aims & Objectives

The present study aimed to observe the prevalence of the various hemoglobinopathies at a tertiary care centre in New Delhi.

Materials & Methods

This study was conducted in the Department of Pathology at ABVIMS and Dr. RML hospital, New Delhi. All patients referred for HPLC examination were included in this study over a period of five years (January 2019-December 2023). Relevant clinical data was collected. Haemogram with peripheral smear examination was done. All specimens were analyzed on BIO RAD Variant II which utilizes the principle of high-performance liquid chromatography (HPLC).

Result

Of the total 6304 cases on which HPLC was performed, hemoglobinopathies was detected in 360 (5.7%) cases. The various abnormal hemoglobin patterns detected were β-thalassemia trait, Hb E trait, Hb D-Punjab trait, Sickle cell trait, Hb E disease, Sickle cell disease, Thalassemia major, Sickle -β thalassemia, E-β thalassemia, Delta-β thalassemia, Hb J Meerut, Hereditary persistence of fetal hemoglobin and Hb Q-India trait. Beta thalassemia trait was the most common hemoglobinopathy found in 225 cases (62.5%); followed by Hb E trait 46 cases (12.7%) and HbD trait 31 cases (8.6%).

Conclusion

The present study highlights the burden of different types of hemoglobinopathies in Northern India. Beta thalassemia trait was found to be the most common hemoglobinopathy in this region. HPLC is a rapid, sensitive and useful method for detection of various hemoglobinopathies.

Benign Hematology-Clinical (BHC) PP-BHC-50

Beyond the Vacuole: Unmasking VEXAS Syndrome in MDS

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Background

The VEXAS syndrome is a recently recognized, acquired monogenic adult onset haemato-inflammatory syndrome marked by novel somatic mutations within the UBA1 gene. It is an acronym that stands for vacuoles, the E1 enzyme, X-linked inheritance, autoinflammatory tendencies, and somatic mutations. It presents as a severe progressive disease displaying varied characteristics that bridge hematologic and rheumatologic domains. In this case we describe the vague presentation of VEXAS syndrome.

Case Presentation

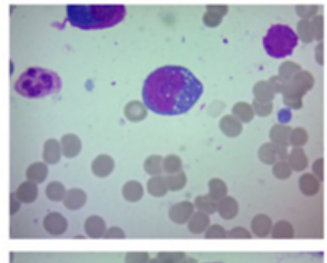
HD, 58-year-old male symptomatic for past 4-5 months. He presented initially with fever, polyarthralgia, Dacryocystitis. He also had a skin redness for which he received steroids with partial responses. He was found to have superficial and deep vein thrombosis elsewhere (Splanchnic and superficial cutaneous veins). He was referred to us for work up of anemia. He did not have ear/nose chondritis. His work up did not fit SLE, Still's disease or Rheumatoid arthritis. He did not have any addictions or any related family history. On examination he was moribund with difficulty in even turning in bed due to pain. He had erythematous rash over both the upper limbs which looked like sweet syndrome. He did not have any palpable nodes. There was no hepatosplenomegaly.

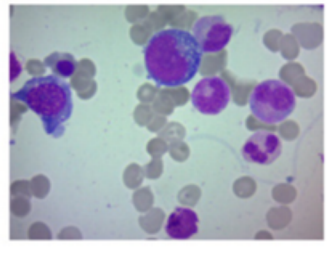
On initial evaluation his hemoglobin was 6.5gm/dL, MCV – 90.45 fL, MCH – 32.66 (pg/RBC), RDW – 14.5, WBC count of 8150, with differential N71/L20/M2/E1/B6, platelet count of 331000/microL. His bone marrow examination showed Hypercellular fragment with M:E Ratio, 2:1, Dyserythropoiesis, >10% Myeloid precursors with giant metamyelocytes, few hypolobated megakaryocytes seen. Vacuolations in bone marrow precursor cells in Myeloid and erythroid precursors were seen. There was no hemophagocytosis - Erythroid hyperplasia with dyserythropoiesis with granulocytic dysplasia. Fig 1 shows erythroid and myeloid progenitors with vacuoles. His UBA1 mutation (Variant c. 121A>G Exon 2) was positive by Sanger sequencing. NGS and karyotype was not done.

The c.121A>G mutation causes a substitution of methionine 41 with valine at the translation initiation site of the cytoplasmic UBA1b isoform. This mutation results in the loss of UBA1b and the expression of a shortened isoform called UBA1c. The UBA1c isoform is catalytically impaired compared to UBA1a and UBA1b.

Diagnosis

VEXAS syndrome with trilineage myelodysplasia





Treatment

Patient was planned for Azacytidine based treatment f/b allogeneic stem cell transplant if responsive but was lost to follow up.

Follow-up

Patient expired at home without getting any MDS directed treatment.

Conclusion

VEXAS syndrome has been recently described with more new cases being reported but can have an ambiguous autoinflammatory presentation from relapsing polychondritis to rare dacryocystitis/thrombosis/sweet syndrome as in our patient emphasising on high index of clinical suspicion and appropriate laboratory testing.

Malignant Hematology-Clinical (MHC) PP-MHC-1

A Fascinating Case of ABH Red Cell Antigenic Modification in Elderly Myelodysplastic Neoplasm Patient

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Background

Blood group antigens (A, B and H) are those complex carbohydrates which are attached to the red blood corpuscles and endothelial cells. These antigens are usually constant throughout the life of an individual, being the inherited traits. However, though rare, there are certain conditions mentioned in literature which may be definitely associated with modification of these antigens, leading to change of blood group e.g. leukemia's and lymphoma's, age related, immunosuppression and patients on chemotherapy.

Case Presentation

Blood group changes may be identified prior to an undiagnosed underlying leukemia or may indicate leukemia relapse.

62 years old male who was regular in getting medical check-ups owing to the service requirement and his initiatives since last 25 yrs was diagnosed as a case of MDS Increased blasts 2 with blasts comprising 09% with one blast showing Auer rod when he came for breathlessness on exertion for last 3 months.

Diagnosis

ABH red cell antigenic modification in a patient with myelodysplastic syndrome with increased blasts (MDS IB-2).

Treatment

When he was transfused for initial few months his blood group remained as B positive, however after a year, blood bank informed of changing of his blood group after repeating the samples.

Follow-up

The patient is still on 6 monthly follow up

Conclusion

Patient had never got transfused before that. It had implications on the morale of the patient as well a bit confusion in the staff as it was one of the first episode for most of them.

The blood group antigenic modifications are reported to be well correlated with the leukemic phase and reversion back on complete remission. Myelodysplastic neoplasm as we know is a kind of pre-leukemic state. The changing of blood group may happen in MDS, however a very few literature is on the records. The importance of knowing is awareness of the incident, clinical significance and impact.

Malignant Hematology-Clinical (MHC) PP-MHC-2

Extranodal DLBCL With Isolated Marrow Relapse After ASCT Treated with Reduced Intensity Fludarabine/busulfan Conditioning as Fifth Line of Management

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Background

DLBCL relapsing after autologous transplant has suboptimal outcomes, with very limited treatment options available.

Case Presentation

Mr. P, 35/M presented with prolonged fever in August 2018 and was diagnosed with extra nodal stage IV DLBCL based on bone marrow biopsy, with PET scan showing isolated involvement of multiple bones, liver and spleen.

Diagnosis

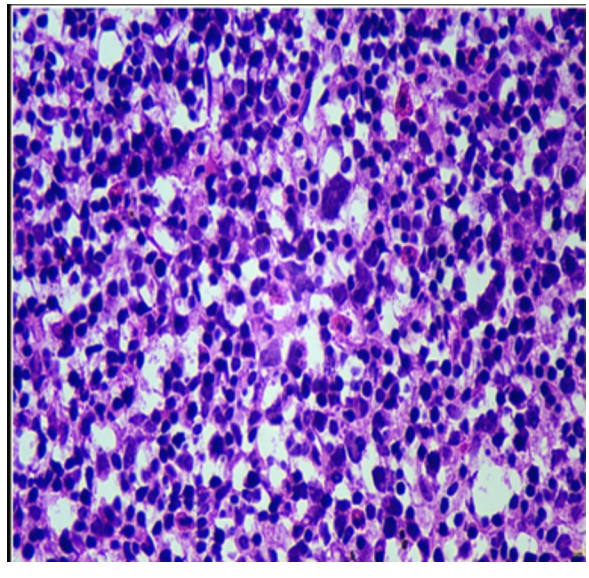
Diffuse Large B Cell Lymphoma, Stage IV.

Treatment

He received six cycles of RCHOP, after which repeat PET in March 2019 showed complete response. He had recurrence of persistent fever after six months, for which a repeat PET scan was done which showed increased uptake in multiple bones, suggesting relapse. He achieved a second CR with two cycles of RGDP, following which an autologous stem cell transplantation (ASCT) with BEAM conditioning was performed in January 2020. Repeat PET after three months in March 2020 again showed CR. In May 2023, he developed asymptomatic cytopenia, which was serially monitored. After WBC count fell to 1000/ul with 65% lymphocytes in PBF, a bone marrow biopsy was advised but refused, and a PET scan performed showed no evidence of disease. BM biopsy was done in February 2024 for further leucopenia, which showed BM infiltration with lymphoma (Fig 1), for which he received two cycles of RDHAP and achieved CR. A fully HLA-matched sibling donor was identified, and the patient underwent a reduced-intensity conditioning transplant with FluBu2/Csa/MTX 15/10/10/10 conditioning. Last dose MTX was skipped in view of jaundice and AKI.

Follow-up

His D28 chimerism was 97% donor, with normalization of counts and no symptoms. He has oral lichen planus like lesions and no other evidence of GVHD.



Conclusion

Our patient highlights the aggressive nature of extranodal DLBCL, characterized by recurrent relapses. Treatment options are limited, with CAR-T and Polatuzumab out of reach of most people in India. RIC AlloHSCT with higher dose of prophylactic methotrexate can provide potential long-term cure with minimal toxicity in younger patients and can prove to be cost effective in the long run.

Malignant Hematology-Clinical (MHC) PP-MHC-3

Primary CD-19 Negative Large Gut Extranodal DLBCL - A Very Rare Case Reported from a Rural Tertiary Care Centre

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Background

Extra-nodal CD19-negative Diffuse Large B-Cell Lymphoma (DLBCL) refers to cases where the lymphoma primarily affects extra-nodal sites, such as the gastrointestinal tract, skin, or central nervous system, and lacks the expression of CD19 which is a common B cell marker. The specific incidence of extra-nodal CD19-negative DLBCL is not well-documented in the literature. However, it is known that CD19-negative DLBCL is rare, representing a small subset of DLBCL cases. Within this small subset, extra-nodal involvement adds an additional layer of rarity.The absence of CD19 can complicate diagnosis and treatment, as standard immunohistochemical panels and targeted therapies that rely on CD19 expression may be ineffective.This rare variant poses significant diagnostic and therapeutic challenges.

Case Presentation

A 70 year old female patient presented with pain abdomen and generalised weakness. On routine examination CBC showed lymphocytosis with presence of reactive lymphocytes, USG whole abdomen showed a mass in recto-sigmoid junction and multiple large inguinal lymph nodes. FNAC of inguinal LNs revealed reactive changes. Biopsy was planned but in the mean time patient developed acute abdomen and underwent exploratory laparotomy with loop ileostomy. Specimen from colonic mass was sent for histopathological examination. Later bone marrow aspiration and peripheral blood smear was also done which came out to be within normal limit.

Diagnosis

On routine histopathological examination diagnosis of poorly differentiated malignancy favouring Non Hodgkin's Lymphoma was done. Following immunohistochemical analysis it was found to be CD 19, CD 3, CD 5, CD10, MUM1, Bcl6 negative and CD 20, CD 15, CD 45, Bcl2, Ki67 strongly positive. So the diagnosis of CD19 negative extra nodal diffuse large B-cell lymphoma was done.

Treatment

Patient underwent exploratory laparotomy and loop ileostomy following which histopathological diagnosis was made. Currently the patient is undergoing CHOP therapy in our institution on a outpatient basis.

Follow-up

Patient is currently hemodynamically stable and further follow up will be done after completion of chemotherapy.

Conclusion

Though CD19 negative extra nodal DLBCL is very rare still we came across a case of extra nodal DLBCL which did not express a common B-cell marker. This subset of DLBCL may complicate treatment because targeted CAR-T therapy in CD19 negative lymphoma might not be beneficial , potentially leading to poorer clinical outcomes. Further research is needed to elucidate the underlying biology of CD19 negative DLBCL and to identify effective treatment approaches for this distinct and challenging group of patients.

Malignant Hematology-Clinical (MHC) PP-MHC-4

Safety and Efficacy of R2CHOP in Untreated Diffuse Large B-cell Lymphoma: A Single Centre Retrospective Study

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Introduction

Diffuse Large B-Cell Lymphoma (DLBCL) is a common lymphoid cancer, accounting for 30% of all non-Hodgkin lymphomas (NHL), with over 50% of patients diagnosed being over 60. The addition of rituximab (R-CHOP) has improved outcomes, but 40% of patients still relapse or become refractory. Lenalidomide, particularly effective in activated B-cell lymphoma, shows promise when combined with R-CHOP (R2CHOP). The REAL07 study in elderly patients reported an 86% complete response rate, though with some grade 3-4 neutropenia. Sanjal H Desai et.al., reported promising PFS, EFS and OS rate at 24 months with this regime i.e., 84.4%, 84.5%, and 97%. New first-line treatments are needed to improve long-term outcomes.

Aims & Objectives

Our study will assess the safety and efficacy of R2CHOP in newly diagnosed LBCL patients in the Indian population, focusing on overall response rate (ORR), response rate (RR) at two years, progression-free survival (PFS), overall survival (OS), and the safety profile of the regimen.

Materials & Methods

This retrospective study will analyze data from patient records (Jan 2017 – Feb 2023) of newly diagnosed DLBCL patients aged 18+ treated with Lenalidomide plus R-CHOP. Descriptive statistics, Kaplan-Meier survival analysis, and log-rank tests will be used, with Chi-square and t-tests for variable analysis. Patients with relapsed/refractory DLBCL or those who received other treatments will be excluded.

Result

The study included 23 patients with a median age of 57 years, with 52.2% ≤ 57 yrs of age. Most (69.6%) had a performance score <2, and 60.9% had an IPI score <3. Stage III-IV disease was found in 56.5%, and 34.8% had extranodal involvement. Duration of lenalidomide was 3.5 (1.4 – 4.2) months. Overall response rates were 69.6%, with 65.2 achieving complete response. The 3-year OS was 79.4%, and PFS was 50.1%. Baseline factors, such as age, score, stage, elevated LDH, and extranodal involvement, did not significantly affect OS or PFS.

Conclusion

In conclusion, R2CHOP showed strong efficacy in untreated Diffuse Large B-Cell Lymphoma, with high response rates and favorable survival. However, relapse and progression in some patients suggest the need for ongoing monitoring and additional strategies for high-risk cases. Overall, it remains an effective and safe treatment option.

Malignant Hematology-Clinical (MHC) PP-MHC-5

Clinical Outcomes of Continuing ABVD in Classical Hodgkin Lymphoma with Interim PET-positivity

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Introduction

Interim positron-emission tomography–computed tomography (iPET-CT) is used to assess early response to chemotherapy and guide further management in classical Hodgkin lymphoma (cHL). Intensification of therapy based on iPET positivity is considered a standard approach, however in practice, many centers continue the ABVD protocol, and there are no randomized trials comparing these 2 approaches. The standard practice in our center has been to continue ABVD in patients who have a Deauville score (DS) of 4, with end-therapy consolidation RT if indicated, based on initial bulk disease and end-of-treatment (EOT) PET positivity.

Aims & Objectives

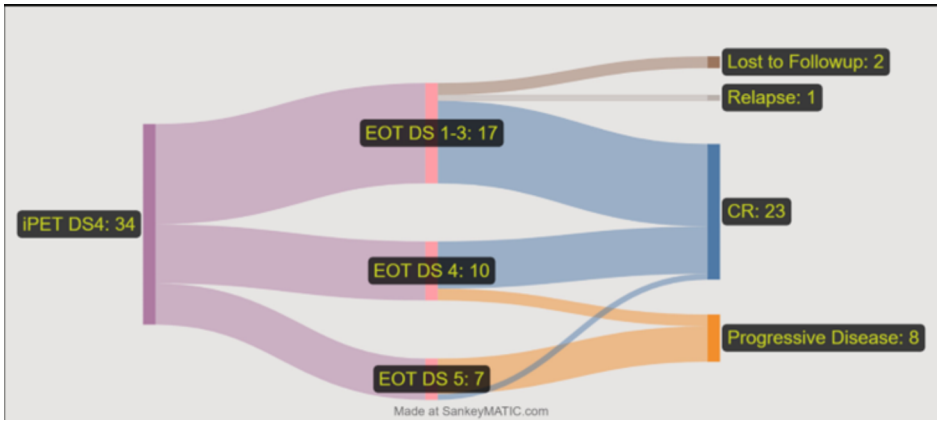
This study aims to document outcomes in patients with DS4 at iPET, who continued on ABVD regimen, with or without consolidation with RT.

Materials & Methods

Retrospective analysis of treatment outcomes in patients with cHL treated with ABVD regimen between 2015-2023, and iPET-CT was done for early response assessment, using the standardized 5-point DS. Event was defined as disease progression, relapse or death due to any cause. Demographic and follow-up data was collected from institutional electronic medical records and analyzed with IBM SPSS software version 23.0.

Result

Out of 425 patients with cHL treated between 2015-2023, 235 patients had an interim PET-CT, and 34 patients (14.4%) had DS4. All 34 patients continued ABVD for a further 4 cycles. At EOT-PET, 17(50%) achieved complete remission (CR) (DS 1-3), 10(29.4%) had persistence of DS4, and 7(20.6%) had radiological progression (DS5). Consolidation RT was given to 15 patients (44.1%).



At a median follow-up of 33 months (Range 10-110), 23 patients were in clinical CR (EOT-PET: DS 1-3 n=14, DS4 n= 8, DS5 n=1), 8 had biopsy-proven progression (EOT-PET: DS5 n=6, DS4 n=2), 1 relapsed (EOT-PET DS2) and 2 were lost to follow-up (Figure 1).

The 2-year event-free survival (EFS) was 76.4 + 7.3 %, with EOT DS1-3, DS4 and DS5 2-year EFS of 100%, 80% and 14.3% respectively (p=0.000).

Conclusion

Continuation of ABVD in patients with iPET-DS4 has acceptable treatment outcomes, with 2-year EFS comparable to the BEACOPP regimen with less toxicity. Prospective trials are needed to definitively compare continuation of ABVD with escalated regimens such as BEACOPP.

Malignant Hematology-Clinical (MHC) PP-MHC-6

Clinical Spectrum and Short-term Outcome of Patients with Acute Myeloid Leukemia from India

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Introduction

Acute Myeloid Leukemia in India presents unique challenges of frailty, infections and poor treatment adherence, necessitating a description of local epidemiology and outcomes and to inform effective interventions.

Aims & Objectives

To describe short term outcomes in patients with AML in India

Materials & Methods

Adult AML patients admitted to a tertiary care center between October 2022 and March 2024 were prospectively evaluated to describe clinical, epidemiological patterns, and one-year survival.

Result

A total of 50 patients were enrolled, with a median age of 54 years (IQR 37-66) and M:F ratio of 1.3:1. Commonest presenting symptoms included fever (80%), cough (30%), and bleeding (18%). Ten (20%) patients were diagnosed to have APML and shifted to Arsenic/ATRA. The median WBC count at baseline was 22,450/µL (IQR 2730-48050). Genetic analysis using RT-PCR detected NPM1, FLT3-ITD, and FLT3-TKD mutations in 16%, 12%, and 4% of patients, respectively. Thirty patients underwent chest imaging, of which 22 (73%) had evidence of active infection. Treatment included HMAs in 11 (22%), HMAs with Venetoclax in 16 (32%) and intensive chemotherapy in 6 (12%) patients. A total of 18% patients did not start any treatment. After three months of follow up, 32% had died, 12% were lost to follow-up and only 50% were continuing treatment. At the end of follow up period, 54% patients had died and 14% were lost to follow up. The median overall survival was 156 days.

Conclusion

This study highlights challenges in the treatment of AML in India. Only a small percentage of patients receive intensive chemotherapy. Early mortality and loss to follow-up remain major challenges.

Malignant Hematology-Clinical (MHC) PP-MHC-7

Tug of War : Chronic Myeloid Leukaemia in Megakaryocytic Blast Crisis V/S Acute Megakaryoblastic Leukaemia (AML-M7)

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Background

Chronic Myeloid Leukemia (CML) in megakaryocytic blast crisis and AML-M7 are rare disorders comprising of <3% and 1.2% of all haematological malignancies respectively. CML in megakaryocytic blast crisis is characterised by the presence of basophilia and megakaryoblast fragments in the peripheral blood which may not be present in AML-M7. Specific difference between the two entities is the presence of BCR-ABL fusion protein of p210kDa, specific for CML. We report a case of young lady with easy bruisability, diagnosed as a case of CML in megakaryocytic blast crisis based on peripheral blood smear(PBS) , bone marrow examination, flow cytometry and molecular studies.

Case Presentation

A 27-year-old lady with no significant co-morbidities presented with easy bruisability following minimal trauma for 03 months duration. On evaluation, she had anaemia (Hb- 10.2 g/dL), leucocytosis (total count - 13,780/µL) and adequate platelets (114x10^3/µL). PBS showed 56% blasts with left shift and increase in basophils and blasts . The blasts were large with high N:C ratio, cytoplasmic blebbing and occasional blast with Auer rods. Ultrasound abdomen revealed hepatosplenomegaly. Bone marrow aspirate showed 59% blasts and biopsy revealed marked marrow fibrosis (Grade II-III) with immature cell aggregates and megakaryocyte clustering. On Flow cytometry, 02 subset of blasts were identified, 65% of which were positive for CD34, CD38, cyCD41 and negative for CD117, HLA-DR. The other subset (27.7%) were positive for CD38, CD34, CD117, HLA-DR and negative for CD13, CD14, CD64. CyMPO was negative in both the population of blast. Thus, confirming the presence of both megakaryoblasts and myeloid blasts.

Diagnosis

Based on morphology and flow cytometry, differential diagnosis were AML-M7 v/s CML in megakaryocytic blast crisis-de novo. Molecular mutation analysis showed the presence of BCR-ABL fusion protein of 210kDa, thus confirming a diagnosis of CML in megakaryocytic blast crisis.

Treatment

The patient was started on Dasatanib, Azacitidine and Venetoclax (6 cycles)

Follow-up

Post 6 cycles, bone marrow was performed for remission status and noted to be in morphological remission. Haematopoetic Stem cell transplant has been planned.

Conclusion

CML in megakaryocytic blast crisis has a poor prognosis with low survival rate. Hence this case report emphasises on differentiating the blast morphologically for early diagnosis and confirming with molecular studies so as to initiate treatment at the earliest.

Malignant Hematology-Clinical (MHC) PP-MHC-8

A Challenging Case of Chronic Myeloid Leukemia (CML) With Compound Mutations Including T315I, Rapidly Progressing to B-lymphoid Blast Crisis

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Background

Pediatric CML constitutes around 3-5% of all childhood malignancies. Treatment with TKIs has revolutionized the treatment of such patients, but presence of TKI resistant clones make it very difficult to prevent progression of the disease.

Case Presentation

A 9-year-old male child presented with fever and hepatosplenomegaly. Peripheral smear revealed marked left-shifted leukocytosis (>4.00 lacs/cumm) with basophilia and 3% blasts. Reverse transcriptase Polymerase Chain Reaction (RT-PCR) detected e14a2 type of p210 transcript. Bone marrow was hypercellular with increased granulopoiesis, myelocyte predominance without increased blast favoring CML in chronic phase. The patient was started on Imatinib at 340 mg/m2/day as per institutional policy. He did showed response initially, but drug was stopped in view of grade IV thrombocytopenia. On recovery, it was restarted but soon TLC started rising. Peripheral blood flow cytometry confirmed the diagnosis of B-lymphoid blast crisis. Mutation analysis by next generation sequencing revealed two-point substitutions in ABL gene i.e E255K and T315I. Child was started on High-risk arm of ICICLE B-ALL Induction protocol along with Dasatinib, due to non-availability of Ponatinib. Post induction, bone marrow was in morphological remission with incomplete count recovery, and undetectable B-MRD by flowcytometry, however, RQ-PCR for BCR-ABL was positive. Since, the presence of compound mutations such as E255K plus T315I confers resistance against all approved TKIs, including Dasatinib, Ponatinib and newer drugs such as Asciminib as per the latest ELN 2023 recommendations, he is being taken up for a matched sibling donor - hematopoietic stem cell transplant.

Conclusion

Prompt detection of such resistant TKI clones by next generation sequencing can guide in precise therapeutic intervention and prevent progression to advanced phases of disease. A more robust data of more such cases and how they response to TKI might answer these questions.

Malignant Hematology-Clinical (MHC) PP-MHC-9

Intravascular Large B Cell Lymphoma - Recognizing the Chameleon

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Background

Intravascular large B-cell lymphoma (IVLBCL) is a rare (less than one per million) and highly aggressive form of lymphoma marked by the nearly exclusive proliferation of large cells within the interiors of blood vessels of all sizes. Here, we discuss our experience dealing with one such case in our hospital.

Case Presentation

A 62-year-old lady, known hypertensive, was admitted to our hospital with cognitive decline, and memory disturbances for one month. Before this, she had left lower limb weakness secondary to a cerebrovascular accident, was on regular physiotherapy, and was ambulatory till about a month before this admission. Examination revealed left hemiparesis, and rest of the systems were normal

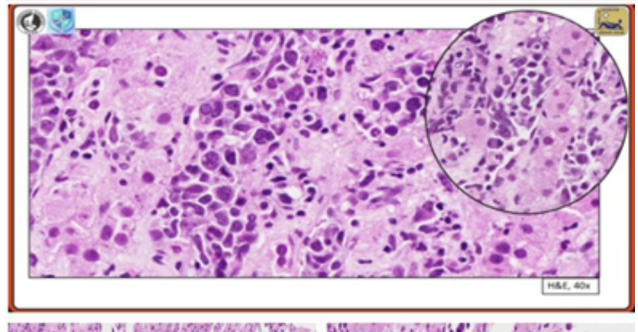
Diagnosis

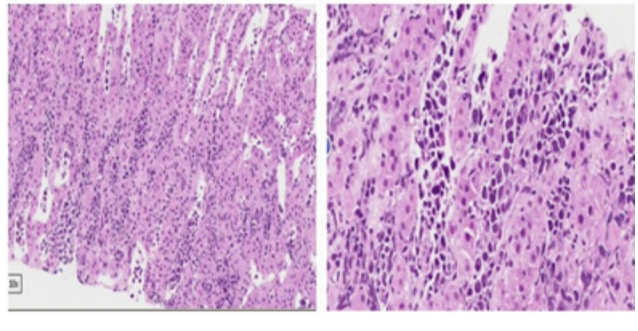
Given the rapidly progressive cognitive decline, MRI(BRAIN) was done which showed similar areas of diffusion restriction in bilateral centrum semi-ovale and fronto-parietal region comparable to MRI(BRAIN) done in 2023. CSF analysis was normal. Given these findings, PETCT was performed, which showed metabolically active lymph nodes (SUV 33) at the root of superior mesenteric artery and aortocaval region and bilateral bulky adrenals - likely neoplastic (? Lymphomatous).

CT-guided biopsy of left adrenal gland was done, and this showed dilated sinusoids filled with dyscohesive medium to large sized atypical lymphoid cells. IHC showed positivity for CD20, MUM1. CD3, CD5 and CD10 were negative with Ki67 of 80%. The features were consistent with Intravascular Large B Cell Lymphoma.

Treatment

She was started on a high-dose methotrexate based chemotherapeutic regimen (MATRix- with thiotepa omitted because of frailty). She achieved CMR after two cycles. She further had 2 cycles of attenuated R-ICE chemotherapy for systemic disease. The course of treatment was complicated by multiple episodes of neutropenic sepsis, which was managed with broad-spectrum antibiotics, Colony stimulation factors, and buffy coat.





Follow-up

She is currently undergoing a Carmustine-thiotepa conditioning autologous transplant

Conclusion

IVLBCL is a rare entity that has multiple presentations. Cognitive decline and memory disturbances have not been described with IVLBCL. Hence this becomes one of the rare presentation of this diverse disease.

Malignant Hematology-Clinical (MHC) PP-MHC-10

Clinical Profile & Treatment Results of Pediatric Acute Myeloid Leukemia Patients : A Single-center Experience from AIIMS Rishikesh

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Introduction

The outcome of acute myeloid leukemia (AML) in childhood has improved considerably in recent past with usage of intensive chemotherapy. Among different protocol, we have been using BFM (Berlin-Frankfurt-Munster) 2004 pediatric AML protocol mainly in children less than 10 years and "7+3" induction regime in adolescent patients (11-18 years).

Aims & Objectives

To study the clinical profile and outcomes of newly diagnosed pediatric AML patients of less than 18 years.

Materials & Methods

This is a single-center, prospective observational study conducted in all newly diagnosed AML patient of less than 18 years. Patients were managed with BFM 2004 pediatric AML protocol mainly in children < 10 years and "7+3" induction regime in adolescent (11-18 years). All patient underwent bone marrow examination at day 14 of induction, post induction, after consolidation and post completion of maintenance along with measurable residual disease (MRD) assessment by flowcytometry method.

Result

Total 20 patients treated between September 2022 till September 2024 were analyzed. Median age was 8.3 years, M: F ratio 2.3:1. As per both BFM 2004 & ELN 2022, 45 % patients were belonging to favorable risk category. AML1: ETO, BCR::ABL1 & NPM1 mutated AML was seen in 40 %, 5 % and 5 % respectively. NGS was done in total 20 % of patients where NRAS was most commonly detected in 10 % of patients. One each patient was Philadelphia positive AML & familial AML (Both monozygotic sisters were NPM1 mutated AML). Fifteen percent of patients had CNS involvement at diagnosis. Total 65 % & 35 % patients received BFM 2004 & '7+3' regimen respectively. Post induction 80 % patient were in complete morphological remission and 70% achieved MRD negative status. Currently 15 % each is receiving BFM & Azacitidine maintenance. One patient has undergone haploidentical allogenic stem cell transplant. Currently 55 % are in complete remission,20 % has relapsed and 15 % patients died. Results are given in Table 1.

Number of patients	n = 20
Age	Median age: 8.3 years
Gender	Male:14 (70%) Female: 6(30%)
AML Risk Groups (BFM 2004)	Favourable risk: 9(45%) Adverse risk: 11(55%)
AML Risk Groups (ELN 2022)	Favourable risk:9 (45%) Intermediate risk:6 (30%) Adverse risk: 5(25%)
AML Multiplex PCR	AML1: ETO :8(40%) BCR::ABL1 (minor):1(5%) NPM1:1(5%)
NGS (n=4)	NRAS:2(10%) CDAN1:1(5%) GATA2:1(5%) NRAS, ZRSR2, SETD2, KMT2A, MLLT10:1(5%)
CNS III status at diagnosis	3(15%)
Induction therapy	BFM 2004 (65%) 7+3:7 (35%)
Consolidation therapy	BFM 2004 (65%) HiDAC: 7(35%)
Maintenance therapy	BFM 2004:3(15%) AZACITIDINE: 3 (15%)
Treatment response post induction	Complete response (CR): 16(80%) Partial Response (PR): 1(5%)
Flow-MRD status post induction	MRD negative (< 0.1%):14(70%) MRD positive (≥ 0.1%):3(15%) Not available:3(15%)
Flow-MRD status post consolidation	MRD negative (< 0.1%):7(35%) MRD positive (≥ 0.1%):1(5%) Not available:12(60%)
Survival status	Alive: 17(85%) Dead: 3(15%)

Conclusion

In our single-center experience in management of pediatric AML, BFM 2004 has been a viable intensive regimen especially in children less than 10 years and "7+3" regimen in adolescent patients.

Malignant Hematology-Clinical (MHC) PP-MHC-11

Successful Long-term Complete Remission in Hodgkin Lymphoma with Experimental Lenalidomide and Celecoxib Therapy : A 3-year Case Study

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Background

5%–10% of Classical Hodgkin Lymphoma (cHL) patients are refractory to initial therapy, and 10%–30% relapse after achieving complete remission (CR). For primary refractory disease, the standard treatment is salvage therapy followed by autologous stem cell transplant (ASCT). Despite this, the 5-year freedom from failure is only 31%, with overall survival (OS) at 43%, meaning most patients relapse. There is limited guidance for patients ineligible for intensive regimens or transplantation.

Case Presentation

A 59-year-old male with Classical Hodgkin Lymphoma, treated with 6 cycles of ABVD and 3 cycles of salvage chemotherapy (GDP) after a relapse, underwent high-dose therapy (BEAM) with ASCT in December 2020. Three months post-ASCT, he achieved a complete metabolic response (CMR), with PET-CT showing retroperitoneal and mesenteric lymph nodes (SUVmax 2.08, DS II). He received 30cGy IGRT. Three months later, PET-CT revealed a supraclavicular node (SUVmax 4.13, DS III) and enlarged abdominal nodes. A Tru-Cut biopsy confirmed relapse. He received 4 doses of nivolumab (every 15 days) and was planned for allogeneic SCT, but new mediastinal nodes (SUVmax 9.2) appeared.

Diagnosis

Relapsed/Refractory Classical Hodgkin Lymphoma

Treatment

Lenalidomide (25 mg, 21/28 days) and celecoxib (200 mg BD) for 6 cycles.

Follow-up

After 6 cycles, PET-CT showed a complete metabolic response. Maintenance lenalidomide (5 mg/day) was initiated. A PET-CT after 12 months confirmed remission, which has been sustained for 30 months until the last follow-up in September 2024.

Conclusion

cHL has a poor prognosis when relapsing after autologous SCT. In this case, the patient was ineligible for allogeneic SCT, making it challenging to achieve a meaningful response with limited treatment options. Although the lenalidomide and celecoxib combination has not been evaluated in clinical trials, the patient achieved CR, sustained for 30 months and continuing at the last follow-up.

Malignant Hematology-Clinical (MHC) PP-MHC-12

Transformation From Multiple Myeloma to Chronic Lymphocytic Leukemia: A Once in a Blue Moon Event

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Background

Multiple myeloma (MM) and chronic lymphocytic leukemia (CLL) are B-cell malignancies predominantly affecting older adults. While treatments for MM have significantly improved survival rates, they have also led to an increased incidence of secondary malignancies, notably acute myeloid leukemia/myelodysplastic syndrome (AML/MDS). Transformation from CLL to MM is rare, with no documented cases of the reverse. This report details an unusual case of a 78-year-old woman who, after being treated for MM, developed CLL eight years later.

Case Presentation

The patient initially presented at age of 70 with weakness and exertional dyspnea, when she was diagnosed with anemia. After ineffective treatment for anemia, on further evaluation she was diagnosed with Multiple myeloma (MM IgM+K, ISS-III) following evaluation for pancytopenia and renal dysfunction. She received twelve cycles of the VTd regimen, transitioning to Lenalidomide maintenance. Due to declining renal function, she was switched to Thalidomide but was lost to follow-up for four years. Upon resuming care, she remained stable on Thalidomide maintenance. Seven months later, she reported increased fatigue, prompting further investigation which revealed elevated total cell counts and atypical lymphoid cells indicative of Chronic Lymphocytic Leukemia (CLL)- Rai Stage IV.

Diagnosis

Initial diagnosis included anemia and renal dysfunction, with bone marrow showing 40% plasma cells and serum electrophoresis revealing a distinct IgM and Kappa band establishing the diagnosis of MM.

Upon developing atypical lymphocytosis, peripheral blood analysis by flowcytometry showed 46% atypical cells, positive for CD45, CD20, CD5, CD200 and deletion13q, confirming CLL. Atypical findings were bright expression of CD20 and FMC-7. (Table 1)

Treatment

In 2017, the patient underwent XII cycles of VTd followed by Lenalidomide maintenance & later was switched to Thalidomide due to renal dysfunction. Upon progression to CLL, she was treated with Acalabrutinib.

Follow-up

Currently, the patient is responding well to Acalabrutinib but continues to require monthly blood transfusions.

Conclusion

Though plasma cell neoplasms and CLL originate from B-cells, the transformation between these malignancies is exceedingly rare. This case prompts further evaluation of the pathophysiology and mechanism of such transition.

MULTIPLE MYELOMA (Year 2017)	
Parameters	
Hb (g/dL)	7.1
TLC (per cumm)	3100
PC (per cumm)	1,00,000
BM Plasma Cells	40%
Total Protein/Albumin (g/dL)	6.6/2.88
Myeloma band	Distinct: IgM+Kappa.
IgG/IgA/IgA (g/L)	12.90/0.284/9.22
Kappa/Lambda chain (mg/L)	58/33.40
Kappa/Lambda Ratio	1.74
Beta 2 microglobulin (ng/mL)	37843
Creatinine (mg/dL)	2.84
Calcium (mg/dL)	6.9

PROGRESSED TO

CHRONIC LYMPHOCYTIC LEUKEMIA (Year 2024)	
Parameters	
PBS	46% atypical cells
Flowcytometry	
Positive for	**Negative for**
CD45	CD10
CD20	CD23
CD200	CD3
CD5	CD38
FMC7	CD138
Lambda Clonality	Kappa
FISH Panel	
Positive for	**Negative for**
13q deletion	t(11:14)

Malignant Hematology-Clinical (MHC) PP-MHC-13

Bortezomib's Blindside : Chalazion's Unexpected Arrival

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Background

Multiple myeloma is a common haematological malignancy with the varied presentation. It responds well to chemotherapy. Most of the regimens includes Bortezomib as a important component of the chemotherapy being the first line for the management of the same. Bortezomib can cause various side effects ranging from nausea ,vomiting to hypersensitivity reactions.

Case Presentation

A case study involving 55 yr old female with multiple myeloma on Chemotherapy presented to OPD with the complaints of bilateral eyelid swelling. On evaluation and ophthalmology cross consultation diagnosed as the case of Bortezomib induced Bilateral Chalazia.

Diagnosis

Bortezomib induced Bilateral chalazia in a case of Multiple Myeloma patient on Borrtezomib based chemotherapy.

Treatment

Patient responded well to conservative management and discontinuation of the Bortezomib and all the symptoms were resolved.

Follow-up

Patient followed up regularly in haematology OPD as well as Ophthalmology OPD with relevant examinations and laboratory investigations.

Conclusion

Chalazion aka tarsal cyst can be one of the rare but hazardous side effect of the first line chemotherapeutic drug for multiple myeloma i.e Bortezomib. Early diagnosis and prompt intervention can prevent the catastrophic eye complications. High index of suspicion is the key to manage the rarely occurring adverse drug reactions like the one involved in the case report.

- Bilateral eyelids showing Chalazion .

- Resolving Chalazion after with-holding Bortezomib

Malignant Hematology-Clinical (MHC) PP-MHC-14

Pediatric Ischemic Stroke in a C/O APML with Sickle Cell Trait

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Background

Acute promyelocytic leukemia(APML), a subset of acute myeloid leukemia is characterised by fusion gene transcript PML-RAR-alpha with presence of large atypical promyelocytes and other myeloid precursors in various stages of development in the peripheral blood and has good prognosis. It typically presents with life threatening bleeding diathesis which worsens with chemotherapy. Thrombotic event as a presentation is rare. Pediatric stroke is one such presentation and can occur in children and is associated with significant morbidity and mortality. It can be due to primary disease itself, or secondary to DIC resulting from bleeds, or triggered by underlying hypercoagulable states.

Case Presentation

We report one such case of 11 year old who presented with right hemiparesis with UMN facial palsy and motor aphasia. Investigations showed leukocytosis(TLC: 31580/microL), (69%)blasts with burst positivity for MPO on cytochemistry and Flowcytometry was consistent with Acute Promyelocytic Leukaemia. PML-RARA fusion gene was detected. HPLC sent as a part of stroke workup revealed the child to be sickle cell trait. MRI revealed left MCA infarct with Left MCA thrombus (M2 segment).

Diagnosis

Left MCA infarct in a c/o high risk APML with sickle cell trait.

Treatment

Child was initially started on Aspirin, Atorvastatin. After diagnosis of APML, Arsenic trioxide 0.15 mg/kg iv, ATRA 25 mg/m² via nasogastric tube and Mitoxantrone was started as per Vellore high risk induction protocol along with Enoxaparin and platelet count was maintained>30000/microL. CBC and PT/aPTT/fibrinogen was monitored twice daily. Platelet concentrate and cyroprecipitate was transfused as required.

Follow-up

She was discharged post induction in morphological complete remission. She was lost to follow up due to poor social support despite contacting on multiple occasions.

Conclusion

This case highlights ischemic stroke as rare primary presentation of pediatric APML. The presence of Sickle trait increases the risk of prothrombotic events. It emphasizes that multiple factors may contribute to the disease process, complicating the situation. Therefore, vigilance is essential for accurate diagnosis and effective treatment as soon as possible to decrease the related morbidity and mortality.

Malignant Hematology-Clinical (MHC) PP-MHC-15

A Mass on the Head : A Rare Presentation of Plasmacytoma

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Background

Plasmacytoma is a rare type of plasma cell malignancy. It commonly involves the upper airway areas and also the scalp. However, a huge mass over the scalp is rare

Case Presentation

A 47-year-old female presented to the neurosurgery outpatient department with an 8-month history of gradually progressive forehead swelling, generalized weakness, and bone pain. Initial evaluation shows Hb-8.9g/dl, creat-0.7mg/dl, LDH-288 IU/l, ESR-68mm, S.globulin-2.8 mg/dl.

Diagnosis

A CEMRI brain scan identified a heterogeneous extra-axial mass lesion involving the frontal bone and multiple small raindrop- like lesions in the calvaria. FNAC of the lesion showed atypical cells with a plasmacytoid appearance and IHC suggestive of Kappa restriction. She was referred to the hematology outpatient department for further investigation. Bone marrow studies revealed plasma cell aggregates positive for CD68 and CD138. Serum protein electrophoresis (SPEP) did not detect a monoclonal peak, but serum free light chain (SFLC) analysis showed an elevated κ/λ (343/26.7) ratio (>100). The patient was diagnosed with skull plasmacytoma and multiple myeloma.

Treatment

She was initiated with the bortezomib, lenalidomide and dexamethasone (VRd) regimen and supportive therapies. After two cycles of chemotherapy, she received 30 Gy of radiotherapy in 10 fractions to the frontal lesion. Gradual improvement was noted, with resolution of her frontal swelling. She continued VRd and received a total of seven cycles of the chemotherapy. However, there was progression of disease and change of chemotherapy to carfilzomib, pomalidomide and dexamethasone (KPd). After five cycles of KPd, she attained complete remission (CR) as evidenced by bone marrow studies and serum protein electrophoresis. She subsequently underwent stem cell transplantation.

Follow-up

Three months on follow up she is currently asymptomatic, remaining on regular followupand on lenalidomide maintenance.

Conclusion

Mass on the head is a rare and frightening presentation of Multiple Myeloma. However, a timely diagnosis and treatment results in gratifying results.

Malignant Hematology-Clinical (MHC) PP-MHC-16

Nivolumab and ICE with Bortezomib in Refractory ALK+ Large B Cell Lymphoma

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Background

Anaplastic lymphoma kinase (ALK) positive large B-cell lymphoma (ALK+ LBCL) is a rare and aggressive form of non-Hodgkin lymphoma (NHL). Its unique characteristics set it apart from other types of diffuse large B-cell lymphoma (DLBCL). It often presents with immunoblastic or plasmablastic histological features and this histomorphology can resemble other lymphomas, making accurate diagnosis critical. The tumor cells typically express CD138, ALK, epithelial membrane antigen (EMA), and immunoglobulin (Ig) A expression. The presence of ALK gene rearrangements is a defining feature. Clinically, this lymphoma behaves more aggressively than typical DLBCL with an unfavorable response to conventional chemotherapy.

Case Presentation

In this clinical scenario, a 30-year-old male presented with a progressive large anterior abdominal wall lesion and a large ulcerative lesion on the skin over the left scapula for 6 months. He had a history of swelling over his left clavicle two years ago which was diagnosed as large cell lymphoma. He has received seven cycles of Cyclophosphamide, Bortezomib, and Dexamethasone and 25 fractions of IMRT at another hospital but PET CT showed active disease.

Diagnosis

A biopsy of the anterior abdominal wall mass showed morphology consistent with large B cell lymphoma and plasmacytoid change. IHC showed ALK 4+, MUM 3+, CD45+. Tumor cells were negative for HMB45, CK, CD20, CD3, CD10, BCL2, CD34, SALL4, CD117, CD31, Synaptophysin, Pax 5, CD4, CD8, CD2, CD30, CD5, CD7, CD79a, CD19, CD56. PET showed metabolically active lymphadenopathy along both sides of the diaphragm with spleen involvement, lung nodules, and muscular deposits. Bone Marrow showed infiltration by Large Cell Lymphoma.

Treatment

The patient received 2 cycles of Dose Adjusted EPOCH (Etoposide, Prednisolone, Vincristine, Cyclophosphamide, Doxorubicin) with weekly Bortezomib but showed partial response. He was then switched to ICE (Ifosphamide, Carboplatin, Etoposide) protocol and the weekly bortezomib was continued. Nivolumab was added in the third and fourth cycles with ICE in view of slow response. The anterior abdominal wall lesion and lesion over the left scapula regressed completely by the third cycle.

Follow-up

The patient received one month of Nivolumab maintenance awaiting an autologous stem cell transplant. He is currently undergoing ASCT.

Conclusion

ALK+ LBCL is a very rare but aggressive malignancy. Given its aggressive nature and unique biological profile, ALK+ LBCL requires specialized therapeutic approaches. Multimodal treatment strategies, including novel targeted therapies, may hold promise for better management.

Malignant Hematology-Clinical (MHC) PP-MHC-17

Necrotizing Granulomatous Lymphadenopathy with Secondary HLH-a Diagnostic Dilemma Tuberculosis vs Lymphoma

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Background

Lymphadenopathy warrants attention even in people who do not exhibit symptoms. When a patient in India appears with chronic lymph node enlargement, tuberculosis is the first possible diagnosis. The following conditions can induce necrotizing granulomatous lymphadenopathy: syphilis, eosinophilic granuloma, yersinia, fungal infections, Hodgkins lymphoma, and cat scratch disease. Since therapy of the underlying diseases may be sufficient for full recovery, it is vital to identify probable triggers of hemophagocytic lymph histiocytosis (HLH), a disorder of defective immune control.

Case Presentation

A 40-year-old male patient presented with complaints of a fever, marked weight loss, left inguinal swelling for 5 months, jaundice for 1 month. No significant medical or past history. Upon inspection pallor, icterus, left inguinal area 6*6cm firm non tender swelling noted. Pancytopenia and a mixed form of jaundice (hepatocellular and cholestatic) are shown by further testing. An HLH work-up revealed hyperferritinemia, hypertriglyceridemia, hypofibrinogenemia, elevated LDH, and other inflammatory markers in the context of pancytopenia with recurrent fever spikes. On bone marrow biopsy features are compatible with HLH.On further evaluation. Necrotizing granulomatous lymphadenitis shown by lymph node biopsy: IHC negative, special stains negative. Serum ACE was elevated three times the upper limit of normal. Urinary calcium vitamin D levels are normal. CMV and HSV PCR negative, ANA IFA and ANA profile negative. Viral serology was negative.

Diagnosis

Necrotizing granulomatous lymphadenitis with secondary HLH (?High grade lymphoma vs TB) with MODS (Respiratory failure,Encephalopathy,AKI,Shock)

Treatment

The patient began receiving empirical antibiotic treatment, which was later upgraded due to the development of febrile neutropenia. Concurrently, steroid therapy started based on the HLH protocol thereafter. Since the patient was not responding, cyclosporine was added. Since biopsy is more likely in favour of tubercular lymphadenitis, second line antitubercular medication was initiated. As the disease activity continued to worsen, IvIg was initiated. Despite 3 weeks of anti-tubercular therapy no improvement in clinical condition and there is further detoriation of pancytopenia, hepatopathy multi organ dysfunction syndrome requiring mechanical ventilation, high vasopressor support expired.

Follow-up

Patient expired during hopsital stay.No follow up.

Conclusion

There is still a diagnostic conundrum between tuberculosis and lymphoma despite technological advancements. A delayed diagnosis results in a dismal prognosis. In our instance, despite thorough inquiry, the aetiology of necrotic lymphadenopathy remained unidentified.

Malignant Hematology-Clinical (MHC) PP-MHC-18

Describing Clinical Outcomes in 17p Deleted Newly Diagnosed Multiple Myeloma - A Single Center Experience

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Introduction

Presence of 17p deletions is associated with poor outcomes in Multiple Myeloma. Only limited data is available from India, where disease presentation and access to novel therapies differ significantly from that of higher income countries.

Aims & Objectives

To analyze clinical outcomes in patients with 17p deleted Multiple Myeloma that were newly diagnosed at our center.

Materials & Methods

We conducted a retrospective analysis of patients with Newly Diagnosed Multiple Myeloma (NDMM) with 17p deletion diagnosed with Interphase FISH analysis at our center from January 2017 to December 2023.Statistical analysis was done with SPSS v26.0.0.0 and R v4.1.2.

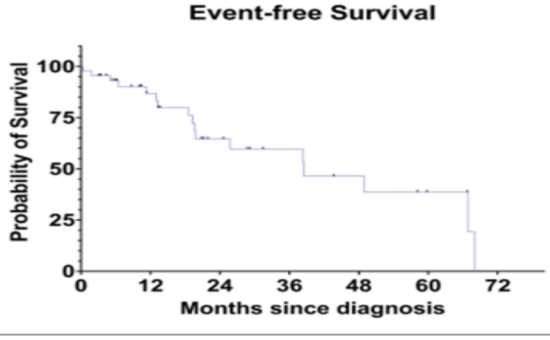
Result

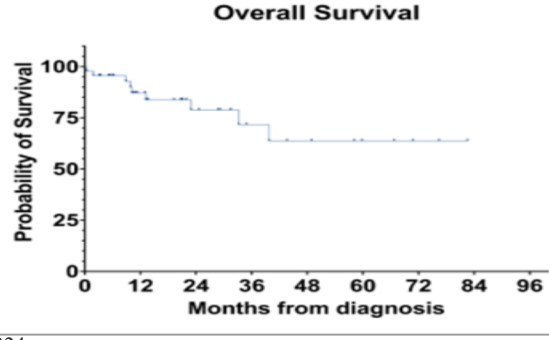
45 patients out of 81 total 17p deletion NDMM cases had been followed-up at least until response assessment or death and were considered for analysis. The median age was 55 years (50-63 years), predominantly male (64.4 %) and R-ISS stage III (53.3 %) at presentation. Induction regimens used were standard triplet regimens - CyBorDex (62.2%), CTD (22.2%) and VLD (13.6%). At end-induction disease assessment, VGPR or better was seen in 80 % (CR=26.7%) and responses inferior to VGPR were noted in 15.5 % (PR=11.1%).

Of the patients followed up, 31.1% (N=14) underwent autologous transplantation (ASCT); 5 patients underwent tandem transplantation. 1 yr EFS was 86.9 % (Median EFS: 38.4 months ,95 % CI 14.5-62.4 months), 1 yr OS was 87.1% (Median OS -not reached) with a median follow-up time of 13.66 months. The median EFS for transplanted patients was 67 months vs 38.5 months for those not transplanted (p=0.125). The median EFS for patients with extramedullary disease (N=6) was 13.2 months vs 48.9 months for patients without (p=0.036). Short median follow-up in this cohort is a limitation in this dataset.

Conclusion

17p deletions portend poor prognosis in Multiple Myeloma in most published literature. However, published Indian long-term outcome data is sparse. In this study we describe a retrospective cohort of TP53 mutation positive NDMM patients. Treatment response, EFS and OS with standard management (Triplet induction +/- ASCT + maintenance) are found to be encouraging despite the limitations of retrospective analysis.





Malignant Hematology-Clinical (MHC) PP-MHC-19

A Case of Myeloproliferative Neoplasm (MPN) With PCM1-JAK2 Rearrangement

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Background

Myeloproliferative neoplasm (MPN) with PCM1-JAK2 rearrangement is a rare and aggressive condition predominantly found in males. The World Health Organization classifies it under "Myeloid/lymphoid Neoplasms with Eosinophilia and TK Fusion Genes," but treatment guidelines remain inconsistent. We present a unique case of a 41-year-old male diagnosed with myeloproliferative neoplasm (MPN) with PCM1-JAK2 rearrangement and his journey towards treatment.

Case Presentation

A 41-year-old male reported with pain in the left hypochondriac region and evident splenomegaly. Investigations revealed significant leucocytosis with a left shift. Provisionally diagnosed as Myeloproliferative neoplasm, he commenced treatment with Hydroxyurea. However, bone marrow assessments suggested Chronic Myeloid leukaemia in its chronic phase. Notably, cytogenetics presented a karyotype with ?t(8;9). Consequently, his treatment shifted to Dasatinib. Next-Generation Sequencing pinpointed a PCM1-JAK2 fusion - merging exon 36 of the PCM1 gene with exon 9 of the JAK2 gene, confirming Myeloid neoplasm with eosinophilia and JAK2 rearrangement. Despite the recognized benefits of Ruxolitinib for MPN with PCM1-JAK2 fusion, the patient elected to continue Hydroxyurea treatment.

Diagnosis

The patient was definitively diagnosed with Myeloid neoplasm with eosinophilia and JAK2 rearrangement, following the detection of PCM1-JAK2 fusion via Next-Generation Sequencing.

Treatment

Initially administered Hydroxyurea based on the provisional diagnosis, the treatment plan was subsequently adjusted to Dasatinib upon further investigation. Although Ruxolitinib was considered, the patient's preference was respected, and he continued with Hydroxyurea.

Follow-up

The patient was followed up regularly, demonstrating a positive response to the treatment. He remains in good health at present.

Conclusion

This case highlights the challenges and intricacies of diagnosing and treating MPN with PCM1-JAK2 rearrangement. The inconsistent responses to Ruxolitinib and the absence of unanimous treatment guidelines emphasize the need for in-depth research. Furthermore, it underscores the pivotal role of patient preferences, emphasizing the essence of comprehensive communication and mutual decision-making in managing such intricate conditions.

Malignant Hematology-Clinical (MHC) PP-MHC-20

Autoimmune Lymphoproliferative Syndrome - A Rare Genetic Condition

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Background

Autoimmune Lymphoproliferative Syndrome (ALPS) is a rare genetic condition caused by defective lymphocyte apoptosis, leading to chronic lymphoproliferation, autoimmunity, and increased lymphoma risk. Mutations in the FAS pathway are often involved. This case report presents a 12-year-old female with ALPS, focusing on her clinical features, diagnostic evaluation, and treatment, including a heterozygous FAS ligand mutation.

Case Presentation

A previously healthy 12-year-old girl presented with 3 months of abdominal distension, low-grade fevers, and fatigue. Physical examination revealed pallor, generalized lymphadenopathy, and marked splenomegaly. Lab results showed leukopenia (WBC 3740/µl), anaemia (Hb 8.9 g/dL), normal platelet count (160,000/µl), and atypical lymphocytes. Serum immunoglobulins were elevated, and anti-dsDNA was positive. Imaging confirmed splenomegaly and widespread lymphadenopathy, with no evidence of malignancy or storage disorders. Fundus examination was normal.

Diagnosis

Flow cytometry detected 48% of CD3 marker Double-negative T cells, 2.26 % of Lymphocytes, 3.25% of CD3 +T cells and 14.79% (CD3+ CD4- CD8-), a hallmark of ALPS. Genetic testing identified a heterozygous FAS ligand gene, confirming the diagnosis of ALPS. Family screening was negative for the FASL mutation.

Treatment

Initial management included corticosteroids (Prednisone 1 mg/kg/day) along with Mycophenolate Mofetil after which lymphadenopathy was reduced. She continued 6 months of therapy after which she voluntarily stopped the medications and had a relapse for which re-initiation of steroids and MMF was considered. However, she has not responded and presented with abdominal distention with gross ascites. 4ltrs of ascitic fluid was tapped twice with no evidence of lymphoma. She was started on Rituximab with sirolimus after which her ascites improved.

Follow-up

The patient is being followed up regularly with a multidisciplinary team, including haematology, immunology alongside genetic counselling. Serial ultrasounds monitor splenomegaly, and regular assessments are conducted to detect any signs of lymphoma or autoimmune cytopenia's.

Conclusion

This case emphasizes the importance of considering ALPS in paediatric patients presenting with unexplained lymphadenopathy and autoimmune cytopenia's. The presence of a FAS ligand mutation highlights the role of apoptosis defects in disease pathogenesis. Early diagnosis and a tailored, long-term management plan are critical to improving patient outcomes and mitigating risks such as malignant transformation.

Malignant Hematology-Clinical (MHC) PP-MHC-21

Chronic Myeloid Leukemia Masquerading as Polycythemia Vera with Myocardial Infarction: An Unusual Presentation

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Background

Myeloproliferative neoplasms (MPN) are clonal haematopoietic stem cell disorders characterized by the proliferation of cells of one or more of the myeloid lineages. As per WHO classification, in suspected MPN cases with polycythemia, Polycythemia vera (PV) is kept as first differential. We hereby present an interesting case of young male with recurrent myocardial infarction and polycythemia turned out to be chronic myeloid leukaemia.

Case Presentation

A 45-year-old male patient presented with anterior wall myocardial infarction. His initial CBC revealed raised Hb (17 gm/dl), thrombocytosis (Platelet count 936 x 109/L) and leukocytosis (TLC 16 x109/L). Peripheral smear showed RBC crowding and overlapping, marked thrombocytosis and neutrophilic leukocytosis with left shift and basophilia.

Bone marrow aspirate smears showed trilineage hematopoiesis with increased megakaryocytes. Bone marrow biopsy was hypercellular (cellularity ~ 80-85%) and showed panmyelosis with proliferation of pleomorphic mature megakaryocytes. His erythropoietin levels were normal. As a part of work up, MPN panel molecular testing was done which was surprisingly negative for JAK2 V617F and JAK2 exon 12. CALR and MPL were also negative. We then got RT-PCR for BCR ABL1 done which was positive for P210 (b3a2, b2a2) major transcript.

Diagnosis

Myeloproliferative neoplasm- Chronic Myeloid Leukaemia presenting as polycythemia leading to myocardial infarction and angina.

Treatment

Patient received initially hydroxyurea therapy and aspirin. He had another episode of angina and evaluated at AIIMS Nagpur. After final diagnosis of Chronic Myeloid Leukaemia he was treated with Imatinib.

Follow-up

Patient was monitored by RQ-PCR for BCR-ABL1. On last follow up after 13 months he was in deep molecular remission. He is completely asymptomatic now and had no recurrence of cardiac symptoms.

Conclusion

CML masquerading as Polycythemia Vera is extremely unusual. Proper diagnostic evaluation of MPNs includes clinical correlation, CBC, PS and bone marrow morphological evaluation and molecular testing. Application of WHO diagnostic criteria using this information prevents misdiagnosis. BCR ABL1 should be tested in all suspected MPNs along with JAK2 V617F, CALR and MPL. This patient enlightened us with the unusual presentation of CML as panmyelosis with rather serious cardiac complications.

Malignant Hematology-Clinical (MHC) PP-MHC-22

An Unusual Presentation of Juvenile Myelomonocytic Leukemia in a Case of Down's Syndrome

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Background

Juvenile myelomonocytic leukemia (JMML) is a rare pediatric myeloproliferative neoplasm overlap disease while Down syndrome or trisomy 21 is a genetic disorder where children are 10-times more at risk of developing leukemia. The association of JMML with Down syndrome is extremely rare and only occasional case reports are available in literature.

Case Presentation

A 19-month-old female known case of Down syndrome presented with petechial rashes over arms, trunk and bilateral lower limbs. There was no history of epistaxis, gingival bleeding, hematuria or melena. There was no relevant family history. On examination there was pallor, however no lymphadenopathy or splenomegaly was noticed. The CBC revealed Hb: 10.2 g/dl, TLC: 59100/mm3, DLC: N82, L8, M9, E1, Plt: 35000/cumm, the differential revealed 02 % circulating blasts. There were 02/100 nRBCs. The patient was advised follow up and subsequently after 1 month the peripheral blood smear revealed leukoerthyroblastosis with 06% circulating blasts while thrombocytopenia persisted (30,000/cumm). Bone marrow aspiration was performed which revealed 07% blasts along with dyspoiesis in the erythroid and myeloid series and a differential of Myeloid leukemia associated with Downs syndrome (ML-DS) was rendered. Flow cytometry revealed 3.5% blasts which were positive for CD34, cMPO, HLA DR, CD117, CD 33. A subsequent Next Generation Sequencing was performed that revealed mutations in PTPN11, NF-1, NRAS genes. Of note, no hot spot mutations in GATA1 gene, known to be associated with Transient Myeloproliferative Disorder (TMD) were seen.

Diagnosis

Based on this a diagnosis of Juvenile Myelomonocytic Leukemia (JMML) associated with Down syndrome was given. The child was kept under follow-up and HLA typing of family members was done in view of a subsequent Hematopoietic Stem Cell Transplantation.

Treatment

Hematopoietic stem cell transplantation was contemplated

Follow-up

The child is on regular follow up.

Conclusion

Although most cases of JMML are not associated with cytogenetic abnormalities, this association with Down syndrome is probably not casual. More cases need to be studied to prove that there is a relation between the two diseases.

Malignant Hematology-Clinical (MHC) PP-MHC-23

Basophilic Blast Phase Transformation of P230 Type BCR::ABL1 Transcript Chronic Myeloid Leukemia – An Exceedingly Rare Complication of a Relatively Indolent Entity

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Background

Blast phase, a dreaded complication of chronic myeloid leukemia (CML), has seen a markedly diminished incidence in the tyrosine kinase inhibitor (TKI) era. Although basophilia is a common feature in both the peripheral blood and the bone marrow during the chronic phase of the disease, transformation to basophilic blast phase is an extremely rare occurrence, with only a handful of cases reported. Here, we report a rare case of CML in progressing to basophilic blast phase in a 65-year-old male patient.

Case Presentation

Patient was a known case of CML diagnosed in 2021 with poor drug compliance. He was referred from outside as a case of myeloid blast phase and was started on 3+7 induction regime. Evaluation at our centre showed bicytopenia with hyperleukocytosis in the peripheral smear (25% blasts and 32

Diagnosis

Overall features were consistent with myeloid blast phase (basophilic blast phase) in a known case of Chronic Myeloid Leukemia.

Treatment

Patient received 3 days 3+7 induction regime before getting referred to our centre, where he was started on tablet dasatinib (140 mg daily) and advised admission, however, was lost to follow up.

Follow-up

The patient was lost to follow up and succumbed to his illness.

Conclusion

Herein, we describe a very rare basophilic blast transformation of CML with a minor type of BCR::ABL1 transcript (p230 type). The case also highlights the importance of morphology besides IPT in the era where diagnosis and therapy are influenced to a large extent by ancillary studies.

Malignant Hematology-Clinical (MHC) PP-MHC-24

Co-occurrence of BCR–ABL1 Translocation and JAK2 V617F Mutation: An Ultra-rare Phenomenon in Myeloproliferative Neoplasms

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Background

Myeloproliferative neoplasms (MPN) are disorders of hematopoietic stem cells defined resulting in an excess production of hematopoietic elements i.e. myeloid, erythroid and/or megakaryocyte lineages. They arise from somatically altered tyrosine kinase signalling, with BCR::ABL1 translocation defining chronic myeloid leukaemia (CML), and JAK2V617F being the most common mutation in the Ph-negative MPNs, which include polycythemia vera (PV), essential thrombocythemia and primary myelofibrosis. These two genetic alterations are usually considered to be mutually exclusive. Here we present a case showing their rare co-occurrence.

Case Presentation

An 86-year-old gentleman, who was diagnosed with PV 5 years back, presented with mild pallor and leucocytosis. There was no organomegaly or lymphadenopathy. His CBC showed mild anemia and leucocytosis (Hb – 105g/L, platelets – 292 x109/L and TLC – 28.9 x109/L). The peripheral blood film showed left shift with 20% myelo-and metamyelocytes, and 5% basophils. The bone marrow was markedly hypercellular (nearly 100% cellularity) with high myeloid:erythroid ratio of 44.5:1 and many dwarf megakaryocytes.

Diagnosis

RT-PCR was positive for BCR::ABL1 translocation. In view of the past history of PV, testing for JAK2V617F was also performed by ARMS-PCR, which showed presence of mutant JAK2V617F allele with an allele burden of 3.6%.Hence, in this patient of PV, a diagnosis of CML in chronic phase was made, with co-occurrence of JAK2V617F.

Treatment

As diagnosis of polycythemia vera was made he was started on hydroxyurea and underwent regular phlebotomies since five years. Following diagnosis of CML in chronic phase, Tab Imatinib 400 mg once daily was started.

Follow-up

As of now patient has responded to imatinib therapy complete hematological response in form of normal CBC and no evidence of extramedullary disease.

Conclusion

Co-occurrence of BCR::ABL1 translocation and JAK2V617F mutation is very rare in MPNs. In a retrospective multi-institutional study by Soderquist et al, a total of 11 cases with co-occurring BCR::ABL1 and JAK2V617F mutations were noted, with an estimated frequency of 0.4%. The sequence of identification of the genetic abnormalities varied: five patients were initially diagnosed with a JAK2 V617F+ myeloproliferative neoplasm, with the subsequent acquisition of BCR–ABL1, similar to our case. Cases that exhibit mixed bone marrow cytologic features (eg, both 'dwarf' and 'cloud-like' megakaryocytes) or that show unexpected changes in bone marrow histomorphology should prompt consideration of the possible coexistence of BCR::ABL1 and JAK2 V617F. Although clinical courses varies, in the absence of tyrosine kinase inhibitor therapy, patients generally demonstrate clinicopathologic features of chronic myeloid leukemia suggesting that BCR::ABL1 has dominant transforming potential in the setting of diminished mutationally activated JAK2.

JAK2 and BCR::ABL1 are driver genomic alterations leading to different types of MPNs. Despite being considered mutually exclusive, our case highlights that they may be present concurrently, with one disease preceding the other. This knowledge is essential to avoid diagnostic confusion and potential error in therapeutic decision making.

Malignant Hematology-Clinical (MHC) PP-MHC-25

The Simultaneous Occurrance of P210 and P190 Transcripts of BCRABL in Chronic Phase Chronic Myeloid Leukemia

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Background

Chronic Myeloid Leukemia is defined by the presence of Philadelphia chromosome with p210 transcript (BCR ABL major) being the prominent break point in chronic phase (CP). P190 is seen in ALL and reported in CML progressing to lymphoid blast crisis. We report a case of Chronic Phase CML having both transcripts simultaneously expressed while in CP.

Case Presentation

A 25-year-old male, diagnosed with chronic myeloid leukemia in 2019, was in major molecular remission on 400 mg imatinib until 2023 when he presented with an acute dengue like illness. He was found to have hyperleucocytosis and recurrence of splenic enlargement despite compliance with TKI. Bone marrow showed 4% blasts, mildly increased reticulin fibrosis. There were no additional chromosomal abnormalities. P210 was quantified at 40.67%. Imatinib resistance mutation analysis was awaited. Therapy was changed to Dasatinib 140 mg for imatinib failure in accelerated phase.

Diagnosis

At initial diagnosis his BCR ABL RQPCR was 35.016%- subsequently was <0.1% with imatinib. At the time of disease progression, this patient had a spleen size of 20 cm. After 3 months of Dasatinib therapy he did not achieve hematological remission. Imatinib resistance mutation analysis by Sanger sequencing showed no tyrosine kinase domain abnormalities. A qualitative BCR ABL RQPCR was analyzed to ascertain the transcript in view of non-response to Dasatinib. This showed both P210 and 190 transcripts

Treatment

Though he fell under ELTS high risk, with apparent TKI resistance, he was unwilling to have a stem cell transplant. He was therefore started on Bosutinib 100 mg ramped up to maximum dose of 400 mg./day over 4 weeks.

Follow-up

He had dramatic response to change in TKI and achieved CHR within 1 month of change in therapy. Spleen size regressed. He reports no adverse events with Bosutinib.

Conclusion

Patients with CP/ (previously defined) AP CML not achieving haematological response, in the absence of tyrosine kinase domain mutations or progression to blast phase, may harbour another BCR ABL transcript. So far, the pathological significance of a concurrent p190 transcript has not been evaluated. Whether these transcripts may be driving the deviation from expected hematological and molecular response remains to be determined.

Malignant Hematology-Clinical (MHC) PP-MHC-26

Triple-negative Myelofibrosis: Data Over the Last Decade From an Eastern Tertiary Care Center

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Introduction

Myelofibrosis (MF) is a subtype of myeloproliferative neoplasm, with 90% of cases driven by mutations in the JAK2, CALR, or MPL genes. Triple-negative MF refers to the absence of all three mutations and accounts for 5-10% of cases. It often has a distinct clinical presentation and poorer prognosis

Aims & Objectives

To evaluate the baseline characteristics, clinical presentation, and outcomes of patients with triple-negative primary myelofibrosis.

Materials & Methods

This retrospective data audit was conducted between January 2012 and July 2024. Baseline clinical and laboratory characteristics parameters were collected, and outcome analyses were performed for patients diagnosed with triple-negative myelofibrosis.

Result

Among the 130 myelofibrosis cases reviewed, 119 (91%) had mutations in JAK2, CALR, or MPL, while 11 cases (8%) were identified as triple-negative in which 6 were lost to follow up after first visit. The median age of triple-negative patients was 58 years (45-70 years.) The male-to-female (M) ratio 3:2. Constitutional symptoms such as fatigability, weight loss, abdominal heaviness were observed in 3 cases, and spleen was noted in 3 cases, with an median spleen size of 12 cm . The median total leukocyte count was 8300 cells/mm3 (range 2200 to 22500 cells /mm3), Median platelet count 90000 cells/mm3(range 14000-2050000 cells/mm3). The median lactate dehydrogenase (LDH) level was 621U/l (range 561 -5348). Circulating blasts were present in 2 cases (range 1-2%,)

Bone marrow analysis showed an average blast percentage of 2% (range 1-3%), and fibrosis was noted in all cases. Three out of five patients evaluated had a normal karyotype, while the remaining two presented with specific karyotypic abnormalities (del 7q, del5q). High-risk disease as per DIPSS-plus criteria was identified in 3 cases.

Three patients received symptomatic treatment with Ruxolitinib or Hydroxyurea, / Prednisolone. Two patients underwent allogeneic hematopoietic stem cell transplantation (allo-HSCT) using matched donors, with 1 sibling and 1 matched unrelated. Both of them died. At the last follow-up, three out of five patients were alive. The median overall survival was 39 months (with a median follow-up of 138 months)

Conclusion

Triple-negative myelofibrosis is a entity characterized by lower WBC, thrombocytopenia, and minimal splenomegaly at presentation. This subset has an overall inferior survival compared to other types of myelofibrosis. Larger, multicenter studies are needed to better delineate its clinical course and develop more effective treatment strategies.

Malignant Hematology-Clinical (MHC) PP-MHC-27

Vanishing Bile Duct Syndrome in Hodgkins Lymphoma; No Longer an Ominous Portent

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Background

Jaundice can complicate or be a presenting symptoms in 3-13% of Hodgkin's lymphoma and the usual suspects are liver involvement, haemolytic anaemia, extra hepatic bile duct obstruction by lymph nodes, rarely paraneoplastic involvement in the form of vanishing bile duct syndrome(VBD). It comprises of a collection of disorders where there is progressive loss of intra hepatic bile ducts more specifically when there is absence of interlobular bile ducts from within portal tracts. One of the known causes of VBD is Hodgkin's lymphoma. In our case report we talk about one such case managed successfully with brentuximab vedotin as a hepato safe debulking agent.

Case Presentation

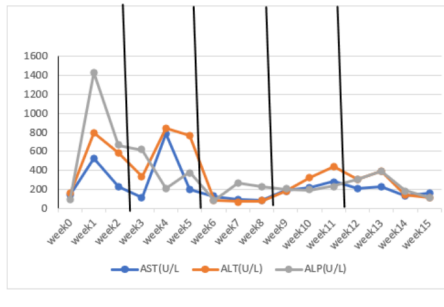
A 8 year old boy presented to the opd with complaints of recurrent anaemia since 5 months, fever and anorexia since 2 months and swelling over neck 1 month, on examination had pallor generalised lymphadenopathy and hepatosplenomegaly, he underwent cervical excision biopsy which revealed classical Hodgkin lymphoma mixed cellularity type, PET CT revealed stage IIIBS(liver was not involved), however patient shortly developed gradually progressive yellowish discolouration of sclera . Investigation showed cholestatic pattern of jaundice. USG whole abdomen was normal. Patient no signs and symptoms of liver disease

Diagnosis

With above tests liver biopsy was done which showed paucity of bile ducts and inflammatory infiltrates in few of the portal tracts s/o vanishing bile duct syndrome.

Treatment

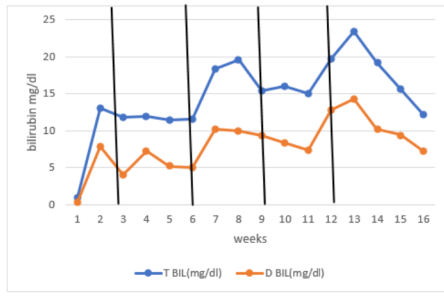
Patient was started on therapy with Gemcitabine 750mg/m2 on day 1 and day 8(hepatosafe dose) and dexamethasone, as a debulking agent along with Urso deoxycholate and l glutamine for supportive care. Initial rise followed by fall was seen of liver enzymes and bilirubin. Repeat PET CT was done to assess for disease status. It showed complete metabolic response DS 1. Cycle 1,2 and 3 of chemotherapy comprised of brentuximab vedotin (at 1.2g/kg) along with it dexamethasone and gemcitabine was given as mentioned previously.



Follow-up

he received 3 such cycles and each time the increase in liver enzymes was reduced from the last. Currently patients' disease is in remission and liver function is also normal.

Graph showing the trend in bilirubin and sgot and sgpt. The solid black line indicates each chemotherapy cycle (debulking f/b cycle 1 , cycle 2, cycle 3)



Conclusion

VBD is a rare presentation of Hodgkins lymphoma.

Patient classically have poor outcome ending in permanent liver failure and death.

Brentuximab vedotin is a safe agent which can be used successfully for debulking and in combination with chemotherapy as definitive therapy for these patients.

Further therapy options must be tailored for these patients in view of the sensitive nature of the disease.

Malignant Hematology-Clinical (MHC) PP-MHC-28

A Single Center Experience of Consecutive vs Alternate Day Schedules of High-dose Cytarabine Consolidation Chemotherapy in Acute Myeloid Leukemia Patients

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Introduction

High-dose cytarabine (HiDAC) delivered every 12th hourly on 1, 3, 5 days(HiDAC-135) is the standard post remission consolidation therapy to prevent relapse in acute myeloid leukaemia(AML). Administration of cytarabine on consecutive days(HiDAC-123), rather than alternate days(135) may hasten the recovery of cytopenia's.

Aims & Objectives

This study aimed to compare the consecutive versus alternative day schedules of HiDAC chemotherapy in terms of treatment outcome and toxicity in AML patients who achieved complete remission after induction and were eligible for intensive consolidation.

Materials & Methods

Eligible Patients were randomized to either to HiDAC-123or HiDAC-135 treatment groups. HiDAC was administered as intravenous infusion over 3hours as per randomisation. Patients were monitored for cytopenia's and complications, received supportive treatment with antibiotics, blood products as needed. Daily complete blood counts(CBC) were performed to track hematological recovery times in each group, documenting parameters like neutropenia, thrombocytopenia recovery times and transfusion requirements.

Result

Total 19 patients were treated between January 2024&September 2024:10 received HiDAC-1 35 and 9 patients received HiDAC-123. Median age was 36years(IQR 27)&17years(IQR 24) in HiDAC-123&135 respectively. Male-to-female ratio was 1:1.1.According to ELN 2022 risk stratification, 52% had favorable risk,26% intermediate risk, & 21% adverse risk AML. The mean time to hematological recovery was shorter in the HiDAC-123 group. The mean time to neutropenia recovery was 13.78days(2.68) for HiDAC-123 compared to 16.10days(1.45) for HiDAC-135(p=0.02). The mean time to recovery of thrombocytopenia& leukopenia were also shorter in HiDAC-123(p=0.01 and p=0.03 respectively).Incidence of Febrile neutropenia was 100% in both groups. There was no significant difference in the requirement of blood products in both schedules. Commonest non-haematological toxicity was cytarabine induced transaminitis. Results are given in table 1.

Characteristics	123, N=9	135, N=10	P value
Age (years)[b]	36 (27)	17(24)	0.37
Gender, n(%)			
male	6(66.7)	7(70)	
female	3(33.3)	3(30)	
Risk category n(%)			
Favourable risk	2(22.2)	8(80)	
Intermediate risk	4(44.4)	1(10)	
High risk	3(33.3)	1(10)	
Baseline TLC[a]	7775 (2334)	5606(2179)	0.02*
Baseline Hb[b]	12(1)	10.50(3)	1.00
Baseline platelet[b]	157000(85500)	157000(122250)	1.00
TLC recovery time[a]	13.67(3.20)	16.22(0.97)	**0.03**
Platelet recovery time[a]	14.67(1.5)	16.60(1.5)	**0.01**
Neutrophil recovery time[a]	13.78(2.68)	16.10(1.45)	**0.02***
Duration of hospital stay[a]	14.89(1.76)	15.6(2.63)	1.00
RDP[b]	9.5(6)	9(2)	0.62
GCSF doses[b]	9(2)	10(2)	0.37
SDP[b]	0.50(1)	0.50(1)	0.07
PRBC[b]	0(1)	0(1)	0.08
Peak neutropenia value[b]	14(75)	17.50(24)	1.0
Peak neutropenia day[a]	10.33(2.12)	12.20(1.58)	**0.01**
Peak TCP[a]	7122(4380)	8000(3620)	0.65
Peak TCP day[a]	11.56(1.67)	12.2(2.66)	0.17
Severity, n(%)			
Neutropenia grade 1 or 2	6(66.7)	8(80)	
Neutropenia grade 3 or 4	9(100)	10(100)	
Thrombocytopenia grade 1 or 2	8(88.9)	7(70)	
Thrombocytopenia grade 3 or 4	9(100)	10(100)	
Duration			
Neutropenia grade 1 or 2 duration[b]	1.5(1)	1.5(1)	1.00
Neutropenia grade 3 or 4 duration[b]	5(1)	6.5(3)	0.17
Nadir TLC [a]	490(211)	441(200)	1.00
Nadir TLC day[a]	10.33(2.16)	12.17(2.13)	**0.01***
Thrombocytopenia grade 1 or 2 duration[b]	2(1)	1(1)	0.31
Thrombocytopenia grade 3 or duration[a]	10.17(3.18)	6.67(1.03)	0.65

a mean (SD), b median (IQR)

*Significant at p value<0.05

Applied unpaired t test for the normally distributed data and mann whitney U test for the not normally distributed data

Conclusion

In our single-centre experience, High-dose cytarabine administered on consecutive days(1,2,3) days resulted in faster hematological recovery compared to alternate day(1,3,5) schedule.

Malignant Hematology-Clinical (MHC) PP-MHC-29

Real World Outcomes of Pediatric Hodgkin Lymphoma in Resource Limited Setting : A Single Centre Study from AIIMS Rishikesh

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Introduction

About 90 % of all newly diagnosed Hodgkin's Lymphoma can be cured with combination chemotherapy and/or radiation therapy with estimated 5 year survival rates of greater than 98%.

Aims & Objectives

To study the treatment outcomes in newly diagnosed pediatric hodgkin's Lymphoma in a resource-constrained setting using various combination chemotherapy with or without radiation.

Materials & Methods

Newly diagnosed case of classical Hodgkin's lymphoma of age less than or equal to 18 years treated between 2017 and 2024 were included in the study.All children underwent staging using FDG-PET at baseline and repeat PET-CT post 2 cycles of chemotherapy.

Result

Total 53 pediatric patients were treated between May 2017 and May 2024.Median age was 11 (IQR 8) years.Male : Female ratio was 3 : 1.As per National Comprehensive Cancer Network risk classification, 15 % ,18.8 % and 66 % had early favourable ,early unfavourable and advanced disease at presentation respectively.22.8 % of advanced disease patients had high IPI score.7.5 % ,26.4 %,43.3% and 22.6 % presented with Stage I ,Stage II,Stage III and Stage IV disease respectively.18.8 % had bulky and 81.1 % had non-bulky disease.92.4 % of the patients received ABVD regimen and 7.54 % received OEPA-COPDAC regimen as first line treatment regimen.15 % of the patients received Radiation therapy post chemotherapy. 81.1 % attained CMR in interim PET while 15.09 % had residual disease and 3.7% defaulted after initial 2 cycles of chemotherapy.13.2 % went on to receive second line treatment with Escalated BEACOPP and 3.7 % received GDP as second line followed by autologous transplantation.Complete response rates among early stage favourable ,unfavourable and advanced disease were 87.5% ,90% and 77.14 % respectively. The median relapse free follow up duration was 30 months (IQR 21-52).Among early stage disease ,27 % received combined chemotherapy with radiation and 72 % received chemotherapy alone of which 15 % presented with relapse.

NUMBER OF PATIENTS	N = 53
AGE	MEDIAN AGE 11 (IQR)
GENDER	Male 40 (75.4%) Female 13 (24.5 %)
STAGE OF THE DISEASE	Stage I : 4 (75.4 %) Stage ii : 14 (26.4%) Stage III : 23 (43.3 %) Stage iv : 12(22.6)
BULK STATUS	Bulky : 10 (18.8 %) Non Bulky : 43 (81.1%)
RISK STRATIFICATION	Favorable : 8 (15%) Unfavourable :10(18.8 %) Advanced disease : 35(66%)
PROTOCOL USED TO TREAT	ABVD : 49 (92.4) OEPA COPDAC:5 (94.3) ESC BEACOPP : 7 (13.2 %) GDP : 2 (3.7 %)
INTERIM PET REMISSION STATUS	Remission : 43 (81.1%) Residual disease : 8 (15 %)
RADIATION THERAPY	8 recived ISRT (15 %)
CURRENT SURVIVAL STATUS	Relapse : 4 (7.5 %) Death : 2 (3.7%) Disease remission : 47 (88.6 %) Relapsed patients who underwent Autologous transplant : 2 (3.7 %)
Median duration of relapse free follow up	907 days - 30 months(Range : 21-52 months)

Conclusion

In our single centre experience combined treatment modality using chemotherapy and radiation is highly effective than chemotherapy alone in early stage disease.

Malignant Hematology-Clinical (MHC) PP-MHC-30

NPM1 Mutated Myeloid Neoplasm with Low Blasts- A Distinct Clinico - Pathological Entity

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Background

NPM1 (Nucleophosphomin 1) mutated AML (Acute myeloid leukemia) accounts for 30-35? ses, and is a distinct entity in the WHO (World Health organization) Haem 5 classification [1]. Unlike other recurrent cytogenetic abnormalities, a blast count of >20% was a necessity to categorize it as AML which has now been abolished, although International Consensus still mandates a 10%cut off [2]. The reported prevalence of NPM1 in MDS (Myelodysplastic syndrome) or CMML (Chronic myelomonocytic leukemia) is as low as less than 2% [3]. NPM1 mutated myeloid neoplasia with less blasts have clusters of CD34 negative and cytoplasmic NPM1 IHC positive on bone marrow trephine. This finding is consistent with AML. These cases respond better to chemotherapy than HMA which is also consistent with an AML diagnosis. The co-mutation profile on NGS does not show myelodysplasia defining mutations, but FLT3, DNMT3A and TET2 [3-4]. Such cases pose diagnostic and therapeutic challenges. This is a series of two such cases with their response outcomes, with discussion on the dichotomy, adding to the armamentarium of clinical medicine.

Case Presentation

CASE 1: A 49-year-old male patient presented with anemia refractory to treatment.

CASE 2: A 44-year-old female patient presented with unexplained pancytopenia and hepatomegaly. Peripheral blood revealed a hemoglobin of 8.6gm/dL, total leukocyte count of 3670/cu mm and platelet count of 24000/cu mm.

Diagnosis

CASE 1: Bone marrow studies revealed a blast count of 2percent, with cellular particles and erythroid predominance. Trephine biopsy showed a dyspoietic marrow with hypercellular marrow spaces and megakaryocyte dysplasia in the form of loose and tight clustering, and variations in nuclear size and lobation. Immunohistochemistry revealed few CD34 positive immature cells, confirming the presence of blasts on a background of myelodysplasia. FISH panel for MDS was negative, and karyotype revealed normal male karyotype. The marrow was subjected to a targeted 50 gene NGS panel which revealed a type A NPM1 variant with a variant allele fraction of 22percent along with TET2 and ASXL1 alterations.

Case 2 : Bone marrow aspirate was dilute and a 200-cell myelogram showed only 1percent abnormal myeloid blast. Megakaryocyte showed hyperlobation. An impression of cellular marrow with myeloid hyperplasia was rendered and further molecular tests were recommended. Cytogenetics were negative for MDS defining lesions and depicted a normal female karyotype. NGS revealed an NPM1 mutation with a variant allele frequency of 12%.

Treatment

CASE 1: In view of the classical NPM1 mutation, the patient was offered 7+3 induction and achieved CR.

Case 2: In view of the NPM1, the patient was offered azacytidine and venetoclax based therapy and now the patient has completed two cycles, awaiting evaluation.

Follow-up

CASE 1: Patient is doing well after 1 year of treatment.

Case 2: Patient has completed 2 cycles of treatment, awaiting disease re-evaluation

Conclusion

These two cases highlight that irrespective of blast count, AML directed therapy has led to response in the two patients. Cases with less than 10% blasts define a subset of NPM1+AML in early stage and need to be treated with intensive chemotherapy and monitored as per NPM1 mutated AM recommendations, irrespective of blast count at diagnosis. Whether the Indian scenario is distinct or not is a question which has to be answered in prospective studies through comprehensive genomic profiling and long term follow up reports.

Malignant Hematology-Clinical (MHC) PP-MHC-31

Psychiatric Manifestations in Children With ALL

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Background

Introduction: Acute lymphoblastic leukemia (ALL) is the most common cancer in children, accounting for approximately 25% of all childhood cancer cases and about 75% of childhood leukemia instances. The diagnosis and treatment of ALL profoundly affect the physical and psychological well-being of both children and their families. Factors such as treatment-related pain, frequent hospitalizations, and side effects from corticosteroids contribute to significant psychiatric issues during therapy

Case Presentation

Aims and Objectives: This study aims to investigate the prevalence of psychiatric symptoms in children diagnosed with ALL at a tertiary care centre. The objective is to quantify these symptoms using the Childhood Psychopathology Measurement Schedule (CPMS) and to explore the relationship between psychiatric manifestations and various phases of chemotherapy.

Diagnosis

Materials & Methods: We conducted a cross-sectional observational study involving 60 children aged 6 to 16 years with ALL undergoing different stages of chemotherapy. Informed written consent was obtained from both the children and their parents. Data collected included demographic information, age at diagnosis, and chemotherapy duration. Each child underwent a comprehensive physical examination and a psychiatric assessment using the CPMS, which identifies disturbed children and classifies childhood psychopathology. A score above 10 indicates the need for further evaluation.

Treatment

Results: The study found that 23.3% of the patients exhibited psychiatric symptoms, predominantly depression and conduct disorders. Early chemotherapy phases correlated with a higher incidence of these issues. Significant associations were identified between psychiatric problems and socioeconomic status as well as the time since diagnosis. However, no significant correlations were observed regarding gender, nutritional status, or specific ALL subtype. Notably, depressive disorders and associated symptoms were more prevalent in the initial stages of treatment.

Follow-up

Results: The study found that 23.3% of the patients exhibited psychiatric symptoms, predominantly depression and conduct disorders. Early chemotherapy phases correlated with a higher incidence of these issues. Significant associations were identified between psychiatric problems and socioeconomic status as well as the time since diagnosis. However, no significant correlations were observed regarding gender, nutritional status, or specific ALL subtype. Notably, depressive disorders and associated symptoms were more prevalent in the initial stages of treatment.

Conclusion

Conclusions: Psychiatric distress can adversely affect treatment adherence and quality of life for children with ALL. Younger patients are more prone to behavioural symptoms, while adolescents may exhibit psychotic features. The psychological effects, including mood swings, anxiety, and depression, are exacerbated by steroid-related reactions, significantly impacting the quality of life for both patients and their families.

Malignant Hematology-Clinical (MHC) PP-MHC-32

A Rare Presentation of ALL as Paraparesis

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Background

Paraneoplastic syndromes, presents as paraparesis in a case of b cell acute lymphoblastic leukemia in children

Case Presentation

3-year-old female presented with h/o fever for last 2 month, followed by difficulty in walking without support, couldnot stand from sitting position, couldn't sit from lying down position. Then she developed difficulty in walking without support. There was no h/o weakness of the upper limb & bowel bladder involvement. no h/o seizure, headache, loss of consciousness, no history suggestive o cranial nerve involvement. There is no h/o weight loss or loss of appetite. There is no/ h/o co ugh cold abdominal pain, vomiting loose stools, dysuria, no rash no joint pain. Rash joint effusion, no oral ulcers, initially she was treated with iv antibiotics and other supportive care

Diagnosis

B ALL /IRG /CNS 1 WITH PARAPARESIS AS PARANEOPLASTIC SYNDROME

Treatment

Received BFM 2002 protocol, pt improved after starting BFM 2002 protocol, after completing induction phase power of the patient improved; now patient has received consolidation, power completely improved, pt doing good.

Follow-up

Power of the limb completely improved, now completed consolidation. Patient doing better.no further weakness was there.

Conclusion

Acute lymphoblastic leukemia is a common leukemia in childhood. They usually present with fever, bone and joint pains, bleeding manifestations, lymphadenopathy and hepatosplenomegaly. Case reports of children presenting with bilateral lower limb weakness in acute lymphoblastic leukemia has been rarely reported, as MRI brain LS spine was normal, EMG, NCV, NCS was normal, neutropenic panel and Electrolytes was normal, diagnosis of paraneoplastic syndrome was made by exclusion

Malignant Hematology-Clinical (MHC) PP-MHC-33

Myeloid Neoplasm with FLIP1L1 PDGFRA Fusion Manifesting as CML

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Background

"Myeloid/Lymphoid neoplasms with eosinophilia and gene rearrangement" is a rare category of Myeloproliferative disorder. These cases typically present with eosinophilia. They rarely present as lymphoid neoplasm or acute myeloid leukemia. They are defined by gene rearrangements involving PDGFRA,PDGFRB or FGFR1. Here we present an unusual case myeloid neoplasm with PDGFRA rearrangement presenting as features suggestive of Chronic Myeloid Leukemia.

Case Presentation

58 yr old male was reffered to us for evaluation of Leucocytosis. His presenting symptoms were pedal oedema and weakness from last 10 days. Clinically he had pallor, oedema, hepatosplenomegaly. CBC showed Hb 5.7, TLC 1,59,000, Platelet count of 41,000. Peripheral smear showed Myelocytes28%, MetaMyelocytes 16%, Polymorphs 40%, Blasts 3%, Lymphocytes11%,Basophils 2%. Peripheral smear was suggestive of CML. ECHO was normal. Bone marrow aspirate was hypercellular, Erythroids were depressed, Myeloids were hyperplastic with increase in basophils, blasts were 3%, Megakaryocytes were reduced. BM biopsy was suggestive of CML with no increase in blasts(CD34/117 was negative) There was grade II fibrosis. BCR ABL translocation done by PCR was negative. It was repeated from two different laboratories. JAK2/ CALR/ MPL was negative. NGS showed presence of FLIP1L1 PDGFRA fusion. As this was rare, we repeated this by FISH. This fusion was found in 180 cells (90% positive).

Diagnosis

Myeloid Neoplasm with FLIP1L1 PDGFRA fusion rearrangement.

Treatment

We have started him on Imatinib 100mg OD from last 1 week.

Follow-up

He is under our regular follow up. WBC count is in decreasing trend. Howevere final response needs to be assessed in subsequent months.

Conclusion

In a patient presenting with leucocytosis and hepatosplenomegaly, after excluding CML and other common myeloproliferative neoplasms, we should look for rare myeloid/lymphoid neoplasms with eosinophilia. In this case we did not suspect this, as eosinophilia was not significant on peripheral smear. We did NGS as we could not categorise him into any specific entity and his TLC count was increasing exponentially. In the literature search i could not find any such case reported so far. As we have recently started him on Tyrosine Kinase Inhibitors, response needs to be assessed.

Malignant Hematology-Clinical (MHC) PP-MHC-34

Hospital-Based Evaluation of upfront Daratumumab in Combination with Triplet Regimen for Treatment of Newly Diagnosed Multiple Myeloma

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Aim

This study analyzes patient outcomes and response rates following treatment with Daratumumab (DARA) in combination with triplet regimen for treatment of newly diagnosed Multiple Myeloma.

Introduction

Multiple myeloma is a malignancy of plasma cells in the bone marrow. Daratumumab, an anti-CD38 monoclonal antibody, is frequently used in combination regimens such as VRD (Bortezomib, Lenalidomide, Dexamethasone) and VCD (Bortezomib, Cyclophosphamide, Dexamethasone), demonstrate significant efficacy. This study aims to provide real-world data on the effectiveness of daratumumab-based regimens in advanced multiple myeloma.

Methods

A retrospective cohort study was conducted at a tertiary care hospital in North India, involving 51 patients diagnosed with Multiple Myeloma who received Daratumumab-based regimens (DARA-VRD and DARA-VCD) between 2023 and 2024. Patients were selected based on performance status and renal and cardiac function. Evaluations occurred after every two treatment cycles. Patients achieving Very Good Partial Response (VGPR) proceeded to Autologous Bone Marrow Transplantation (BMT), while those not eligible for ASCT received at least Six cycles followed by maintenance therapy. The study monitored survival rate and mortality during treatment and follow-up.

Results

The cohort included 51 patients, median age 59 years (range 32–84), comprising 60.7% males and 39.2% females. Treatment distribution showed that 54.9% received the DARA-VRD regimen, while 45.1% received DARA-VCD. In the study, response rate were assessed after every 2 Cycles underwent Bone Marrow Transplantation (BMT).The overall survival rate was 82.3%, and the mortality rate was 7.8%.

Conclusion

Daratumumab-based regimens are effective for advanced multiple myeloma, with high survival rates observed even in high-risk patients. The findings support daratumumab integration into standard treatment strategies and encourage further studies to assess long-term benefits and refine protocols for diverse populations.

Malignant Hematology-Clinical (MHC) PP-MHC-35

Upfront Pembrolizumab with AVD in Hodgkins's Lymphoma: Study from Tertiary Centre in India

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Background

Hodgkin lymphoma (HL) is one of the most curable forms of cancer, with high treatment success rates. Advances in treatment options, including chemotherapy, radiation therapy, and immunotherapy, have significantly improved the prognosis for patients with HL.

Methods

We performed a retrospective study of 15 HL patients, including adolescents and elderly, treated at two tertiary centers in north India between 2023 and 2024. The treatment regimen consisted of the sequential administration of Pembrolizumab with Adriamycin, Vinblastine, and Dacarbazine (AVD). Pembrolizumab (IV, 200 mg) was administered every 21 days starting on cycle 1, day 1, followed by interim assessment with PET-CT. Patients who achieved partial or complete metabolic response were subsequently given six cycles of AVD (doxorubicin [IV, 25 mg/m2], vinblastine [IV, 6 mg/m2], and dacarbazine [IV, 375 mg/m2]).

Results

This study includes patients with a median age of 43 years, spanning from 16 to 74 years. The cohort comprises 66.7% males and 33.3% females. All patients were advanced stage (stage III or IV). The distribution of the International Prognostic Score (IPS) is as follows: 46.7% with scores of 0-1, 20% with a score of 2, 13.3% with a score of 3, and 20% with a score of ≥4. B symptoms are present in 46.7% of the patients. After three cycles pembrolizumab immunotherapy, the observed responses are: 46.6% with a complete response, 40.0% with a partial response, 6% with progressive disease, and 6% resulting in death. Following the administration of six AVD cycles of Pembrolizumab 14 patients are evaluable as 1 is still on treatment, the complete metabolic response is 78.5%, with 14.2 % showing refractory disease.

Conclusion

Sequential pembrolizumab followed by AVD is a promising first-line treatment for advanced-stage Hodgkin's lymphoma, but it doesn't always result in a fairytale outcome for every patient. Here, we demonstrate that sequential Pembrolizumab-AVD therapy has shown a refractory response in 14.2 % patients, whereas it achieved 100% complete response rates in studies conducted worldwide. This suggests potential regional differences in treatment efficacy or patient response. Further studies to explore the underlying reasons and to optimize therapeutic strategies for Hodgkin Lymphoma in diverse populations.

Malignant Hematology-Clinical (MHC) PP-MHC-36

High Grade Primary Bone Marrow Diffuse Large B-Cell Lymphoma Presenting as Cold Agglutinin Disease

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Background

Diffuse Large B-cell Lymphoma is a heterogenous subtype of lymphoma comprising around 30% of all NHLs. We describe a case of DLBCL presenting with isolated marrow disease and Cold Agglutinin disease, a finding rarely reported.

Case Presentation

A 60 year old man, farmer from Maharashtra state presented to us with complains of extreme lethargy and generalised weakness since 2 months. He did not have any history of fever, bony pains or bleeding manifestations and neither had any comorbidities or previous significant medical history. On examination, he had severe anaemia with mild icterus and mild splenomegaly. No external lymphadenopathy was found. Rest of the systemic examination was unremarkable.

Diagnosis

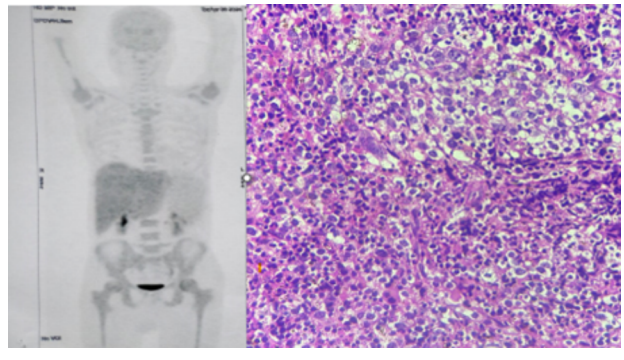
Hemogram revealed haemoglobin of 3.4gm/dL, haematocrit 4.9%, MCV 108.9fL and MCHC 69.4g/dL. Peripheral Smear showed Anisopoikilocytois with agglutinated RBCs, normocytic normochromic admixed with spherocytes, polychromatophils and nRBCs while 6% atypical cells were noted. Post Incubation normalization of MCHC and Hematocrit was noted. Serum Bilirubin was 2.5gm/dL- predominantly indirect with Sr. LDH and Uric Acid being 1191 IU/L and 11.8 mg/dL respectively. Direct and Indirect Coombs test showed Grade 4 positivity, but Monospecific DAT could not be done; although peripheral blood smear was favoring CAD. Bone marrow aspirate demonstrated 9% atypical lymphoid cells which on flow cytometry had high forward and side scatter with bright CD19 and CD20 and negative CD5, CD10. On bone marrow biopsy infiltration by clusters and sheets of these atypical cells was noted which on IHC were immunoreactive for CD20, MUM-1, Bcl-6, C-MYC and Ki67 favoring a double expressor DLBCL. Baseline CSF Analysis had no Malignant cells. On PET-CT, except for Diffuse metabolic activity in Axial and appendicular skeleton, surprisingly no lymphadenopathy was found, confirming it to be a Primary Bone Marrow DLBCL with Secondary CAD.

Treatment

5 cycles of R-CHOP with 2 Intrathecal Methotrexate have been administered, and patient is in follow up with resolved AIHA.

Conclusion

The association of CAD and exclusively extranodal DLBCL is extremely rare, with scarcely any case reports published worldwide. This needs further clinicopathological analyses to clarify the biological and clinical features of this subtype.



Malignant Hematology-Clinical (MHC) PP-MHC-37

Beyond the Nodes : A Rare Case of Mantle Cell Lymphoma with Extensive Subcutaneous Involvement

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Background

Mantle cell lymphoma (MCL) is a rare subtype of non-Hodgkin lymphoma.

Case Presentation

A 43 year-old male presented with multiple subcutaneous soft tissue masses. Biopsy revealed lymphoma. Results: Imaging showed widespread subcutaneous involvement. Flowcytometry confirmed the diagnosis of MCL. On Treatment with RCHOP

Conclusion

This case highlights an atypical presentation of MCL, emphasizing the importance of considering lymphoma in the differential diagnosis of soft tissue masses.

Malignant Hematology-Clinical (MHC) PP-MHC-38

Management of the Advanced Stage Hodgkin Lymphoma

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Introduction

Hodgkin lymphoma (HL) is a relatively common lymphoid malignancy representing one of the frequent and commonly curable types of cancer in young adults. The therapeutic approaches to patients depend on the stage, prognostic factors, comorbidities and toxicity profile.

Aim

The assessment of management options in the advanced stages of HL.

Material & Methods

The enrolled HL patients were diagnosed and treated at the Institute of Oncology from Moldova between 2018-2023. The histological type was identified according to 2022 WHO classification of hematologic neoplasms. The staging was realized according to Lugano Classification of Malignant Lymphomas. ABVD and BEACOPP regimens served as the first-line treatment options.

Results

Females comprised 62% of all HL cases. The prevalent age group was 40-50 years (rate = 36%). Nodular sclerosis proved to be the most common type of HL (87%), according to histopathological and immunohistochemical studies. Lymphoid depletion was revealed in 5% of cases, mixed cellularity - in 7%, and one case was with unspecified histological type. The main symptoms were: peripheral lymph nodes enlargement (100% of cases), cough and breath shortness (78% of cases with mediastinum involvement). The stage of HL was IIIB in 68% of patients at diagnosis. The patients were treated with ABVD and BEACOPP combined chemotherapy. Radiotherapy was performed in cases with residual tumor masses and in bulky-disease. Complete responses were obtained in 35% of cases, partial responses - in 38%. Treatment failure or relapses were registered in 27% of cases. The following post-chemotherapy toxicities were recorded: gastrointestinal disturbances in 98% of cases, grade 1-3 neutropenia in 78%, toxic liver disease in 42%. Five-year overall survival and progression-free survival proved to be higher in cases with complete responses, treated with BEACOPP regimen.

Conclusions

Current management approaches allowed to achieve the response rate of 73% in the advanced stages of HL. BEACOPP regimen remains the first-line treatment option in the advanced stage HL due to the higher complete response rate and survival.

Malignant Hematology-Clinical (MHC) PP-MHC-39

Diagnosis and Management Approaches to Patients with the Advanced Stage Non-Hodgkin Lymphomas

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Introduction

Non-Hodgkin lymphomas (NHL) are common types of cancer in adults. 60-70% of patients with NHL may be curable. The therapeutic approach to each patient depends on the immunohistochemical subtype, stage, prognostic factors, comorbidities, and toxicity profile.

Aim

The evaluation of diagnosis and management options in patients with the advanced stages of NHL.

Material & Methods

Our cohort study included 84 patients with immunohistochemically confirmed diagnosis of generalized nodal NHL analyzed in terms of short- and long-term response. Staging was realized according to Lugano Classification of Malignant Lymphomas. Mainly used antineoplastic regimens were: combined immuno-chemotherapy (R-CHOP, R-COP, BR) and conventional chemotherapy (CHOP, CHOEP).

Results

Patients age ranged between 40-78 years. The group of patients aged 60-70 years was most common (37%). All patients were diagnosed with several sites of the involved lymph nodes. B symptoms were detected in 68% of patients. Diffuse large B-cell lymphoma was identified in 57% of cases, lymphocytic lymphoma - in 13%. Marginal zone and lymphoblastic NHL proved to be less frequent types at diagnosis. Immunohistochemical studies revealed CD20-positive NHL in 95% of patients. Complete responses were obtained under immuno-chemotherapy regimens in 70% of cases. Complete responses were achieved only in 13% of patients treated with combination chemotherapy and radiation therapy. Post-chemotherapy adverse events were: pancytopenia (39%), stomatitis (89%), respiratory infections (53%), nausea, vomiting (85%). Overall survival and progression-free survival rates were higher after combined immuno-chemotherapy R-CHOP and BR.

Conclusions

The majority of patients achieved higher rates of complete responses, overall and progression-free survivals after combined treatment with chemotherapy and rituximab. Our and international studies showed that maintenance therapy with anti-CD20 antibodies increased the complete responses span and survival of patients with B-cell NHL.

Malignant Hematology-Clinical (MHC) PP-MHC-40

Parvovirus B19-Associated Red Cell Aplasia in a 52-Year-Old Male with Mantle Cell Lymphoma Post BR Therapy

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Introduction

Mantle cell lymphoma (MCL) is an aggressive form of non-Hodgkin's lymphoma that often requires immunosuppressive chemotherapy such as Bendamustine and Rituximab (BR). Immunosuppression increases the risk of viral infections, including parvovirus B19, which can cause pure red cell aplasia (PRCA). PRCA is a condition where the bone marrow ceases to produce red blood cells, leading to severe anemia. This case highlights a rare but serious complication in a patient treated with BR for MCL.

Aim and Objectives

Aim: To report a rare case of Parvovirus B19-induced PRCA in a patient with mantle cell lymphoma undergoing chemotherapy.

Objectives:

1. To describe the clinical presentation and diagnostic process of Parvovirus B19-associated PRCA.
2. To explore the relationship between immunosuppressive therapy for mantle cell lymphoma and the development of PRCA.
3. To emphasize the importance of early recognition and treatment of PRCA in patients receiving chemotherapy.

Case Presentation

A 52-year-old male with mantle cell lymphoma was treated with six cycles of BR therapy. After completing chemotherapy, the patient presented with severe anemia. Diagnostic investigations revealed pure red cell aplasia, which was confirmed to be secondary to Parvovirus B19 infection based on PCR and serology results. The patient had no prior history of anemia or bone marrow disorders, and his anemia was directly linked to the recent chemotherapy.

Results

The patient's bone marrow showed an absence of erythroid precursors, confirming the diagnosis of red cell aplasia. Parvovirus B19 PCR and serology tests were positive, indicating a viral etiology. The likely cause was immunosuppression induced by BR therapy, which predisposed the patient to Parvovirus B19 infection and the subsequent development of PRCA. Treatment included supportive care, and antiviral therapies were considered based on clinical guidelines.

Conclusion

Parvovirus B19-induced PRCA is a rare but serious complication in immunocompromised patients undergoing chemotherapy. Early recognition of PRCA and timely diagnostic testing for Parvovirus B19 are crucial to prevent severe anemia and improve clinical outcomes. This case emphasizes the need for vigilance in monitoring patients receiving immunosuppressive therapy for mantle cell lymphoma.

Additionally, the small sample size limits the generalizability of these findings, as this is a single-case report.

Malignant Hematology-Clinical (MHC) PP-MHC-41

Plasma Cell Leukemia with Renal Amyloidosis : A Case Report

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Background

Amyloidosis is a condition marked by the deposition of abnormal amyloid proteins in organs and tissues. Plasma cell dyscrasias, including plasma cell leukemia, are associated with systemic amyloid deposition, especially in organs like the kidneys. Renal involvement often manifests as nephrotic syndrome or renal insufficiency, with a poor prognosis if untreated. Here, we present a case of renal amyloidosis in a patient with suspected plasma cell leukemia, an uncommon and aggressive form of multiple myeloma.

Case Presentation

A 49-year-old female presented with suspected amyloidosis. A USG-guided biopsy from the left kidney revealed amyloid deposits, confirmed by Congo red staining, which displayed apple-green birefringence under polarized light. Histology showed pinkish deposits in the glomeruli, with focal glomerular sclerosis but no signs of atypia or granuloma formation. A bone marrow biopsy demonstrated normocellular marrow with normal myelopoiesis and erythropoiesis. There was a mild increase in plasma cells (7%), some forming small groups with intracytoplasmic and intranuclear inclusions.

Diagnosis

The histomorphological and bone marrow findings, in conjunction with the renal biopsy, led to a preliminary diagnosis of plasma cell leukemia with amyloidosis. Plasmacytosis and amyloid deposition pointed toward a plasma cell dyscrasia. Further diagnostic tests, including serum protein electrophoresis, immunofixation, and immunophenotyping, were advised to confirm the clonal nature of the plasma cells.

Follow-Up

The patient was scheduled for regular follow-up with serial renal function tests and bone marrow examinations to monitor disease progression. Immunophenotyping and additional biochemical tests were planned to assess treatment response. Trephine biopsy was to be performed to better evaluate the bone marrow's plasma cell population.

Conclusion

This case highlights the complex interplay between plasma cell dyscrasia and amyloidosis, emphasizing the importance of a comprehensive diagnostic approach in plasma cell leukemia. Early recognition and treatment are essential to managing this rare but aggressive form of plasma cell malignancy. Multidisciplinary care, including chemotherapy and supportive treatment, can help improve outcomes in such cases.

Malignant Hematology-Clinical (MHC) PP-MHC-42

Mixed Phenotype Acute Leukemia, B/T (MPAL, B/T) – A Rare Case Report

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Background

Mixed Phenotype Acute Leukemia (MPAL) is a rare and aggressive form of acute leukemia characterized by the co-expression of markers from more than one hematopoietic lineage, most commonly B- and T-cell markers. MPAL accounts for approximately 2-5% of all acute leukemia cases and is associated with poor prognosis due to its complex nature and challenging treatment requirements.

Case Presentation

A 39-year-old female from West Bengal, India, presented with signs of acute leukemia. Her complete blood count (CBC) showed a hemoglobin level of 12.4 gm/dL, RBC count of 4.58 million/mm^3, a low total leukocyte count (TLC) of 3,070 cells/µl, and a platelet count of 0.37×10^5/µl. The differential count showed 93% neutrophils and 5% lymphocytes. Bone marrow biopsy revealed 90% hypercellularity and 29% blasts. Immunophenotyping confirmed co-expression of B-cell markers (CD19, PAX5, CD79a) and T-cell markers (CD3, CD5, CD7, CD1a), establishing a diagnosis of Mixed Phenotype Acute Leukemia, B/T (MPAL, B/T).

Diagnosis

The diagnosis of MPAL, B/T was made based on the following key findings:

Co-expression of T-lineage markers (cyCD3, CD5, CD7, CD1a) and B-lineage markers (CD19, PAX5, CD79a). Immunohistochemistry and flow cytometry were instrumental in confirming the dual lineage involvement, with CD19 and PAX5 identifying the B-cell component and CD3, CD5, and CD7 confirming the T-cell component. A bone marrow biopsy revealed 29% blasts, marked hypercellularity (90%), and lymphoid blasts with a high nucleus-to-cytoplasm ratio, further supporting the diagnosis of acute leukemia.

Conclusion

MPAL, B/T, is a rare, aggressive leukemia requiring a precise diagnosis through immunophenotyping and flow cytometry. The dual-lineage expression of B- and T-cell markers highlights the complexity of this case. Early diagnosis and aggressive treatment, often involving multi-lineage chemotherapy and potentially stem cell transplantation, are critical to improving outcomes. Close monitoring and further cytogenetic studies are essential for tailoring treatment and improving the patient's prognosis, as MPAL has a higher risk of relapse compared to other types of acute leukemia.

Malignant Hematology-Clinical (MHC) PP-MHC-43

Role of Next Generation Sequencing in T-ALL: A Report of Two Cases

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Background

Acute lymphoblastic leukemia (ALL) is a hematological malignancy characterized by theuncontrolled proliferation of immature lymphoid cells. Significant advancements have been made in understanding the biology of ALL, resulting in remarkable improvements in its diagnosis, treatment, and monitoring. However, in India, next-generation sequencing (NGS) is often not utilized for T-ALL, despite its potential to provide valuable insights into disease biology and guide treatment decisions.

Case Reports

We present two cases of T-ALL to highlight the clinical utility of NGS.

Case 1: A 15-year-old boy presented with symptoms of easy fatuguability and breathlessness on exertion. NGS revealed a novel NUP214/ABL1 fusion with CDKN2A, CDKN2B deletion. This genetic alteration is associated with a specific molecular subtype of ALL, which can inform treatment decisions. Targeted therapy with Dasatinib was initiated, resulting in a favorable response and achieving minimal residual disease negativity.

Case 2: A 1-year-old boy was diagnosed with T-ALL. NGS identified a germline FANCA mutation, indicating an underlying genetic predisposition to the disease. The patient underwent matched unrelated allogeneic hematopoietic stem cell transplantation (HSCT). As this patient was otherwise not a candidate for stem cell transplant based on this information we were able to decide on Allo HSCT on this patient.

Conclusion

These cases demonstrate the significant role of NGS in T-ALL management. By identifying novel genetic alterations and providing insights into disease biology, NGS can inform

treatment decisions and improve outcomes. The routine integration of NGS into clinical practice is warranted, especially in complex cases or when standard therapies fail. Further research is needed to explore the full potential of NGS in T-ALL and to develop targeted therapies based on specific genetic alterations.

Miscellaneous/Molecular Hematology (MH) PP-MH-1

VEXAS Syndrome Versus MDS : A Diagnostic Conundrum

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Background

The new entity, VEXAS syndrome is an acquired auto-inflammatory disease associated with hematological disorders such as multiple myeloma, MDS etc. We encountered a challenging case where next generation sequencing came to our rescue in making the correct diagnosis.

Case Presentation

A 55-year male presented with transfusion dependent refractory anemia for six months. Peripheral smear shows normocytic normochromic to macrocytic anemia with no abnormal cells. Serum protein electrophoresis showed an abnormal M band with a concentration of 400mg/dl along with high Serum free light chain ratio and serum immunofixation showing cross reactivity with IgG Kappa. PET scan showed diffuse low-grade metabolic activity in the marrow with no evidence of bony lytic lesions. Bone marrow aspirate smears revealed cellular marrow with <5% plasma cells and significant dysmegakaryopoeisis in the form of micro-megakaryocytes and multi-nucleation. Flow cytometry showed 3.4% normal myeloid blasts along-with 0.7% clonal abnormal plasma cells and no definite evidence of dyspoeisis in any of the three lineages. Cytogenetics by FISH did not reveal any abnormality. The clinician suspected it to be a case of VEXAS syndrome. However, NGS showed two pathogenic mutations in the form of point substitution (stop gain) in STAG2 gene along with in-frame deletion in SRSF2 gene with VAF of 75.84% and 30.47% respectively. A final diagnosis of MDS with concomitant MGUS was favored over VEXAS syndrome.

Conclusion

The molecular landscape in VEXAS related MDS is not typical of classical MDS, in which myeloid neoplasia gene mutations such as SRSF2 and STAG2 in the present case are common, large clones are present, and multiple genes are often involved.

Miscellaneous/Molecular Hematology (MH) PP-MH-2

PAX5 fusions in Precursor B cell Lymphoblastic Leukemias : A Single Centre Experience

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Introduction

PAX5 alterations in B-ALL include point mutations, copy number alterations and fusions. PAX5 fusions involving different partner genes are found in 2.5% of pediatric and 01% of adult B-ALL patients. These are known to be NCN high risk category.

Aim and objective

To study the utility of RNA sequencing in PAX5 rearranged B-ALL patients and correlate with cytogenetic and clinical profile.

Methodology

It was a retrospective observational study in which all newly diagnosed B-ALL patients in whom RNA sequencing was performed at baseline were included. The B-ALL patients with PAX-5 fusions on RNA sequencing were studied for correlation with MRD studies and treatment outcomes.

Results

PAX5 fusions were observed in 2.1% pediatric and 3.44% adult B-ALL patients in our study. CD25, CD10 and CD33/CD15 were found in 37.5%, 100% and 37.5% of our patients respectively. The partner genes involved were mostly ETV6 (37.5%) followed by ZCCHC7 (25%), ELN, NOL4L and CBFBT2A3 (12.5% each). Most common exon affected in PAX5 gene is exon 4 followed by exon 5. None of the cases had CNS involvement. RNA sequencing revealed concordance with FISH results in three patients. However, partner genes could not be ascertained by FISH technique. Two patients had IKZF1 deletions. None of the patients was steroid refractory. 12.5% of patients showed post induction MRD positivity. None of the patients showed relapse or refractory disease.

Conclusion

This is an upcoming entity as per the new WHO classification of lymphoid neoplasms. Our patients showed better outcomes in comparison with published literature. More comprehensive data is required to make definitive opinion about its clinical significance in Indian patients.

Miscellaneous/Molecular Hematology (MH) PP-MH-3

Spectrum of Mutations in the Globin Gene Cluster Prevalent in the Thalassemia Cohort of West Bengal

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Introduction

As per the latest global epidemiology data, worldwide prevalence of Beta thalassemia ranges from 3-4%. As per 2016 report, published by Ministry of Health and Family welfare, there are 42 millions β-thalassemia carriers and more than 150000 thalassemia patients in India. In eastern India especially West Bengal, HbE-Beta thalassemia is more prevalent and its phenotype varies from severe anaemia to thalassemia intermedia. Phenotypic severity lies on the type of mutation present. 954 DNA variants in HBB gene are reported in globin gene server and more than 400 mutations cause thalassemia. Data from various regions on Indian population, revealed that more than 80 different mutations characterize the Indian thalassemia population. Present panel based molecular screening is able to characterize 90-95% of thalassemia but 10-5% remains undefined.

Aims & Objectives

To investigate underlying molecular defects in globin gene cluster including HBB and HBA genes and assist in the diagnosis of 422 unexplained cases of hemoglobinopathy.

Materials & Methods

In a prospective study from 2015-2023, 422 suspected cases of hemoglobinopathy were referred for genetic screening of beta and alpha globin genes. After written informed consent, CBC and HPLC were done for all cases. Genomic DNA was isolated using Qiagen Blood DNA kit. Initially seven most common mutations were investigated by ARMS-PCR method and then DNA sequencing was done. Alpha thalassemia and δβ-thalassemia determinants were investigated where required by GAP-PCR.

Result

In 123 cases, ARMS-PCR gave complete result. Alpha thalassemia (αα/α-3.7) deletion was found in 18 cases whereas alpha (ααα3.7anti) triplication was found in 48 cases. δβ-thalassemia was present in 19 cases. DNA sequencing revealed 11 different rare mutations in 34 (8%) cases. Four Hb variants were found in 10 (2.3%) cases. Mutations in the promoter region are present at 20 (4.7%). Out of 422 cases, no mutation was detected in 51 (11.3%) which remain undefined.

Conclusion

In the recent study on prenatal screening from our institute, in 7.3% of risk couples, no mutations could be detected by ARMS-PCR method. In the present study, we are able to characterize 10.4 cases having rare mutations by HBB gene sequencing. These cases if remained undetected, will further increase the burden of thalassemia in India.

Miscellaneous/Molecular Hematology (MH) PP-MH-4

NPM1 mutated AML with concurrent DNMT3A mutation, and FLT3-internal tandem duplication has outcomes similar to European Leukemia Net Adverse Risk Category

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Introduction

Previously our group (Patkar et al, *Blood Cancer Journal* 2019) and others have indicated that *NPM1* mutated acute myeloid leukemia (AML) with concurrent *DNMT3A* and *FLT3*-internal tandem duplication triple mutated AML (TM-AML) may have inferior outcomes. The European LeukemiaNet 2022 (ELN-22) risk stratification doesn't take *DNMT3A* mutations into account. Here, we demonstrate that this subset of AML has an inferior outcome as compared to *NPM1* mutated AML.

Aim & Objective

NPM1 mutated AML with concurrent DNMT3A mutation, and FLT3-internal tandem duplication has outcomes similar to European LeukemiaNet Adverse Risk Category & we demonstrate that this subset of AML has an exceedingly inferior outcome as compared to NPM1 mutated AML and should be considered as a distinct AML entity.

Methods

506 patients of adult AML (≥18 years) uniformly treated with "3 + 7" induction were accrued over 10 years (2012 – 2023). Diagnostic samples were sequenced using a 50-gene myeloid panel (till 2020) and subsequently using a 135-gene panel. Cases were risk-stratified as per ELN22 recommendations. Post induction MRD was evaluated using 10-color or 16-color flow cytometry (PI MFC-MRD). Patient characteristics (WBC counts, age) of this TM-AML subset against *NPM1* mutated AML were evaluated. The outcomes of TM-AML with other ELN-22 risk groups were compared. The prognostic impact of TM-AML on overall survival (OS) and relapse-free survival (RFS) was computed using the Kaplan–Meier method and compared using log-rank test for time-to-event analyses.

Results

The median age of the overall cohort was 35 years with a median follow-up of 29.5 months. The median OS was 80 months and the median RFS was 52.3 months. Based on ELN22 recommendations, patients were classified as favorable (n=275), intermediate (n=157), or adverse risk (n=75). AML with *NPM1* mutation was the commonest entity (n=144, 28.4%) in our cohort of which 15 cases of concurrent *NPM1, FLT3-ITD, and DNMT3A* triple mutated AML were detected. TM AML cases presented with a higher WBC count ($p = 0.001$) as compared to ELN22 intermediate and adverse risk groups. TM AML cases showed an inferior OS ($p = 0.01$) and RFS ($p = 0.0001$) compared to AML with *NPM1* mutated cases. In comparison with ELN22 intermediate risk AML cases, TM AML showed inferior OS ($p = 0.01$) and RFS ($p = 0.002$).

Conclusion

De novo AML patients with concurrent DNMT3A, FLT3 and NPM1 mutations present with higher WBC count and have outcomes comparable to ELN-22 adverse risk AML.

Miscellaneous/Molecular Hematology (MH) PP-MH-5

Non-Invasive Foetal Sex Determination with Cell Free DNA From Maternal Plasma Using Droplet Digital PCR

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Introduction

Fetal sex determination is useful for families at risk of X-linked disorders for genetic counselling or intervention if necessary. Currently this is performed through invasive procedures such as amniocentesis and chorionic villus sampling (CVS), with a 1% risk of miscarriage.

Aims & Objectives

The aim of this study is to identify the utility of ddPCR for determining sex of the foetus using circulating cell free fetal (ccff) DNA in maternal plasma and to validate by comparing with the Chorionic villus sample (CVS) results.

Materials & Methods

Twenty six pregnant women who came for prenatal diagnosis of inherited disorders from March 2024 to July 2024 were included in this study. Blood samples were collected in EDTA tubes from pregnant women at 10-12wks gestational age. Plasma was separated within 3 hours from sample collection according to the protocol. DNA was extracted from 4 mL of maternal plasma by using the QIAvac Vacuum system. We employed droplet digital PCR (ddPCR) to evaluate the determination of fetal sex. ZFY (region on Y-chromosome) probe was tagged with FAM and is read on channel 1. ZFX (region on X-chromosome) probe was tagged with VIC and is read on channel 2. A minimum of > 4 droplets was considered positive for any channel.

Result

Median age and gestational age of the cohort were 28 years and 13 weeks respectively. Among the 37 cases, there were 10 cases of haemophilia, 22 cases of beta thalassemia, and one case each of alpha thalassemia, F13 deficiency, BTK, JAK3 and Glanzmann's thrombasthenia. Out of 37 samples 17 were showed both ZFY and ZFX amplification on ddPCR, rest of 20 were showed only ZFX amplification. Concordance 100% CVS sampling based sex determination.

Conclusion

The ddPCR is a robust, efficient and reliable method for fetal sex determination from maternal plasma. Invasive prenatal diagnosis if necessary can be limited to male foetuses in couples with X-linked disorders.

Miscellaneous/Molecular Hematology (MH) PP-MH-6

The Study Establishes that NUDT15 Polymorphism Plays More Significant Role Over TPMT Polymorphism in Determining the Risk of Thiopurine Drug Related Toxicity

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Introduction

Clinical Pharmacogenetics Implementation Consortium (CPIC) Guideline,2018 focus on gene-drug pairs for clinical relevance and actionable recommendation to alter a dose based on the genotype-phenotype relationship. Thiopurine drugs (azathioprine, mercaptopurine, and thioguanine) are commonly prescribed to treat patients having Acute Lymphoblastic Leukemias (ALL) and Autoimmune Disease. These drugs are metabolized to the active 6-thioguanine nucleotide (6-TGN) which is further metabolized by Thiopurine S-Methyltransferase (TPMT) Nudix Hydrolase 15 (NUDT15). Genetic variants in TPMT and NUDT15 can lead to accumulation of 6-TGN, leading to increased risk of drug-related toxicity with standard doses of thiopurine drugs.

Aims & Objectives

The objective of the study was to establish and compare the frequency of NUDT15 and TPMT polymorphism in our population.

Materials & Methods

We performed retrospective analysis of 29 samples in our lab for NUDT15 and TPMT polymorphism in past two years. Total genomic DNA was isolated and purified from peripheral blood leukocytes using QIAamp DNA Blood Mini Kit 51106 QIAGEN. The NUDT15 polymorphism analysis in exon 1 and exon 3 were performed by Sanger sequencing and TPMT polymorphism was performed by restriction fragment length polymorphism (RFLP).

Result

TPMT and NUDT15 polymorphism analysis were performed for 29 patients. Out of these 66% (N=19) had NUDT15*1/*1 (wild type), phenotypically normal metabolizer, whereas 31% (N=9) of NUDT15*3 allele (Heterozygous), phenotypically intermediate metabolizer and 3% (N=1) of NUDT15*3 allele (Homozygous), phenotypically poor metabolizer. Only 7% (N=2) showed TPMT polymorphism*1/*3C (Heterozygous) phenotypically Intermediate metabolizer.

Conclusion

Our study shows the frequency of NUDT15 polymorphism are more common as compared to TPMT polymorphism. Detecting NUDT15 polymorphism along with TPMT polymorphism is important for clinico-pharmacogenetic implementation and guiding the dosage of Thiopurine therapy. Although the number of cases in our study is small and a larger cohort of cases would require to establish that the frequency of NUDT15 and TPMT polymorphism in Indian population, we conclude that NUDT15 polymorphisms are common than TPMT polymorphism.

Miscellaneous/Molecular Hematology (MH) PP-MH-7

Paradigms and Challenges of Pre-PCR Processing and RQ-PCR Assay: A Single Centre Experience

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Introduction

The goal of pre-PCR processing in RQ-PCR is to convert a complex biological samples (blood, bone marrow, fluids) into a PCR-amplifiable sample. This mainly involves lysis of the red blood cells and separating out WBCs to process for DNA/RNA extraction and archival of samples. This is important because PCR inhibitors can significantly reduce the sensitivity and kinetics of diagnostic/real-time quantitative PCR when applied directly to biological samples. The general practice in most part of our country is to outsource molecular tests to reference laboratories as setting up of a molecular lab involves heavy investment, skilled technicians and strict quality control implementation. It thus becomes important for the reference laboratories that receive samples after a delay of at-least 24-48 hours to ensure optimal and reproducible Pre-PCR processing methodology. We, as a referral molecular laboratory, validated the different steps of Pre-PCR processing at 0 hour, 24 hours and 48 hours using in-house prepared reagents and demonstrated consistent results at different time-points (RNA and DNA/cDNA concentration on Nanodrop and/or Qubit/gel electrophoresis run/OD ratios as well as ABL copy numbers, to ensure that samples from peripheral centres, also achieve accurate results. We also compared the IS-NCN% of BCR-ABL (P210) assay using in-house prepared plasmid controls and primers/probes, with readymade kits and pDNA standards (SIGMA), diluted in salmon DNA, in order to find out whether pDNA standards can serve as a cheaper alternative to the multitude of readymade kits available in the market. The results are intriguing and need to be discussed.

Miscellaneous/Molecular Hematology (MH) PP-MH-8

Preimplantation Genetic Testing for Monogenic Disorders (PGT-M) in Hematological Cases

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Introduction

Hematological disorders like thalassemia, sickle-cell anemia and glucose-6-phosphate dehydrogenase deficiency (G6PD) are very prevalent in India. Preventive strategies are therefore extremely important to control the disorder from passing on to the next generation. To avoid the trauma of termination of multiple affected pregnancies, Preimplantation Genetic Testing (PGT) through in vitro fertilization (IVF) technology is useful to select unaffected (for pathogenic variant) euploid embryos for implantation. An HLA matched unaffected euploid embryo can also be selected through PGT for 'savior sibling' to cure previous affected child using hematopoietic stem cell transplant (HSCT).

Aims & Objectives

To offer PGT for couples where both partners were carriers of hematological disorders and for selection of HLA matched unaffected euploid embryos if required.

Materials & Methods

PGT for monogenic disorder (PGT-M) was offered for 28 couples heterozygous for hematological disorders (19 b-thalassemia with 4 HLA matching, 4 sickle cell anemia, 2 b-thalassemia/sickle cell anemia and 1 each of hemochromatosis, MTHFR and G6PD deficiency with MTHFR). During the IVF cycle, trophectoderm cells biopsied from blastocyst stage embryos were subjected to aneuploidy screening by PGT-A followed by PGT-M for pathogenic variants. Unaffected euploid embryos were selected for implantation for 18/28 (64%) couples. Prenatal diagnosis reconfirmed the PGT results. For 1/4 cases of PGT-M for b-thalassemia with HLA matching of embryos with the affected child, the single HLA matched unaffected euploid embryo was used for implantation.

Result

The results of PGT for 28 couples are summarized in Table 1. Pregnancy achieved in 16/18 (89%) couples, 4 are ongoing (25%) and full term healthy delivery in 11 couples (69%) (8 b-thalassemia, 2 sickle cell anemia, 1 MTHFR). For G6PD with MTHFR variants, a twin pregnancy occurred but miscarried in the first trimester. For b-thalassemia, all 8 pregnant women (100%) delivered healthy unaffected children. One of these was a HLA identical brother acted as a savior sib for the cure of his elder b-thalassemia affected sister. This is the first reported HLA matched birth from Maharashtra and the second in India. For other 3 couples no HLA matched embryo was available. New cycles are ongoing.

Disorder	Couple	No. of cycles	No. of unaffected euploid embryos	No. of Embryos Transferred	Pregnant	Aborted	Delivered
β-Thalassemia	1	1	6	1	1	-	1
	2	3	3	3	-	N/A	N/A
	3	1	5	1	1	-	1
	4	1	2	1	1	-	1
	5	1	All 4 embryos with chromosomal aneuploidy	No embryo for transfer	N/A	N/A	N/A
	6	1	3	Embryo transfer awaited	N/A	N/A	N/A
	7	1	5	2	1	-	1
	8	1	5	2	1	-	1
	9	2	2	1	1	N/A	1
	10	1	2	2	-	N/A	N/A
	11	2	5	1	1	-	1
	12	1	1	1	1 (ongoing)	N/A	-
	13	1	2	1	1 (ongoing)	N/A	-
	14	1	7	1	1 (ongoing)	N/A	-
	15	1	1	1	1 (ongoing)	N/A	-
β-Thalassemia with HLA matching	16	3	6, of which only 1 HLA matched	1 with HLA matched embryo	1	-	1
	17	3	7, of which not a single HLA matched	No embryo transfer done	N/A	N/A	N/A
	18	1	No euploid unaffected embryo	No embryo for transfer	N/A	N/A	N/A
	19	2	4, of which not a single HLA matched	No embryo transfer done	N/A	N/A	N/A
β-Thalassemia / Sickle Cell Anemia	1	1	All embryos affected	No embryo for transfer	N/A	N/A	N/A
	2	1	All embryos affected	No embryo for transfer	N/A	N/A	N/A
Sickle Cell Anemia	1	1	2	Embryo transfer awaited	N/A	N/A	N/A
	2	2	Both embryos with aneuploidy	No embryo transfer	N/A	N/A	N/A
	3	1	2	1	1	-	1
	4	1	2	1	1	-	1
G6PD with MTHFR	1	1	3	1	1 (Twin)	1	N/A
Hemo-chromatosis	1	1	1	Embryo transfer awaited	N/A	N/A	N/A
MTHFR	1	1	4	1	1	N/A	1

Table 1: Results of PGT for hematological disorders on 28 couples, showing 11 livebirths (69%) and 4 ongoing (25%) from 16 pregnancies. This shows success rate of 94%. (N/A: Not Applicable)

Conclusion

PGT through IVF is now available in India and at our center for hematological (89% PGT successful unaffected pregnancies) and many other monogenic disorders to get an unaffected, even HLA matched, chromosomally normal child.

Miscellaneous/Molecular Hematology (MH) PP-MH-9

RASopathies Mimicking Juvenile Myelomonocytic Leukemia: A Report of Four Cases

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Background

Juvenile myelomonocytic leukemia (JMML) is an aggressive myeloproliferative neoplasm in early childhood driven by RAS pathway mutations, often presenting with granulocytosis, monocytosis, and organ infiltration. Hematopoietic stem cell transplant (HSCT) remains the only curative therapy for JMML. However, germline RAS mutations, characteristic of RASopathies, can mimic JMML, presenting with transient myeloproliferative features but typically resolving spontaneously. Distinguishing somatic from germline mutations is crucial for ensuring proper management and avoiding overtreatment with aggressive therapies like HSCT.

Case Presentation

We report four male patients aged 10 months to 1 year 11 months who presented with fever, splenomegaly, and elevated total leukocyte counts (TLC) (Table 1). Clinical suspicion of JMML arose due to monocytosis and splenomegaly in all cases.

Diagnosis

Bone marrow immunophenotyping revealed no abnormal myeloid blasts in three cases, while one case showed subtle abnormalities (CD25 and CD11b expression) in the stem cell compartment, suggestive of JMML. Cytogenetic analysis using FISH was negative for BCR::ABL1 and monosomy 7 in all four cases. Next-generation sequencing using a 137-hematolymphoid gene panel identified NRAS mutations (p. Gly12Ala, Gly13Asp and Gly12Asp in 2 cases) with variant allele frequencies (VAF) greater than 45% in all cases. The NRAS variant were present in exon 2 in all four cases (Gly12Ala, Gly13Asp, and Gly12Asp in 2 cases). Given the high VAF (>25%), peripheral blood T cells were sorted using flow cytometry to confirm germline status. All four patients had the same NRAS variant in T cells, confirming the germline nature of the variants.

Treatment

Three patients were treated with Azacytidine. One patient developed thrombocytopenia and peripheral blood blasts and was subsequently treated with OMCT alongside Azacytidine. The fourth patient showed spontaneous clinical improvement and did not require therapy.

SN	Age	Gender	Clinical findings	Bone marrow aspirate and immunophenotype	Treatment and follow-up
1	1 year	Male	Fever, cough (1 month), splenomegaly; TLC: 78.8 x 10^9 /L, AMC: 5.55 x 10^9 /L	60% blasts/hematogones; No evidence of dyspoiesis or abnormal blasts	Treated with Azacytidine (5 cycles). TLC reduced to 7.58 x 10^9 /L, spleen regressed to just palpable. No transfusions at 6 months follow-up.
2	10 months	Male	Fever, progressive abdominal distension, left axillary swelling; TLC: 57.7 x 10^9 /L, AMC: 11.31 x 10^9 /L	10% blasts/hematogones; No evidence of dyspoiesis or abnormal blasts	Initially on Azacytidine; developed thrombocytopenia with 2% blasts. Started on OMCT + Azacytidine. TLC reduced to 9.4 x 10^9 /L at 3 months follow-up.
3	1 year 11 months	Male	Fever (1 month), abdominal distension (6 months); TLC: 20.68 x 10^9 /L, AMC: 1.89 x 10^9 /L	8% blasts/hematogones; CD11b+ and CD25+ myeloid blasts; suspicious of JMML	On Azacytidine (5 cycles). Spleen size reduced (9 cm to 2 cm below costal margin), TLC reduced to 10.04 x 10^9 /L at 5 months follow-up.
4	1 year 3 months	Male	Pallor (1 month), hepatosplenomegaly; TLC: 53 x 10^9 /L, AMC:1.90 x 10^9 /L	50% blasts/hematogones. No evidence of dyspoiesis or abnormal blasts	No therapy initiated. Splenomegaly resolved, patient playful and transfusion-independent for 3 months. TLC reduced to 30.2 x 10^9 /L at 4 months follow-up.

Follow-up

Over 3 to 6 months, all patients demonstrated reductions in spleen size and TLC. Three patients remained transfusion-independent.

Conclusion

In cases of suspected JMML with high VAF (>25%) RAS pathway mutations, it is critical to assess for germline variants. RASopathies can mimic JMML but often have a more favorable prognosis, resolving spontaneously. Early recognition of germline mutations can prevent unnecessary aggressive treatments like HSCT and improve patient outcomes.

Miscellaneous/Molecular Hematology (MH) PP-MH-10

Genomic landscape of Chronic Myelomonocytic Leukemia

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Introduction

Chronic myelomonocytic Leukemia (CMML) is a clonal disorder of hematopoietic cells presenting with myeloproliferative and myelodysplastic features. Such E et al incorporated molecular genetic data into the existing CMML-specific prognostic scoring system (CPSS) resulting in an integrated clinical/pathological/genetic risk stratification tool.

Aims and objectives

Studying the genomic landscape in CMML patients and to correlate with CPSS-Mol score.

Materials and methods

We studied 58 cases of CMML diagnosed from 2018-2024. Baseline clinical characteristics of the patients, including age, sex, CBC counts were noted. Bone marrow aspirate (BMA) samples were examined for blast count, monocytes and dyspoiesis. Cytogenetic findings were noted, wherever available. DNA was extracted and processed for NGS to study the mutational profile of these patients. CPSS-Mol scores were calculated *using Calculate by Qx MD.*

Results

Median age of the cohort was 60 years (M:F=1.8). Distinction between myelodysplastic (MD) and myeloproliferative (MP) CMML could be made in 50 cases, based on WBC count cut-off of $13x10^9$/L, majority (62%) being MP CMML. On BMA examination, 38% cases were classified as CMML-1 and 62% as CMML 2, based on blast percentage. On cytogenetics, 17% cases showed an abnormality, including monosomy 7(45%), trisomy 8, del(20q), del(7q) and trisomy 21. Of the 58 cases, 96.5% had at least 1 mutation and included *NRAS*(31.03%), *RUNX1*(25.86%), *SRSF2*(24.13%), *CBL*(22.41%),

ASXL1(17.24%) and *DNMT3A*(15.5%). All these genes, except *DNMT3A,* are included in the recommended minimal gene set for diagnosis of CMML (WHO 2022). Most common mutations in MP-CMML included *NRAS*(18%), *TET2*(13.7%) and *ASXL1*(8.6%), whereas for MD-CMML it was *RUNX1*(15.51%), *SRSF2*(12.06%), *TET2*(10.34%). Copy number analysis was available in 24 patients, comprising loss of chromosome 7 (8.33%), gain in chromosome 8(4.16%), gain in chromosome 21(4.16%), and deletion in chromosome 5q(4.16%). On applying CPSS-Mol score, 16% patients could be grouped as intermediate-1, 45% as intermediate-2, and 38.6% as high risk. The most common mutation in intermediate-1 group was *TET2,* in intermediate-2 was *NRAS* and in high was *RUNX1.*

Conclusion

CMML can be difficult to diagnose with morphology overlapping with other entities of MDS and/or MPN. Mutational profile can be a helpful diagnostic and stratification parameter in such cases.

Miscellaneous/Molecular Hematology (MH) PP-MH-11

Non-invasive Prenatal Diagnosis of Beta Thalassemia Using Maternal Plasma by DDPCR

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Introduction

Prenatal diagnosis of beta-thalassemia traditionally relied on chorionic villus sampling (CVS) or amniocentesis, which carry a risk of miscarriage in 1

Aims & Objectives

The aim of this study is to identify the performance of ddPCR for analyzing specific β-thalassemia mutations in ccff-DNA of maternal plasma and compare with the CVS results.

Materials & Methods

Peripheral blood samples of beta thalassaemia couples with an IVS I-5(G>C) mutation were included in the study. Plasma DNA was extracted by the QIAVac Vaccum Systems. A Novel assay combining haplotype and mutation dosage analysis by ddPCR was performed by targeting a common polymorphism, Codon 2 T>C by allele specific primers and Tagged probes for IVS I-5(G>C) and IVS I-5(G=) respectively. Two ddPCR reactions were done, one targeting the 'T' allele and the other targeting the 'C' allele for all the samples (maternal plasma). Genomic DNA based sequencing of mother and father was also performed using the same allele specific primers to identify the allele carrying mutation in the parents. The assay was standardized with 5 genomic DNA (1-10ng/ul) samples and validated on 13 maternal plasma samples.

Result

Thirteen couples who came for PND of beta thalassaemia were included. The median gestational age was 13 weeks [Range: 11-19 weeks]. Assay was standardized for the primer-probe concentration and reaction set-up was performed on normal controls and patient's genomic DNA. Among these five were wild type, seven were heterozygous and one showed homozygous according to the new assay. ddPCR results were 100% concordant with the CVS results. Foetal Fraction [FF]was calculated by allele specificity and FF was ranged 0.5-2.5% among the validation cohort.

Conclusion

Performing haplotype and mutation dosage-based assay on maternal plasma showed 100% concordance with CVS sampling. Bigger validation cohort is being included to increase the confidence of the assay. One limitation observed was that, in cases where the foetus shared same alleles as mother, estimating foetal fraction was not possible by this method.

Miscellaneous/Molecular Hematology (MH) PP-MH-12

Measurement of T-Cell Receptor Excision Circles (REC) and Kappa Receptor Excision Circles (KREC) for the Screening of Suspected Severe Combined Immunodeficiency (SCID) Patients Using DD-PCR

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Introduction

Severe combined immune deficiency (SCID) is a potentially fatal primary immunodeficiency characterized by the absence of T and/or B lymphocytes. Various genes and their variants have been associated with SCID. T-cell Receptor Excision Circles (TREC) and Kappa Receptor Excision Circles (KREC) are good indicators of impaired development of T-cells and B-cells respectively. Screening for TREC and KREC is a useful tool for the screening of SCID

Aims & Objectives

In this study we standardise a ddPCR based assay to screen for TREC and KREC levels in the genomic DNA samples of the suspected PID cases .&To standardise the assay on genomic DNA samples from healthy controls and known SCID patients

Materials & Methods

Previously diagnosed cases of SCID with confirmed molecular defects (n=10) and 10 healthy controls were included for the standardisation of the assay. DNA samples were diluted to the range of 1-10 ng/uL concentration. The DD-PCR assay was developed using specific primers and probes to detect TREC/KREC, and a reference gene Ribonuclease P/MRP subunit p30 (RPP30) from DNA samples. TREC and KREC values were calculated as percentages with the control gene (RPP30).

Result

Based on the TREC and KREC values on the healthy control DNA, Median and Inter Quartile Ranges (IQR) were calculated. TREC and KREC values were defined to be reduced if they are less than the 1st quartile. All the 10 PID cases showed TREC values less than the 1st quartile. KREC values were seen to be decreased in 5/10 cases with the rest showing values within the IQR. This variation in TREC and KREC values correlated with the genetic variants identified by NGS suggesting T-B- SCID and T-B+ SCID respectively.

Conclusion

ddPCR based assay to measure TREC and KREC is a robust technique to screen suspected patients for SCID. The assay is designed and standardised in such a way that it can also be employed in non-invasive prenatal screening of foetuses suspected to have SCID. It also gives us the clue about the disorder in the foetus whether it is T-B- SCID and T-B+ SCID.

Miscellaneous/Molecular Hematology (MH) PP-MH-13

Molecular Subtyping of B-cell Acute Lymphoblastic Leukemia and its Impact on Measurable Residual Disease Outcomes: A Descriptive Study

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Introduction

A morphology and immunophenotyping are used to diagnose B-cell acute lymphoblastic leukemia (B-ALL), which is subtyped based on molecular and cytogenetic abnormalities, form the basis for risk stratification, and are associated with prognostic and therapeutic implications. We aim to characterize B-ALL cases based on molecular subtypes in our cohort

Aims & Objectives

1. To determine molecular subtypes and measurable residual disease status of B-ALL.

2. To correlate the molecular subtype of B-ALL with measurable residual disease status.

Materials & Methods

We retrieved all the B-ALL cases received in the molecular hematology laboratory for common B-ALL RT-PCR-based fusion transcript assessment from January 2018 to December 2023 [BCR::ABL1, ETV6::RUNX1, MLL::AF4, and E2A::PBX1]. The RNA-based targeted fusion panel NGS was done in RT-PCR-negative cases. A flow-cytometry-based end-induction measurable residual disease (EOI-MRD) assessment was retrieved.

Result

The total number of B-ALL samples received was 1020. Of these, 676 cases had molecular and MRD data (Table 1). The median age of presentation was 7 years (range:0-63) with a male-to-female ratio of 1.7:1. One-hundred-eighty-seven cases (27.6%) were positive for one of the four fusion transcripts tested. Among the RT-PCR positive cases, the ETV6::RUNX1 positivity was seen in almost 50% (n=94) of cases, followed by BCR::ABL1(n=47, 25.1%), E2A::PBX1 (n=40, 21.3%), and MLL::AF4 (n=6, 3.2%) positivity. The EOI-MRD was positive in 29% (n=197) and negative in 71% (n=479) cases. The EOI-MRD positivity was higher in BCR::ABL1 (n=24, 51.1%) and MLL::AF4 (n=3, 50%) positive cases while lower in ETV6::RUNX1 (n=17, 18%) and E2A::PBX1 (n=8, 20%) positive cases. NGS for the targeted fusion panel was done in 37 RT-PCR-negative cases. NGS detected fusion in 9 cases (24.3%), of which 7 cases (66.7%) showed MRD-positivity, while no fusion was detected in the remaining 28 cases (80.5%) and showed MRD-positivity in 8 cases (28.6%).

De-novo B-ALL cases with Molecular and MRD data(January2018-December2023)

Baseline Characteristics	All cases (n=676)	RT-PCR POSITIVE (n=187) (27.6%)	RT-PCR NEGATIVE (n=489) (72.4%)
Median Age (yrs)(ranges)	7 (0-63)	6 (0-63)	7 (0-60)
Age-group wise distribution			
Children (≤ 15 years)	484 (71.6%)	143(76.4%)	341(69.7%)
Adolescent-young adult (16-39 years)	147 (21.7%)	33(17.6%)	114(23.3%)
Adult (≥40 years)	45 (6.7%)	11(5.8%)	34(6.9%)
Gender wise distribution			
Male	429 (63.5%)	119(63.6%)	310(63.3%)
Female	247 (36.5%)	68(36.3%)	179(36.6%)
M:F ratio	1.7:1	1.7:1	1.7:1
End-Induction MRD			
MRD-Negative	479 (71%)	136(72.7%)	343(70.1%)
MRD-Positive	197 (29%)	51(27.2%)	146(29.8%)

Conclusion

The molecular subtype of B-ALL has an impact on end-induction MRD outcome. It is mandatory to perform molecular subtyping of B-ALL for better risk stratification and to improve the possible outcome by treatment intensification.

Miscellaneous/Molecular Hematology (MH) PP-MH-14

RAS-associated Autoimmune Leukoproliferative Disorder (RALD) - A Case Report

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Background

Ras-associated autoimmune leukoproliferative disorder (RALD) is a rare genetic condition characterised by autoimmune manifestations and lymphoproliferation. It is primarily caused by somatic mutations in the NRAS or KRAS genes involved in cell signaling. Clinically this condition overlaps with autoimmune lymphoproliferative disorder (ALPS) in having immune cytopenias, lymphoproliferation, lymphadenopathy, splenomegaly and increased TCR??+ double negative cells (DNTs). It also has an overlapping phenotype with Juvenile myelomonocytic leukaemia (JMML), which is an MDS/MPN condition commonly affecting children and adolescents. In this report we discuss an interesting cases of RALD that we encountered in our practice.

Case Presentation

A 3-Month-old male child presented with abdominal distension, intermittent fever and cough for 3 weeks. On examination the child was found to have massive hepatosplenomegaly. Peripheral blood counts revealed bicytopenia with monocytosis of 2054 monocytes/uL. In view of bicytopenia, bone marrow examination was performed which showed trilineage haematopoiesis with erythrophagocytosis with scattered CD34+ cells. A primary differential of haemophagocytic lymphohistiocytosis and JMML were considered. Lymphocyte subset analysis revealed elevated TCRαβ + (DNTs), which included autoimmune lymphoproliferative syndrome (ALPS) to the differentials. A clinical exome panel by (NGS) was sent for molecular testing which showed a variant in KRAS, KRAS:c.38G>A (VAF – 19%); this is a heterozygous missense variant in exon 2 of the KRAS gene that results in the amino acid substitution of Aspartic acid for Glycine at codon13 (p.Gly13Asp;ENST00000311936.8), which was reported to be associated with RALD and JMML. Additional analysis by karyotyping and targeted gene showed no significant alteration. Buccal cells were also subjected to the sequencing of KRAS mutation is not present in the Buccal swab sample (somatic origin).The patient improved with treatment and due to the indolent course, he was finally diagnosed with RALD.

Conclusion

RALD is a rare genetic disorder with overlapping phenotype with ALPS and JMML. High clinical suspicion is required to diagnose the entity.

Miscellaneous/Molecular Hematology (MH) PP-MH-15

RNASEQ Reveals Dysregulated Tumor Associated Antigens in Chronic Lymphocytic Leukemia (CLL)

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Introduction

Expression of unique tumor associated antigens (TAA) or novel neoantigens (NeoAg) on cancer cells forms the basis of identification of potential targets of immunotherapy followed by their evaluation in clinical trials. These unique targets arise from somatic mutations (SNPs, ins/dels, frameshifts, neoORFs, lnc encoded peptides) that occur during tumor evolution. Limited number of studies have been conducted on identification of TAA in CLL and hence press upon more studies in similar direction.

Aims & Objectives

The main aim of the study was to identify unique TAAs in CLL.

Materials & Methods

This study was conducted after obtaining approved from the AIIMS's ethics committee. WES (Twist Whole Exome library prep kit) & WTS (NEB Ultra II directional RNA-Seq Library Prep kit) were performed on malignant CLL B cells (CD45+CD19+CD5+) & paired Neutrophils (CD45+CD15+CD16+CD56-) in 53 CLL patients and NGS libraries were run on Illumina NovaSeq6000. Data was processed with in-house established bioinformatics pipelines that identified somatic variants, differential gene expression, and predicted HLA–neopeptide bindings.

Result

Differential gene expression revealed topmost highly expressed genes e.g FMOD, SFTPB, IGSF3 in CLL that could be considered as putative TAAs & explored further. Several somatic mutations were identified in common drivers such as TP53(8%), SF3B1(19%), NOTCH1(15%), CHD2(6%) & others. Further analysis revealed a series of HLA-A2 restricted putative neoepitopes derived from C16ORF57, SF3B1, NFKB1E & other NeoAgs. The NFKB1E neoepitope, for example, originated from a frameshift deletion in 2 patients & was predicted to be restricted not only by HLA-A*02:11 (most common A2 allele in North Indians) but also other versatile subtypes A*02:01 (Caucasian, Gambian, Japanese) /*02:02 (Gambian) /*02:05 (Gambian, N Indians) /*02:06 (Japanese) /*02:07 (Japanese, N Indians).

Conclusion

Similar studies are warranted to investigate immunogenic potential of TAA & NeoAgs that could aid in personalized immunotherapeutic approach for treatment of CLL and other cancers. Activation of NeoAg specific cytotoxic T cells in conjunction with checkpoint blockage/ CART/ adjuvants/ conventional therapies could augment anti tumor immune responses.

Miscellaneous/Molecular Hematology (MH) PP-MH-16

Characterization of the Kinase Domain Mutation by Sequencing Assay in TKI-resistant CML Patients : A Single Centre Experience

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Introduction

A kinase domain (KD) mutation in the BCR-ABL1 gene is a common mechanism of resistance to tyrosine kinase inhibitors (TKIs) in patients with chronic myeloid leukemia (CML). They are found in 40–50% of patients with CML with TKI resistance.

Aims & Objectives

To find out the prevalence as well as describe the different kinase domain mutations observed in TKI-resistant CML patients.

Materials & Methods

It was a two-year retrospective observational study, involving CML patients on TKIs, who showed sub-optimal response to therapy or TKI failure, at different time-points i.e 6 months, 12 months and thereafter. The patients were tested by Sanger sequencing on ABI 3500XL(Thermo-fisher).

Result

Out of a total of one-hundred and seventy CML patients, non-respondent to TKIs, during the given period, thirty-six were positive for kinase domain mutations (21.2%), while 23.52% (40/170) had splice site variant ([p. R362fs*21(deletion-frameshift), c.1086_1270del185). 9/40(22.5%) patients with splice-site variant also had concomitant pathogenic KD point mutations. 8/36(22.2%) KDM-positive patients had compound mutations. The commonest affected sites of KD mutations in our study were between the SH2-SH3 contact residues (32.6%), followed by P-Loop (26.1%) and adjacent to SH2 contact region (17.4%). T315I was the commonest KD mutation detected in our study, followed by F359C/I/V(16.6%) AND E2555K/V (11.1%). Median age at KD mutation detection was 39 years (Range: 9-78 years) with an M:F ratio of 3:1. The IS-NCN% at which KD mutations were detected, varied between 0.326 to 276.754, at different stages of CML treatment.

Conclusion

In resource-constrained settings, patients who are not in complete cytogenetic remission, may only be taken up for kinase domain mutational analysis at six months and beyond, without impairing patient care.

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