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PATHOLOGICAL EVALUATION OF BONE MARROW BIOPSY IN PANCYTOPENIA CASES WITH SPECIAL REFERENCE TO BONE MARROW IMPRINT CYTOLOGY: A HOSPITAL BASED STUDY

Pathology

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ABSTRACT

Introduction: Pancytopenia is an important clinico-hematological condition and mainly presents in the form of anemia, leucopenia and thrombocytopenia. There are varying trends in its clinical patterns, treatment modalities and outcome. **Materials and Methods:** A hospital-based observational study was done in the department of Pathology, AMCH, Dibrugarh, Assam, from June 2021-May 2022 in patients above 12 years admitted in Medicine ward fulfilling the inclusion criteria were included in this study. All the participants underwent detailed clinical examinations and baseline investigations followed by bone marrow examinations. **Results:** Out of 72 participants, 41 were males and 31 were females with male to female ratio of 1.32:1. Mean age was 45.39 ± 15.49 years. Megaloblastic anemia was the commonest cause that was observed in 30.5% (22) cases followed by Aplastic anemia 18% (13) and MDS 16.7% (12). Anisocytosis, reticulocytosis and hypercellular marrow were the most common hematological picture. **Conclusion:** The severity of pancytopenia and underlying pathology determines the management and prognosis. Thus, comprehensive clinical and hematological evaluation of pancytopenia cases is utmost necessary to identify the correct cause.

KEYWORDS

Pancytopenia, Bone marrow aspiration, Bone marrow biopsy, Megaloblastic anemia, Assam.

Pancytopenia itself is not a disease entity but a triad of findings in the presence of a disease which cause the different mechanisms like infections, destruction of marrow tissue by toxins, radiations, replacement of normal tissues by malignant tissues. Some other causes of pancytopenia are myelodysplastic syndrome, myelofibrosis, lymphoma, tuberculosis, multiple myeloma, storage diseases, SLE, metastatic deposits.[1] Pancytopenia mainly presents in the form of anemia, leucopenia and thrombocytopenia. Platelets are the first to be affected as they have the shortest half-life leading to throm bocytopenia. Anemia develops the slowest in pancytopenia cases.[2]

Patients with pancytopenia usually presents with generalized weakness, fatigue, shortness of breath, pallor, prolonged fever and tendency to bleed. Systemic examination shows jaundice, hepatomegaly, splenomegaly and lymphadenopathy.[3] Pancytopenia is one of the most common indications for bone marrow examination to evaluate the underlying pathology, although a complete hematological examination with good clinical examination is necessary. A comprehensive medical history, meticulous clinical examination, complete blood count (CBC) and peripheral blood smear (PBS) examination and further investigations like immunophenotyping, cytogenetics or molecular studies forms a valuable diagnostic aid.[4] Bone marrow aspirate smears provide the best assessment of the morphology of hematopoietic cells. Bone marrow biopsy can be used for assessment of marrow activity and marrow cellularity in disorders like aplastic anemia. In case of local marrow fibrosis in disorders like metastatic cancers and granulomatous diseases where marrow cannot be aspirated, the lesions are best seen in biopsies.[5]

AIMS AND OBJECTIVES:

1. To find out the primary bone marrow causes of pancytopenia.
2. To evaluate the clinico-pathological spectrum of pancytopenia cases.
3. To evaluate the spectrum of bone marrow morphology in pancytopenia cases.
4. To evaluate the diagnostic utility of bone marrow imprint cytology in cases presenting with pancytopenia.

MATERIALS AND METHODS:

The present study was undertaken in 13 years old and above patients presenting with pancytopenia in the Department of Medicine, Assam Medical College and Hospital, Dibrugarh, Assam, with the purpose of identifying the primary bone marrow causes of pancytopenia in patients admitted in the Medicine ward. This study was conducted under the guidance of the Department of Pathology, Assam Medical College and Hospital, Dibrugarh.

Inclusion criteria-

Patients of either gender belonging to the age group of ≥13 years presenting with pancytopenia:

1. Hemoglobin <13.5 g/dl in male or <11.5 g/dl in female.[6]
2. Total leukocyte count <4000/cc.[6] and
3. Platelet count <1,00,000/cc)[7] were included in the study.

Exclusion criteria-

1. Cases undergoing drug therapy for pancytopenia.
2. Patient not giving consent.
3. Patients undergoing chemotherapy or having immunosuppressive condition like retroviral infections.
4. Patient with bleeding diathesis, skin infections, osteomyelitis or osteogenesis imperfecta.
5. Pregnant women.

Written, informed consent was taken from each of the participants. Relevant medical history were elicited including symptoms such as fever, lethargy, breathlessness, bone pains, night sweats, malaise, and weight loss. History of any previous treatment, intake of or exposure to potentially toxic chemicals, agents or drugs, radiation exposure, smoking status, alcohol intake, and other addictions, were also recorded. A detailed physical examination of every patient was done for pallor, jaundice, petechiae/purpura/ecchymoses, hepato-splenomegaly, lymphadenopathy, sternal tenderness, dermatological manifestations, and gum hypertrophy. Evidence of hypersplenism and primary malignancy was searched for, wherever necessary. Basic hematological investigations, routine investigations, and BM examination were performed in each case.

Peripheral blood film (PBF) was examined for the presence of anisopoikilocytosis, circulating erythroblasts, hypo or hypersegmented neutrophils, abnormally increased or decreased granulation in neutrophils, immature WBCs, and lymphocytosis. BM aspiration and trephine biopsy were carried out by standard methods. Stains such as Leishman stain, Giemsa stain, Hematoxylin and Eosin stain were used. Myeloperoxidase special stain, Periodic Acid–Schiff and Perl's stain on aspirate smears were used, wherever indicated.

DATA ANALYSIS:

The data collected were entered into MS Excel spreadsheets and

analysis was carried out using the Statistical Package for the Social Sciences (SPSS) for Windows, Version 25.0. Categorical variables were presented in number and percentage (%).

RESULTS:

The study included 72 participants, out of which 41 were males and 31 were females, with a male to female ratio of 1.32:1. The majority of the study participants belonged to the age group 51-60 years (25.0%) and the overall mean age of the study participants was 45.39 ± 15.49 years. The most common presenting symptoms were generalized weakness (seen in 62 patients), followed by bleeding manifestations (51 patients) and fever (38 patients). Other less common symptoms were dyspnoea, abdominal pain and bone pain. On examination, all study participants were found to have pallor. Other signs observed were petechiae (29 patients), ecchymosis (10 patients), purpuric patches (8 patients), bleeding gums (4 patients), splenomegaly (11 patients), pedal edema (7 patients) and icterus (3 patients). The most common PBF findings were anisocytosis (66.7%), followed by normocytic (43%) and macrocytic (33.3%) blood picture. Macrocytosis with hyper segmented neutrophils were seen in 16 patients (22.2 %). Atypical cell was observed in only 1 patient.

On BM examination, 55.6% of the study participants had hypercellular bone marrow, followed by normocellular (23.6%) and hypocellular bone marrow (20.8%). 41.7% of the study participants showed erythroid hyperplasia and 30.5% showed megaloblastic maturation. The most common causes of pancytopenia were found to be megaloblastic anemia (30.5%), followed by aplastic anemia (18%), MDS (16.7%) and plasma cell myeloma (15.3%). (Table 1). The diagnostic accuracy was found to be more in the bone marrow trephine biopsy (100%), followed by bone marrow imprint cytology (94.4%) and bone marrow aspiration cytology (87.5%). Taking the bone marrow biopsy as the gold standard, it has been observed that bone marrow imprint cytology was more reliable than the bone marrow aspiration cytology in the diagnosis of pancytopenia. (Table 2). 56.9 % of the study population had normal iron stores while 33.3 % had increased iron stores and 9.8 % had iron deficiency. In the study population, normal iron stores were seen in 59.1 % cases of megaloblastic anemia, 61.5 % cases of aplastic anemia, 58.4 % cases of MDS, 90.9 % cases of plasma cell myeloma and 66.7 % cases of hypersplenism.

Table 1: Classification of different causes of pancytopenia in the study participants

Bone marrow findings	Number	Percentage
Megaloblastic anemia	22	30.5
Aplastic anemia	13	18
Myelodysplastic syndrome	12	16.7
Plasma cell myeloma	11	15.3
Hypersplenism	9	12.5
Acute Leukemia	3	4.2
Gaucher Disease	1	1.4
Hemophagocytic lymphohistiocytosis (HLH)	1	1.4
Total	72	100

Table 2: Causes of pancytopenia diagnosed on bone marrow aspiration cytology, bone marrow imprint cytology and bone marrow biopsy along with correlation of bone marrow aspirate and imprint cytology with bone marrow trephine biopsy as the Gold standard

Diagnosis	Number of cases	BMA cytology	BMI cytology	BMB	Correlation of BMA cytology & BMB (%)	Correlation of BMI cytology & BMB (%)
Megaloblastic anemia	22	19	20	22	86.4	90.9
Aplastic anemia	13	12	13	13	92.3	100
MDS	12	9	11	12	75	91.7
Multiple myeloma	11	11	11	11	100	100
Hypersplenism	9	7	8	9	77.8	88.9
Acute Leukemia	3	3	3	3	100	100
Gaucher disease	1	1	1	1	100	100
HLH	1	1	1	1	100	100
Total	72	63	68	72	-	-

*BMA= Bone marrow aspiration, BMB= Bone marrow biopsy, BMI= Bone marrow imprints, MDS= Myelodysplastic syndrome, HLH= Hemophagocytic lymphohistiocytosis

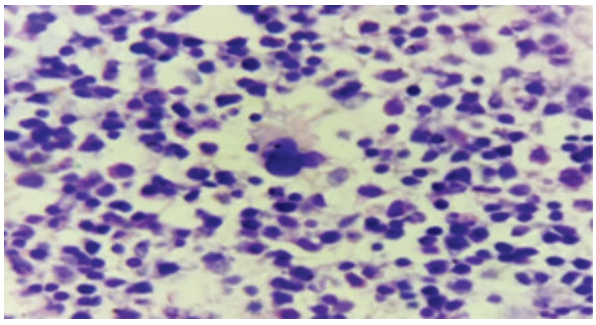

Figure 1. Bone marrow trephine biopsy shows erythroid hyperplasia with megaloblasts having delicate nuclear membrane.

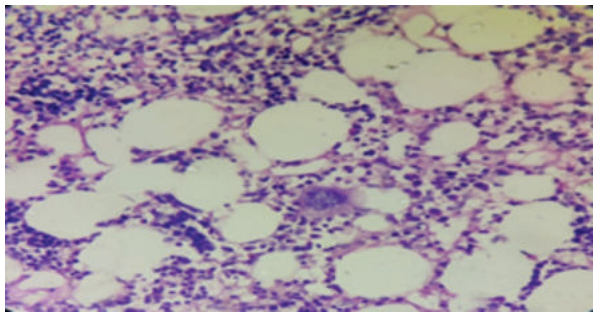

Figure 2: Trephine biopsy shows hypolobated megakaryocyte and quadrinucleate gigantoblast and erythroid precursor having nuclear budding.

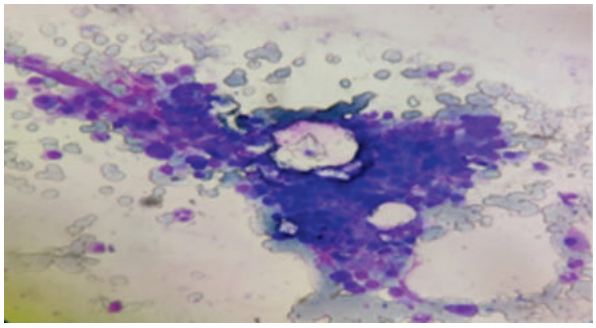

Figure 3: Bone marrow imprint shows increased plasma cells intermingled with few erythroid and myeloid precursors.

DISCUSSIONS:

In the present study, majority belonged to the age group 51-60 years (25.0%) and majority of the study participants were male (56.9%) and a male : female ratio was 1.32:1. Although in a study done by Anjum et al in India, majority of the cases were in age group 29-38 years and male:female ratio was 1.5:1.8 The commonest age group of pancytopenia was found to be 51-60 years in this study in contrast to other studies where common age group was below 40 years.9 The finding in this study and other studies indicates male preponderance in pancytopenia.

In the present study, the most common causes of pancytopenia were found to be megaloblastic anemia (30.5%), followed by aplastic anemia (18%), MDS (16.7%) and plasma cell myeloma (15.3%). Similar findings were seen in a study done by Dubey et al and Anjum et al in India where megaloblastic anemia was the commonest cause of pancytopenia followed by aplastic anemia 8,10 The findings in this study are comparable to the above studies, which indicates that nutritional anemia is common in India.

In the present study, out of 72 participants, 72 (100%) had pallor

followed by weakness (86.1%), bleeding tendencies (70.8%) and fever (52.8%). Mangal and Sinha et al, Gayathri and Rao et al in their study in India also found that pallor was the most common clinical presentation followed by fever, splenomegaly, lymphadenopathy, hepatomegaly and icterus.1,11 The most common PBS findings were anisocytosis (66.7%) followed by normocytic (43%) and macrocytic (33.3%) blood picture in this study. The findings in this study is comparable to P Agarwal et al and S M Sale et al.12,13

Present study showed that hypercellular bone marrow (55.6%) was most common morphological bone marrow changes followed by normocellular (23.6%) and hypocellular bone marrow (20.8%), 41.7% of the study participants showed erythroid hyperplasia and 30.5% showed megaloblastic maturation which is in accordance with study done by A.N. et al and N Rohira et al 14,15

Diagnostic accuracy was found to be more in the bone marrow trephine biopsy (100%), followed by bone marrow imprint cytology (94.4%) and bone marrow aspiration cytology (87.5%) in this study Taking the bone marrow biopsy as the gold standard, in the present study it has been observed that bone marrow imprint cytology was more reliable than the bone marrow aspiration cytology in the diagnosis of pancytopenia and the finding is comparable to previous studies done by Pant et al and G Taori et al.16,17 However V Tilak et al found that the diagnostic accuracy was 87.3% in bone marrow imprint cytology and 75.8% in bone marrow aspiration cytology.18

CONCLUSIONS

The present study indicates that a detailed primary hematological investigations like complete blood count (CBC), reticulocyte count and peripheral blood smear (PBS) study along with bone marrow examination in patients with pancytopenia is helpful to understand the disease process and to rule out the causes of pancytopenia. It is also useful in planning further investigations and management. In my study, the most common cause of pancytopenia was megaloblastic anemia which indicates the prevalence of nutritional anemia in this study area. It is also concluded that bone marrow imprints are equally useful as bone marrow biopsy in the diagnosis of pancytopenia, therefore it can be a standard practice for bone marrow evaluation.

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