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Bone Marrow Study in Hematological Disorders: A One Year Retrospective Study in a Tertiary Care Hospital of North East India

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Abstract: ***Background: Most often, bone marrow is involved in hematological and non-hematological disorders, which are diagnosed by two separate but interrelated techniques viz. bone marrow aspiration (BMA) and bone marrow biopsy (BMB). Aim: The main objective of this study was finding out the causes of hematological disorders by evaluating the bone marrow aspiration cytology and bone marrow biopsy and correlating both these parameters to arrive at a more conclusive final diagnosis. Results: Out of 125 cases of BMA cases studied, 35 cases had also undergone BMB. Among study subjects, 61.29% were male and 38.71% were female with age group ranging from 6 months to 70 years. In our study 30.65% cases were Acute leukemias, 16.13% (20) cases of anemias and 11.29% (14) cases with platelet disorders. Among anemias, Megaloblastic anemia was most common followed by Iron deficiency anaemia and combined nutritional deficiency anemia. Others were Myelodysplastic syndrome, plasma cell dyscrasias, myeloproliferative neoplasm, one case of hemophagocytic syndrome. Conclusion: The study concludes that bone marrow examination is the basic cornerstone to arrive at the diagnosis of most hematological and non-hematological disorders.***

Keywords: bone marrow aspiration, bone marrow biopsy, hematological disorders

1. Introduction

Bone marrow examination is useful in the diagnosis of both hematological and non-hematological disorders. The two most important techniques used for the diagnosis of hematological disorders are bone marrow aspiration and trephine biopsy. Bone marrow aspiration (BMA) is the most frequent and safe invasive procedure done routinely in the hospitals for the diagnosis and management of hematological disorder.[1-3]

Bone marrow aspiration (BMA) alone is usually sufficient to diagnose nutritional anaemias, most of the acute leukaemias and Immune thrombocytopenias whereas Trephine biopsy provide important diagnostic clue in patients with granulomatous disease, myelofibrosis and bone marrow infiltration. Bone marrow aspiration is useful in making out better individual cell morphology with bone marrow biopsy in bone marrow architectural pattern and distribution.[4]

Hence, we attempted this study with the aim of finding out the causes of haematological disorders by evaluating the bone marrow aspiration cytology and bone marrow biopsy and correlating both these parameters to arrive at a more conclusive final diagnosis.

2. Literature Survey

Kibria SG et al[2] in their study on bone marrow examination of 177 cases of suspected hematological disorders found that among the malignant hematological disorders, Acute Myeloid Leukemia (AML) was the most common disorders followed by Acute Lymphoblastic Leukemia, MDS, CML and Multiple Myeloma. Among the non-malignant hematological disorders, Combined (both iron and folic acid and /or Vitamin B12) deficiency anemia was the most common disorder followeb by aplastic anemia.

Atla BL et al[4] in their study among 105 cases, age of patients ranged from 1 to 68 yrs with mean age of 32.4 yrs and male predominance (1.5:1). Bone marrow aspiration was diagnostic in 53(50%) cases and trephine biopsy was diagnostic in 52(50%) cases. Anemias (50%) and leukemias (16%) are most common hematological disorders. Among the anemias, megaloblastic anemia was the most common (40%) cause of hematological non-malignancies. Among leukemias, acute myeloid leukemias were common cause of hematological malignancies.

In the study undertaken by Sreedevi P et al[5] of 43 cases of bone marrow aspiration ,9 cases were erythroid hyperplasia, 7 cases Idiopathic Thrombocytopenic Purpura, Megaloblastic anemia was 5 cases (11.8%) , Hypoplastic marrow was seen in 4 cases and Acute leukemias in 3 cases . Rest were Chronic myeloid leukemia, Multiple myeloma, Gauchers disease, Infiltrative marrow, Transient Myeloproliferative Disorder, Congenital Dyserythropoietic Anemia, Myelofibrosis and Megakaryocytic hyperplasia .

According to the study Pudasaini S et al[6] out of 57 cases of bone marrow aspiration studied, erythroid hyperplasia was seen in 12 cases (21%). Megaloblastic anemia was seen in 7 cases (12.3%) and microcytic anemia was seen in 4 cases (7%). There were 6 cases (10.5%) of Idiopathic Thrombocytopenic Purpura. Acute leukemia was diagnosed in 7 cases (12.3%) and among this acute myeloid leukemia (10.5%) was more common than acute lymphoid leukemia (1.8%). Myelodysplastic syndrome and multiple myeloma was seen in 3.5 % cases each. Aplastic anemia and Kalaazar was seen in 5.3% and 1.8% cases respectively.

Ranabhat S et al[7] in their study found that out of One hundred and fifty-nine patients included in their study, Anemia was the largest group followed by malignancy, infection and miscellaneous diseases. Regarding individual diseases, Megaloblastic anemia was the most common hematological disorder followed by Immune Thrombocytopenic Purpura, leukemia and aplastic anemia.

3. Materials and Methods

The study was a hospital based retrospective study done in the Department of Pathology, Gauhati Medical College and Hospital in association with department of Medicine and Paediatrics for a period of one year from March 2017 to February 2018. There were total 125 cases. PBS along with necessary hematological and clinical parameters were also noted in all cases of suspected hematological disorders. Among them trephine biopsy were done in 35 cases. Giemsa stain was used routinely for bone marrow aspiration and Haematoxylin and Eosin stain for trephine biopsy .Special stains like viz. Iron stain, Periodic Acid Schiff (PAS) stain and Myeloperoxidase (MPO) were used wherever indicated.

Bone marrow aspiration/Bone marrow biopsy procedure: In all our cases, we have taken material from the posterior superior iliac spine which is the most suitable and safe site for both aspiration and biopsy. Other sites- sternum and medial side of tibia. Salah needle was used for bone marrow aspiration. Jamshidi needle was used for bone marrow biopsy.

4. Results

In the present study 125 patients were subjected to bone marrow aspiration out of which 35 cases had also done bone marrow biopsy. Cytochemical stains were done on selected cases and when essential. Among the study subjects, 61.29% were male and 38.71% were females. The age group of patients ranged from 6 months to 70 years. Maximum patients were from the age group of 0-10 years (27.42%)

Regarding cellularity, 8% cases had hypocellular marrow,59.2% had a hypercellular marrow and 34% had normocellular marrow. In our study 30.65% cases were of Acute leukemias. There were 16.13% (20) cases of anemias. Among the anaemias, 16 cases were of Megaloblastic anemia and 2 cases each of Iron deficiency anaemia and combined nutritional deficiency anemia.

There were 11.29% (14) cases with platelet disorders. These cases had megakaryocytic hyperplasia with abnormal lobulations of megakaryocytes. Clinically these patients presented with multiple, tiny, petechial spots over the body. A diagnosis of Immune thrombocytopenic purpura was made after exclusion of all other causes of thrombocytopenia. Majority of these patients were in the pediatric age group.

4.84% (6) cases showed morphology suggestive of Myelodysplastic syndrome. All 6 cases were above 50 years of age. However Perl's stain was not done and hence classification of MDS could not be made. Serum Vitamin 12 and serum folic acid was done to rule out Megaloblastic anaemia.3.23% cases had plasmacytosis and were advised to do serum protein electrophoresis.

Besides we encountered one interesting case of Haemophagocytic syndrome in a case of Systemic idiopathic juvenile rheumatoid arthritis. The patient had leucocytosis which is unusual in haemophagocytic syndrome. It was believed to be the intial stage of hemophagocytosis where we noted occasional macrophages engulfing polymorphs, erythroid precursors and platelets. Later the patient was started on steroids based on our diagnosis and eventually the patient recovered.

In another case a patient presented with pancytopenia. Total leucocyte count was only 900 cells/mm3.When we examined bone marrow, it was packed with faggots. The case was provisionally diagnosed as Hypergranular variant of Acute Promyelocytic leukaemia. The patient was started on All trans retinoic acid and eventually good response was observed within two days.

Table 1: Distribution of cases according to age group

Age group (Yrs)	No of cases	Percentage (%)
0-10	34	27.4
20-Nov	16	12.9
21-30	23	18.4
31-40	10	8.06
41-50	18	14.52
51-60	18	14.52
61-70	6	4.84

Table 2: Distribution of cases according cellularity

Cellularity	No of cases	Percentage(%)
Hypocellular	10	8.01
Hypercellular	74	59.2
Normocellular	41	33.06

Table 3: Distribution of hematological cases according to diagnosis in bone marrow aspiration smears

Hematological condition	No of cases	Percentage (%)
Leukaemias	38	30.65
Anaemias	20	16.13
Platelet disorders	14	11.29
Normal	12	9.68
Myelodysplastic syndrome	6	4.84
Myeloproliferative neoplasm	1	0.8
Plasma cell dyscrasias	4	3.23
Lymphoproliferative disorder	6	4.84
Others	12	9.68
Inconclusive	12	9.68

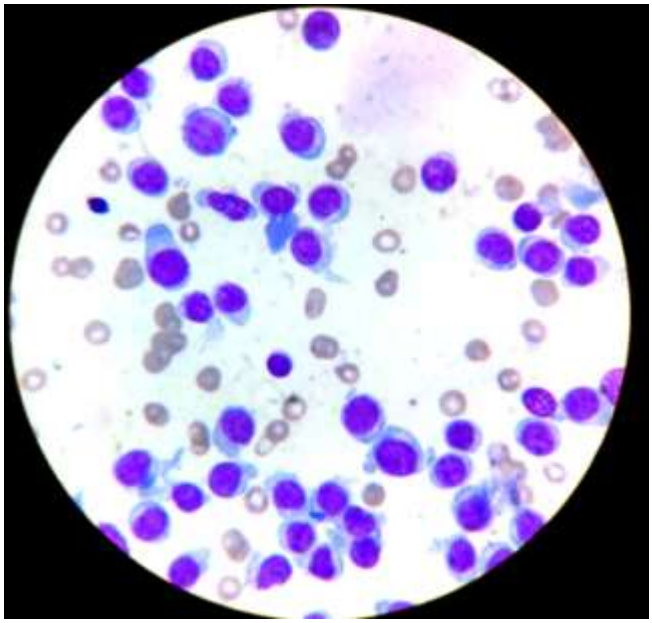

Figure 1: Acute leukaemia(Morphology suggestive ofAML M5a) Giemsa 100x10

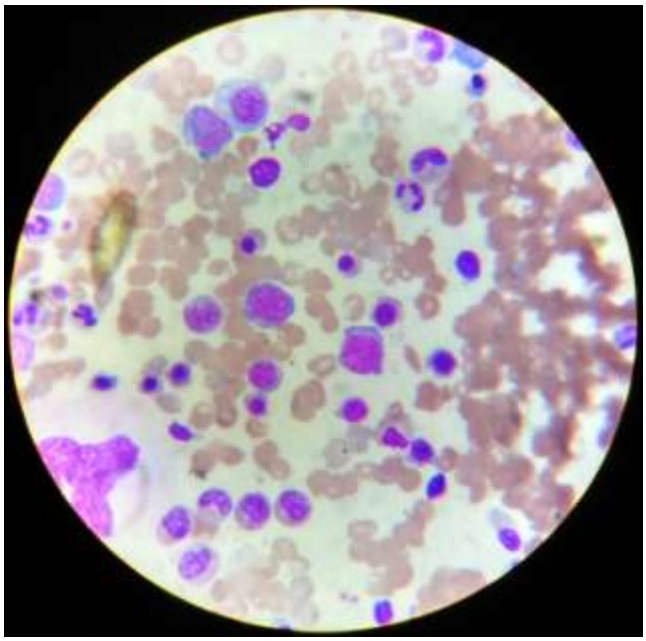

Figure 2: Early Megaloblasts with sieve like chromatin pattern in a case of Megaloblastic anaemia, Giemsa 100x10

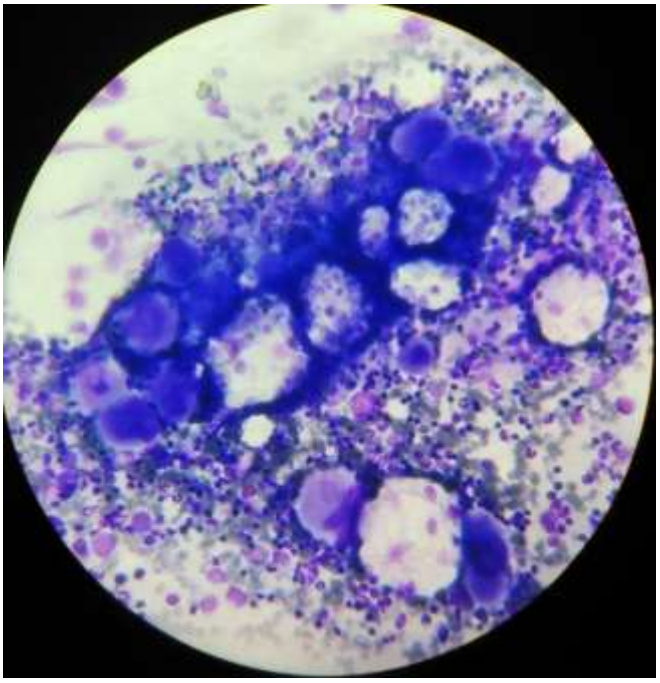

Figure 3: Megakaryocytic hyperplasia with abnormal lobulation of megakaryocytes in a case of Immune thrombocytopenic purpura.Giemsa 40x10.

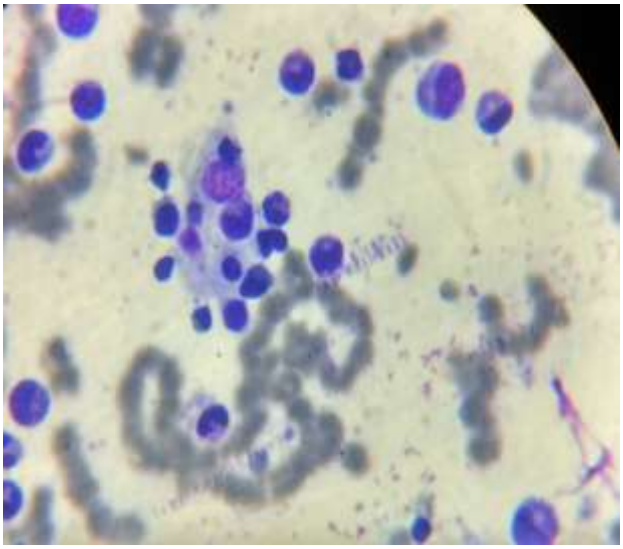

Figure 4: Haemophagocytosis in a case of Macrophage activation syndrome showing engulfment of myeloid precursors and erythroid precursors by a macrophage.Giemsa 40x10

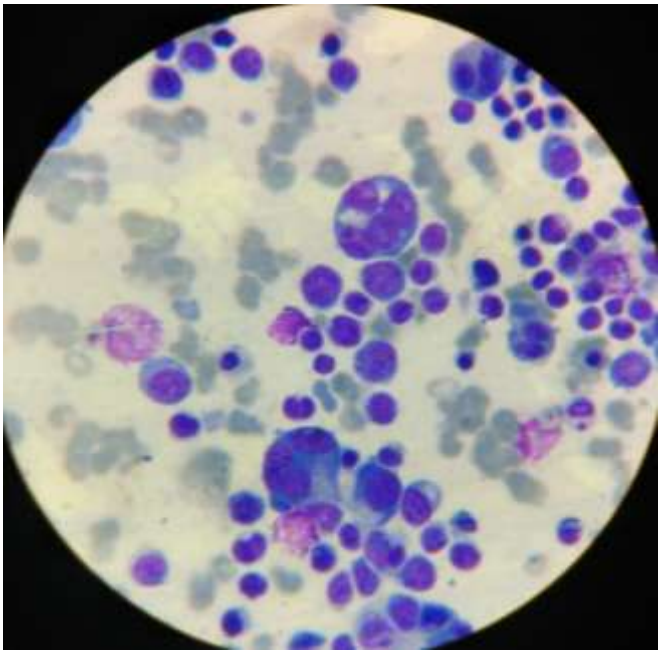

Figure 5: Hydroxyurea induced dyserythropoetic changes in bone marrow aspirate of a case of Acute leukemia.Giemsa 40x10

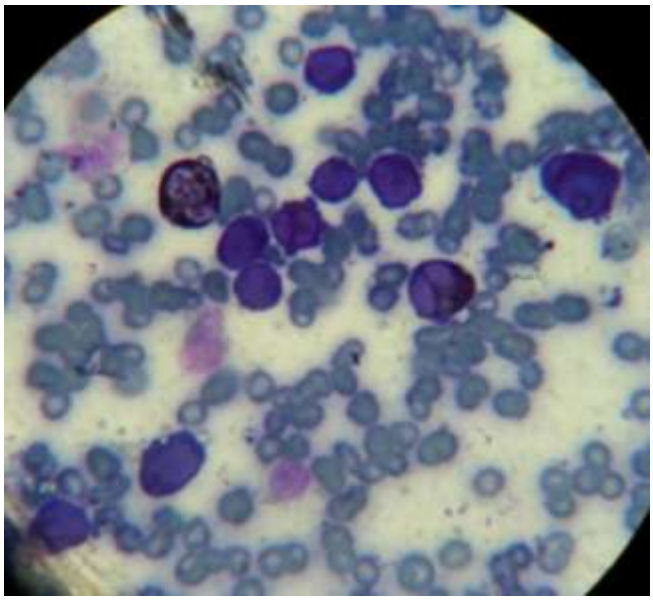

Figure 6: Atypical promyelocyte showing strong SBB positivity in a case of Acute promyelocytic leukaemia.

5. Discussion

The spectrum of hematological disorders is very wide and bone marrow examination is safe procedure and is a useful tool in making a final diagnosis. In our study most common age group was 0-10 years(27.4%).Similar finding was seen in a study done by Sreedevi P et al[5] from Andhra Pradesh, India. They reported 27.9% of cases in between 0 and 10 years. However different results were seen in study done by Pudasaini S et al[6] from Kathmandu, Nepal. They reported only 7% of cases in the paediatric age group. Maximum number of cases were in the 31-45 years of age group.

Male: Female ratio in our study was 1.6:1.It was different from the study done by Pudasaini S et al[6] from Kathmandu, Nepal where they reported almost equal number of cases.(M:F=1:1.1)

The commonest indication of Bone marrow study was pancytopenia. In the present study 33 cases (26.4%) were subjected to bone marrow examination for pancytopenia. Similar findings were observed in the study of Atla BL et al[4] from Andhra Pradesh where they found 37 % cases being subjected to bone marrow examination for evaluation of pancytopenia. Study by Pudasaini S et al[6] from Kathmandu reported a higher percentage of cases evaluated for bone marrow (50%) followed by 36% cases of bicytopenia. The commonest cause for pancytopenia was found to be megaloblastic anaemia followed by Myelodysplastic syndrome. Megaloblastic anemia accounted for 48.5% of all pancytopenic cases which was similar to the study done by Atla et al[4] who found 54% of pancytopenic cases as Megaloblastic anaemia and another similar study by Gayatri et al[8].

Majority of the bone marrow aspiration smears showed a hypercelular marrow for the age of the patient. It was obvious because megaloblastic anaemia, acute leukaemias and myelodysplastic syndromes usually present as pancytopenia with a cellular marrow. Pudasaini S et al[6] from Kathmandu, Nepal also found a hypercellular marrow in 61.4% cases .They reported megaloblastic anaemia and acute leukaemias 12.3% each.

There were 38 cases of leukaemia.20 cases had a morphological feature of Acute myeloid leukemia while 18 cases had features of Acute lymphoblastic leukaemia. We reported a higher percentage of leukemias in our study compared to Pudasaini S et al[6](12.3%),Kaur M et al[9](10%), Sreedevi P et al[5](7%) etc. This may due to the fact that bone marrow study is a routine procedure in hematological evaluation of leukemia in our institution.

We encountered 3.23% cases of Plasma cell dyscrasias. All of the cases had trephine biopsy done. A higher percentage of plasma cells were reported in all the cases. Similar findings were seen in studies of Pudasini S et al[6] who reported 3.5% cases of plasma cell dyscrasias. A higher proportion of such cases were seen in the study of Kibria et al[2] (9.04%), Laishram et al[3](20.5%) etc.

Disorders of platelet were seen in 11.29% cases. These cases were mostly in the paediatric age group and diagnosed as Immune thrombocytopenic purpura. Bone marrow aspiration was done to rule out other causes of thrombocytopenia. Kibria et al[2] reported 6.21%, Pudasini S et al[6] also found 10.5% cases of platelet disorders similar t0 our study and Laishram et al[3] found 14.5% of platelet disorders.

6. Conclusion

Bone marrow examination still remains today the basic cornerstone for diagnosis of hematological disorders and also for understanding disease progression, for prognostication and therapeutic evaluation with its relatively easier procedure and cost effectiveness. Combining both the

procedures done together helped us to study the cytomorphology of the cells along with the pattern of distribution of the cells , hence help in making the diagnosis accurately. Furthermore, using ancillary techniques such as flow cytometry bears extra advantage in further typing of various diseases.

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