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Study of haematological disorders detected by bone marrow examination at tertiary care hospital

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ABSTRACT

Bone marrow aspiration & biopsy examination is often required for diagnosis & management of haematological disorders which have diverse modes of presentation. Mostly of the haematological disorders present as anaemia, which are diagnosed by bone marrow aspiration (BMA) and bone marrow biopsy (BMB). I n the department of pathology, the study was conducted to compare the role of bone marrow aspirate and trephine biopsy for diagnosing the haematological diseases and indications.

Materials and Methods: To check the role of bone marrow aspiration and biopsy in the diagnosis of haematological disorders this is the aim of study. In the department of pathology at tertiary care teaching hospital this study was conducted over a period of 2 years from November 2016 to October 2018. A total of 572 cases were included in this study.

Results: In the present study, both aspiration and biopsy cases were available are 572 were included. The age ranged from 6 months to 84 years. The 326(56.99%) were males and 246(43%) were females with M: F=1.32 :1. Clinical indications for bone-marrow examination, The most common indication was pancytopenia of 201 cases (35.13%) followed by anaemia 167 cases (29.19%), malignancy 79 cases (13.81%), Hepatosplenomegaly 48 cases (8.39%), thrombocytopenia 47 cases (8.21%) and fever 30 cases (5.24 %). Most of the cases had hypercellular bone marrow (53%) followed by normocellular marrow (32%) and hypocellular marrow (15%).

1. Introduction

In the developing world than developed countries the spectrum of haematological disorders is relatively different.[1] By detail clinical examination and few simple investigations diagnosis can be done most of the time. But, without bone marrow examination, the diagnosis is usually not a confirmatory. Bone marrow is involved in variety of haematological disorders include nutritional deficiency diseases, acute leukaemia, myeloproliferative neoplasm (MPN), haemato-lymphoid neoplasm, and nonhematological disorders include infectious diseases infiltrating the bone marrow such as parasitic infections, tuberculosis and metastatic deposits.[2]

Indications for bone marrow examination can be summarised, depending upon the clinical diagnosis & peripheral blood examination.[3] Biopsy of bone marrow is an adjunct to the study of haematological disorders which are quite frequent in all age groups.[4] Sometime, due to inadequate sample on aspiration, and a biopsy needs to be performed simultaneously.[5]

To identify the indications for a bone-marrow examination, to correlate between bone-marrow aspiration and biopsy findings the study was conducted. It aims to assess the diagnostic value of bone marrow examination, clinical indications and to know the age wise incidence and male to female ratio.

2. Materials and Methods

In the department of pathology at tertiary care teaching hospital this study was done during the period between November 2016 to Oct 2018, this was record base observational study. A total of 580 cases were included in

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this study. Leishman stain was used to stained aspiration slides. In all cases iron stores was done with the help of Perl's stain. In all the cases of leukaemia myeloperoxidase staning was done. Haematoxylin and Eosin stain used for trephine biopsy & peocessed. Reticulin stain was done in all the case for fibrosis grading and WHO grading system was used. Complete blood count (CBC), Peripheral smear examination (PBF) was done in all cases. In the diagnosis of haematological and nonhematological disorders the role of bone marrow examination was reviewed in the study. Then data was manually collected and analysed. Where both aspiration and biopsy are available these are the cases included in the study & cases where biopsy was not available were excluded.

3. Results

Over a period of two years in the present study, bone marrow aspirations were done was 580. Present study included 572 cases in which both aspiration and biopsy were available. In the Table 1 shows the age & sex distribution of the patients. The age ranged from 6 months to 84 years. The 326(56.99%) were males and 246(43 %) were females with M:F=1.32:1. Maximum number of hematological disorders patients who underwent bone marrow aspiration was 227(39.68 %) in the age group of 21 to 3 0 years.

Table 1: Age and sex wise distribution.

Age group	Males	Females	Total
0 -20	82 (14.33%)	52(9.09%)	134(23.42%)
21 -40	109 (19.05%)	118(20.62%)	227(39.68%)
41 -60	81 (14.16%)	60(9.87%)	141(24.65%)
61 - 80	45 (7.86%)	22(3.84%)	67(11.71%)
>81	3 (0.52%)	-	3(0.52%)
Total	320 (55.94%)	252(44.05%)	572(100%)

In our study the clinical indication for bone-marrow examination was the most common indication as shown in Table 2 was pancytopenia of 201 cases (35.13%) followed by anaemia 167 cases (29.19%), malignancy 79 cases (13.81%), Hepatosplenomegaly 48 cases (8.39%), thrombocytopenia 47 cases (8.21 %) and fever 30 cases (5.24%).

Table 2: Indication of Bone marrow examination.

Indications	No. of cases	Percentages
Pancytopenia	201	35.13%
Anaemia	167	29.19%
Malignancy	79	13.81%
Hepatosplenomegaly	48	8.39%
Thrombocytopenia	47	8.21%
Fever	30	5.24%
Total	572	

Study showed the cases of hypercellular bone marrow (53%) followed by normocellular marrow (32%) and hypocellular marrow (15%).

Table 3: FoIIoing are the Haematological disorders among study subjects on aspiration.

Disorders	Total	Percentages
Megaloblastic Anaemia	163	28.49%
Dimorphic Anaemia	74	12.93%
Reactive Marrow	49	8.56%
Nutritional Anaemia	46	8.04%
Acute myeloid Leukaemia	35	6.11%
Normal bone marrow	30	5.24%
ITP	28	4.89%
CML	21	3.67%
Iron Deficiency Anaemia	19	3.32%
ALL	17	2.66%
Chronic lymphoproliferative disorder (CLPD)	15	2.62%
Anaemia of chronic disorders	14	2.44%
Dry tap	12	2.09%
A particulate marrow	11	1.92%
Aplastic anaemia	7	1.22%
Leukemoid Reaction	7	1.22%
Hypersplenism	6	1.04%
Plasma cytosis	4	0.69%
MDS	4	0.69 %
Multiple myeloma	3	0.52%
Myelofibrosis	3	0.52%
Eosinophilia	1	0.17%
Plasma cell leukaemia	1	0.17%
Hairy cell leukaemia	1	0.17%
Juvenile myelomonocytic Leukaemia	1	0.17%
Total	572	

In Table 3 shows bone marrow aspiration findings and Table 4 shows bone marrow biopsy findings respectively.

In present study anaemia was the most common presentation which of 380 cases (66.43%) followed by Acute leukaemia of 52 cases (9.09%). Megaloblastic anaemia was most common among the anaemia which of 163 cases (28.49%) followed by dimorphic anaemia of 74 cases (12.93%), nutritional anaemia of 46 cases (8.04%) and aplastic anaemia of 11 cases (1.92%).

Amongst the leukaemia acute leukaemia was seen in 52 cases in which 35(6.11%) cases of acute myeloid leukaemia and 17(2.66%) cases of acute lymphoblastic leukaemia seen. In 28(4.89%) number cases of idiopathic thrombocytopenic purpura (ITP) seen, in which 12 cases were ITP with erythroid hyperplasia and remaining 16 cases were only ITP seen.

Also seen 21 cases (3.67%) of chronic myeloid leukaemia & 4 cases (0.69%) shows a plasma cytosis. For staging of non-Hodgkin's lymphomas, received 9 bone marrow cases among which infiltration seen in 5 cases (0.87%). Among staging in Hodgkin's lymphoma 1

Table 4: Following are the histopathological diagnosis of haematological disorders.

Diagnosis	No of cases (n)	% of cases
Erythroid hyperplasia	380	66.43%
Acute myeloid leukaemia	35	6.11%
Normal study	30	5.24%
ITP	28	4.89%
Chronic myeloid leukaemia (CML)	21	3.67%
Acute lymphoblastic leukaemia	17	2.97%
Chronic lymphoproliferative disorder (CLPD)	14	2.44%
Aplastic anaemia	11	1.92%
Inadequate biopsy	9	1.57%
NHL	5	0.87%
Plasma cytosis	4	0.69%
Myelodysplastic syndrome (MDS)	4	0.69%
Multiple Myeloma	3	0.52%
Myelofibrosis (MF)	3	0.52%
Granulomatous pathology	2	0.34%
Eosinophilia	1	0.17%
Hypersplenism	1	0.17%
Hodgkin's Lymphoma	1	0.17%
Myeloproliferative disorder	1	0.17%
Hairy cell leukaemia	1	0.17%
Metastasis	1	0.17%
Total	572	

case was positive for infiltration. After correlation with biochemical, radiological and clinical findings multiple myeloma seen in 3(0.52%) cases which showed 4 0% plasma cells with plasma blasts. Also seen 3 cases (0.52%) of myelofibrosis Figure 1.

Also seen a one (4.6%) cases of adenocarcinoma deposits in bone marrow biopsy Figure 2 and few cases of myeloproliferative neoplasms seen in present study.

In the present study one cases each of plasma cell leukaemia and Hairy cell leukaemia seen. In previously treated megaloblastic anaemia case, myelodysplastic syndrome (MDS) was diagnosed after clinical correlation which was not responding to treatment.

Diagnos is of 2 case of granulomatous pathology were done on bone marrow biopsy with aspiration showing reactive marrow. Also seen an eosinophilia in 1 case.

Special stain done in cases of AML, ALL like Myeloperoxidase done in AML which shows diffuse positivity in cases of Acute myeloid leukaemia. Block like PAS positivity seen in cases of ALL. Also seen grade III positivity in cases of myelofibrosis.

In the present study diagnostic accuracy of bone marrow aspiration findings is very well corelated with the bone marrow findings.

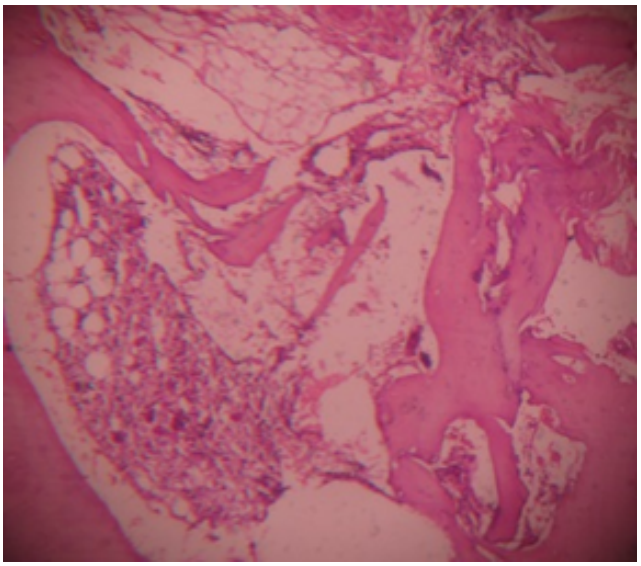

Fig. 1: Bone marrow biopsy showing myelofibrosis (Haematoxylin & Eosin stained).

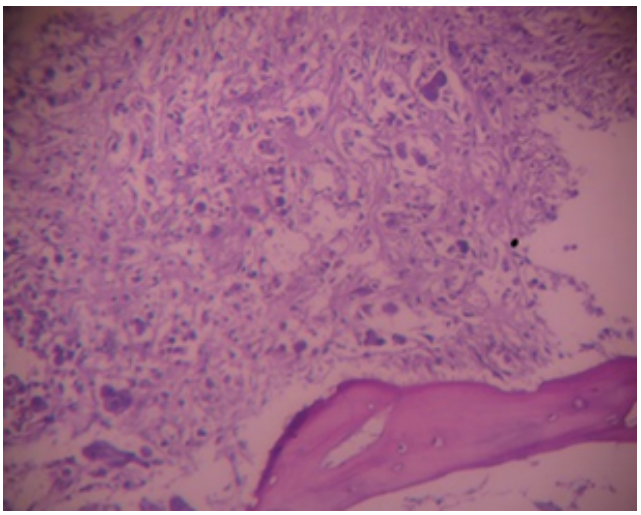

Fig. 2: Metastatic deposits seen in bone marrow biopsy (Haematoxylin & Eosin stained).

4. Discussion

Bone-marrow is the principle site of haematopoiesis. Haematological disorders include a wide range of diseases ranging from reactive hyperplasia to haematological malignancies. Bone marrow aspiration and trephine biopsy these are two procedures done for diagnosis of haematological and non-haematological disorders and are very much complimentary to each other. For correct diagnosis it is a combination of both procedure where clues gathered from examination of several different preparations for a correct diagnosis.[6] This is helpful in follow up for the patients undergoing chemotherapy.[7,8]

In our study w e included the cases were both aspiration and biopsy were available are 572. Present study showed, the age ranged from 6 months to 84 years, most common age group of 21 to 30 years. Pudasaini et al, study showed the majority of the patients were between 31–45 years.[9]

In our study m ales is to female ratio was M: F of 1.32:1. The commonest clinical presentation was pancytopenia (35.13% of cases) seen in our study was followed by anaemia (29.19%), malignancy (13.81%), hepatosplenomegaly (8.39%), thrombocytopenia (8.21%) and fever (5.24 %). In the study done by Ahmed et al, pancytopenia was the commonest presentation and anaemia is the second common indication similar to our study.[10] Bhatnagar et al. study from India shows incidence of pancytopenia in 54.5% cases, which is also nearest to present study.[11]

In our study seen are hypercellular bone marrow (53 %) followed by normocellular marrow (32 %) and hypocellular marrow (15 %). Most common finding in present study was anaemia (380 cases) followed by Acute myeloid leukaemia (Figure 1). Among anaemias most common anaemia was megaloblastic (163 cases) anaemia (Figure 2) was followed by dimorphic deficiency anaemia (74 cases), nutritional anaemia & aplastic anaemia. Various studies reported throughout the world in which the most common cause of pancytopenia is aplastic anaemia.[12,13]

But study done by us showed megaloblastic anaemia was the commonest cause of pancytopenia followed by leukaemia. Some studies conducted in India showed megaloblastic anaemia is the major cause of pancytopenia. Among leukaemia acute leukaemia (52 cases) was most common cause and acute myeloid leukaemia showed in 35 cases and 17 cases of acute lymphoblastic leukaemia.

Erythroid hyperplasia with either megaloblastic proliferation or micro normoblastic erythropoiesis seen in both BMA and BMB examination. The study conducted by Ch Toi P et al., these findings are similar.[14] But BMB iron stained sections showed differences in iron content from that of BMA smears. Stuart-Smith SE et al., have also shown in a study that aspirate smears reflect bone marrow iron stores more reliably than trephine biopsy sections.[15]

In the present study due to increase in fibrosis dry tap seen on trephine sections in 4 out of 52 cases of acute leukaemia. A cute lymphoblastic and acute myeloblastic leukaemia shows marked increase in reticulin may lead to dry tap seen in the study of Bird and Jacobs. One cases of metastatic lesions were diagnosed on biopsy sections with the respective aspirate smears not showing metastatic deposits. So, a dry tap or inadequate aspiration should always be accompanied by trephine biopsy to arrive at a final diagnosis. Primary was unknown in this case of metastatic deposits were IHC was used on biopsy for identifying the primary site.

On biopsy section one case of Chronic Lymphocytic Leukaemia (CLL) with diffuse involvement of marrow was seen but on aspiration showed only marrow involved. Trephine biopsy always include in case of CLL along with bone marrow aspiration because bone marrow aspirate gives very little information. While trephine biopsy examination the pattern of marrow involvement by leukemic cells can only analysed. Also, trephine biopsy permits an exact assessment of extent of infiltration and gives information of prognostic importance.[16]

The 1 case was positive for infiltration among staging in Hodgkin's lymphoma. We received 9 bone marrow cases f or staging of non-Hodgkin's lymphomas we case out of which 5 cases showing evidence of infiltration of marrow involvement in biopsy. This could be explained by focal pattern of infiltration and fibrosis seen on biopsy. In the study of Kumar, A showed involvement on biopsy in 27 cases (55.10%) by lymphoma.[17,18] Unilateral positivity was found in four cases (14.81% cases). Marrow involvement by NHL incidence was 55.1%. After doing trephine biopsy, diagnosis of aplastic anaemia only confirmed, as the accurate tool to assess marrow cellularity is the trephine biopsy. BMB gives the qualitative and quantitative assessment of cellularity hence is of almost importance in diagnosing a plastic anaemia.[19]

Trephine biopsy added information about fibrosis, cellularity and morphology of megakaryocytes in chronic myeloproliferative neoplasm (MPNS). One cases of Hodgkin's lymphoma infiltration and 2 cases of granulomatous pathology were diagnosed on biopsy alone with their corresponding aspirate smears showing reactive marrow only.

In our study 3 cases of multiple myeloma showed 40% plasma blasts, one case of eosinophilia and few cases of myeloproliferative neoplasm seen in present study.

Previously treated but not responding to the treatment, the case of megaloblastic anaemia was diagnosed as Myelodysplastic syndrome (MDS). For confirm diagnosis the bone marrow aspiration and trephine biopsy are complementary to each other this is reported in the Gupta et al study. Cases of metastatic lesions of adenocarcinoma shows cellular aspirate and marrow fibrosis were diagnosed on biopsy alone this was observed in present study similarly few cases of focal NHL infiltration on biopsy with normal aspirate noted. All cases of Granulomatous pathology and Hodgkin's lymphoma infiltration were diagnosed by biopsy alone in the present study.

To conclude, Bone marrow aspiration and biopsy examination were complementary to each other and well corelated. On bone marrow examination, well cytomorphological details are seen in recognising the abnormal hematopoietic cells or the non-native cells in case of nonhematological disorders. But on other hand a bone marrow trephine biopsy examination gives idea

about arrangement of hematopoietic cells within the marrow framework and provides more view of the cellularity of the marrow and provides infiltration to be recognized clearly. For diagnostic purpose both the procedures can be done simultaneously.

5. Conflict of Interest

None.

6. Source of Funding

None.

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