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Original Article

Correlation of bone marrow aspiration and biopsy findings in diagnosing hematological disorders – a study of 89 cases

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Keywords:

Bone marrow aspiration;
Haematological disorder;
Anemia;
Leukemia;
Aplastic anemia;
Myelofibrosis.

ABSTRACT

Background: Bone marrow examination is an important diagnostic tool to evaluate various disorders which includes both neoplastic and non- neoplastic hematological diseases. Few studies have compared the relative value of aspirate with trephine biopsy. The present study was conducted to compare the role of bone marrow aspirate and trephine biopsy to formulate an effective and rapid method for diagnosing wide spectrum of hematological diseases.

Materials and Methods: This is a three year retrospective study done from July 2010 to June 2013. A total of 95 cases presented with clinical haematological disorders; of which only 89 were biopsied and the correlation done. All the smears and sections were reviewed for morphological details and findings on aspirate and biopsy and compared to each other.

Results: Out of the 89 cases selected for study; bone marrow aspiration revealed diagnostic materials in 75 cases and 14 cases were inconclusive for a definite diagnosis. The diagnostic accuracy of the bone marrow aspiration cytology was 84.26%. Eighty eight cases were diagnosed on trephine biopsy of bone marrow with diagnostic accuracy of 98.87%.

Conclusion: Both the aspiration cytology and trephine biopsy complement each other for evaluating any haematological disorder. Though cellular morphology is better understood in marrow aspirates and is equally effective to biopsy in diagnosing various anemias and leukemias; however it is the histopathological study of trephine biopsy that gives well preserved marrow architecture with its all cellular and stromal components. modalities including radiological, microbiological and serological tests.

INTRODUCTION

The adult haematopoietic system includes tissues and organs involved in the proliferation, maturation and destruction of haematopoietic cells. These organs and tissues include the bone marrow, thymus, spleen and lymph nodes. Bone marrow is the site of myeloid, erythroid, and megakaryocytic as well as lymphoid cell development.[1]

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Bone marrow examination is an important diagnostic tool to evaluate various disorders including both neoplastic and non-neoplastic hematological diseases. The bone marrow evaluation may either confirm clinically suspected disease or may provide the previously unsuspected diagnosis.[2,3] Bone marrow aspiration is the most frequent and safe invasive procedure done routinely in the hospitals for the diagnosis and management of hematological disorder.[4] In case of trephine biopsy, the greater value is that it can provide information about the structure of relatively large pieces of marrow. At the same time, morphological features

of individual cells can be identified.[5]

Bone marrow aspiration (BMA) cytology and bone marrow biopsy (BMB) are two main basic preparations for bone marrow evaluation in our country. Although various studies have been conducted regarding the role of bone marrow aspirate cytology and trephine biopsy for diagnosing various hematological disorders but fewer studies have compared the relative value of aspirate with trephine biopsy.[6-8]

The present study was conducted to compare the role of bone marrow aspirate cytology and trephine biopsy to formulate an effective and rapid method for diagnosing wide spectrum of hematological diseases.

MATERIALS AND METHODS

This was a three year retrospective study done in the department of pathology, Kathmandu Model Hospital, from July 2010 to June 2013. A total of 95 cases presented with clinical haematological disorders; of which only 89 were biopsied and the correlation done. All the smears and sections were reviewed for morphological details and findings on aspirate and biopsy and compared to each other. A detailed history, clinical findings, routine relevant laboratory investigations and radiological findings were carried out in each case.

Only those cases in which bone marrow examination was done by using BMA and BMB were included in the study. The standard technique was employed for obtaining the aspirate samples using the Salah's needle from posterior superior iliac spine. The trephine biopsy was performed using Jamshidi needle with the length of the biopsy core ranging from 1 to 3 cm. The biopsy was then fixed for minimum of 24 hours in 10% buffered formalin and then decalcified overnight in mixture of 8% hydrochloric acid and 10% formic acid in equal amounts. The fixation of the biopsy core was followed by automated tissue processing, paraffin embedding and sectioning. All the aspirate smears were routinely stained by Jenner Giemsa while the trephine biopsy sections were stained by routine Hematoxylin and Eosin stain. The relevant cytochemistry and immunochemistry staining was performed as and when required. All the smears and sections were reviewed for morphological details by two pathologists and the findings on BMA and BMB were compared and the final correlation done.

RESULTS

A total of 75 cases were diagnosed on BMA cytology with erythroid hyperplasia as the commonest diagnosis (N=10; 13.33%). Megaloblastic anemia and acute leukemia were diagnosed as the second common diagnosis (N= 9 each; 12%). Diagnosis on bone marrow aspiration and bone marrow biopsy are shown in Table 1&2.

A total of 88 cases could be diagnosed on bone marrow biopsy. Megaloblastic anemia was the commonest diagnosis (N=15; 17.04%). The overall diagnostic accuracy of bone marrow aspiration cytology in diagnosing haematological disorders was 84.26% and the diagnostic accuracy of bone marrow biopsy was 98.87%.

Table 1: Diagnosis on bone marrow aspiration (BMA) cytology

BMA diagnosis	No of cases	Percentage of cases
Erythroid hyperplasia	10	13.33%
Micronormoblastic anemia	8	10.66%
Megaloblastic anemia	9	12%
Mixed erythropoiesis	4	5.33%
Malarial infection	4	5.33%
Leishmaniasis	2	2.66%
Granulomatous inflammation	1	1.33%
Immune thrombocytopenia	7	9.33%
Acute leukemia	9	12%
Chronic myeloid leukemia (CML)	5	6.66%
Chronic lymphoid leukemia (CLL)	2	2.66%
Multiple myeloma	2	2.66%
Lymphoma	1	1.33%
Myelodysplastic syndrome	2	2.66%
Normal marrow	9	12%
TOTAL CASES	**75**	**100%**

Table 2: Histopathological diagnosis of lesions based on trephine biopsy

Histopathological diagnosis	No of cases	Percentage of cases
Micronormoblastic anemia	12	13.63%
Megaloblastic anemia	15	17.04%
Hyoplastic/ Aplastic anemia	6	6.81%
Myelofibrosis	2	2.27%
Malarial infection	4	4.54%
Leishmaniasis	2	2.27%
Granulomatous inflammation	3	3.40%
Immune thrombocytopenia	12	13.63%
Acute Lymphoid Leukaemia (ALL)	7	7.95%
Acute myeloid leukemia (AML)	5	5.68%
Chronic myeloid leukemia (CML)	5	5.68%
Chronic lymphoid leukemia (CLL)	2	2.27%
Multiple myeloma	2	2.27%
Lymphoma (NHL)	1	1.13%
Myelodysplastic syndrome	2	2.27%
Normal marrow	**8**	**9%**
TOTAL CASES	**88**	**100%**

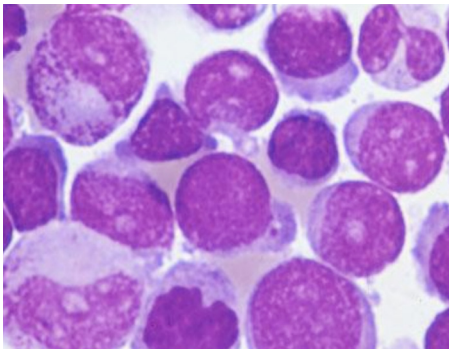

Figure 1: *Bone marrow aspirate showing myeloblasts with auer rods in AML (Giemsa stain, X100).*

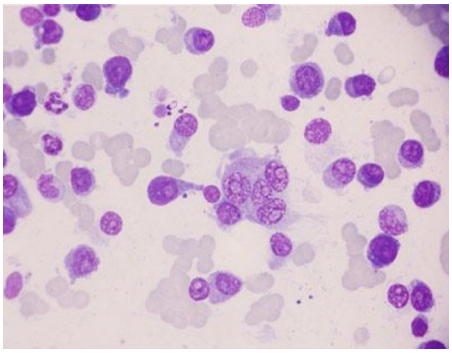

Figure 2: *Bone marrow aspirate showing neoplastic plasma cells (Giemsa stain, X100).*

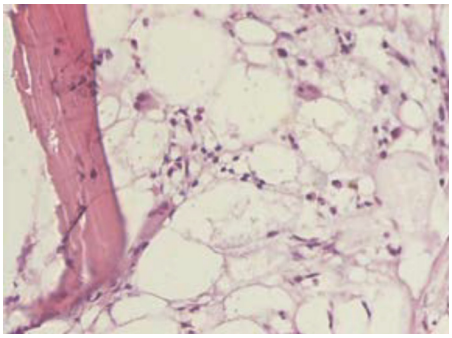

Figure 3: *Bone marrow biopsy showing hypocellular bone marrow fragments with absence of haematopoietic cells and its replacement with fat cells (HE stain, X100.)*

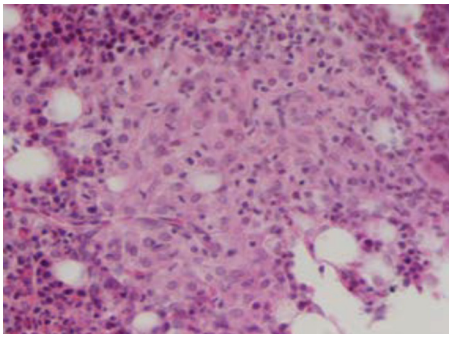

Figure 4: *Bone marrow biopsy showing ill-defined epithelioid cell granulomas (H&E stain, X400).*

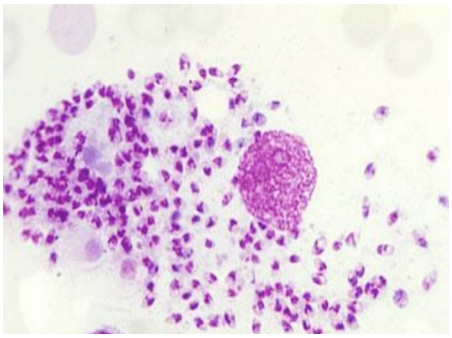

Figure 5: *Bone marrow aspirate smears showing LD bodies (Giemsa stain, X400).*

DISCUSSION

The comparative evaluation of BMA and BMB is essential so that more rapid and efficient method may be defined for diagnosing various hematological disorders. The present study observed that the diagnostic accuracy of BMB was higher (98.87%) in comparison to BMA (84.26%) in diagnosing various hematological disorders. Smita Chandra and Harish Chandra have also given the diagnostic accuracy of BMA as 77.5% and that of BMB as 99.2% in diagnosing hematological disorders.[9]

Erythroid hyperplasia was the most common diagnosis in BMA accounting for a total of 10 cases (13.33%) in our study. Similar incidence (14%) was shown in a study by Khodke et al.[10] Jha et al in their study showed an incidence of 19.6%.[11] Those cases diagnosed as erythroid hyperplasia on BMA in our study was further diagnosed on trephine biopsy as micronormoblastic anemia-2 cases and 4 cases each of megaloblastic anemia and Idiopathic Thrombocytopenic Purpura.

Megaloblastic anemia was the second commonest diagnosis amongst the BMA cases accounting for a total of 9 cases (12%). Megaloblastic anemia was a common cause of pancytopenia in a study conducted by Tilak N et al.[12] The high prevalence of nutritional anemia has been cited for the increased frequency of megaloblastic anemia.[13] We could not find the exact deficiency leading to megaloblastic anemia as serum Vitamin B^{12} and folic acid levels were not assessed. In a study done by Gayathri et al[14] megaloblastic anemia was the commonest cause of pancytopenia and was the commonest finding in BMA.

Micronormoblastic anemia was diagnosed in 8 cases (10.66%) on BMA in our study. Two cases each of erythroid hyperplasia and mixed erythropoiesis were diagnosed as micronormoblastic anemia on BMB accounting for a total of 12 cases (13.63%) amongst the BMB diagnosis. However,

in a study done by Ahmad et al,[23] 8% cases were microcytic anemia and diagnosed as iron deficiency anemia.[15]

Nine cases (12%) of acute leukemia; acute lymphoblastic leukemia and acute myeloid leukemia (fig.1); were diagnosed in BMA in our study compared to 12 cases which were diagnosed on BMB. The predominant reason for not diagnosing acute leukemia on BMA in our case was dry tap either due to marrow fibrosis or tightly packed marrow by leukemic cells. Other malignancies diagnosed in our study were CML- 5 cases, 2 cases each of CLL, Multiple myeloma (fig. 2) and MDS and 1 case of lymphoma. Both bone marrow aspiration and trephine biopsy were complementary in all the other cases of malignancies diagnosed in our study. While aspiration smears were observed to be most effective for studying cellular morphology, biopsy on the other hand, was helpful in assessing marrow cellularity. Our findings are comparable to the study by James et al who observed that combined procedures of aspiration and biopsy gave a higher yield and are essential in patients with leukemia and lymphoma.[16] Hence, it is important that both the aspirated and biopsy material should be examined together, since the two methods are often complementary.[17]

Our study of haematological disorders showed that 2 cases in whom BMA yielded dry tap was diagnosed as myelofibrosis on trephine biopsy. Trephine biopsy was also superior to BMA in diagnosing 6 cases of hypoplastic/ aplastic anemia (fig. 3) similar to study by Gupta N et al.[18] Sabharwal et al [8] included 7 cases (23.3%) of myelofibrosis which were diagnosed on trephine biopsy sections. Trephine biopsy was also better than bone marrow aspiration in the diagnosis of myelodysplastic syndrome since it showed the presence of aggregates of immature myeloid precursor cells. In a study done by Humphries of 87 cases of dry tap on marrow aspiration, obtained trephine biopsies which showed significant pathology.[19] Dry tap with marrow aspiration were due to fibrosis and hypercellularity. The frequent diseases diagnosed on bone marrow biopsy in cases where aspiration yielded dry tap were metastasic cancers, chronic myeloid leukaemia, idiopathic myelofibrosis and aplastic anemias. Hence, the finding of a dry tap should never be dismissed as being due to faulty technique and always needs a bone marrow biopsy.

Two cases of multiple myeloma and one case of lymphoma were included in the present study and all the cases reflected 100% positive results for both the aspirate smears and biopsy sections. However, trephine biopsy by virtue of providing architectural pattern was superior for the staging and exact categorization of lymphoma. Sabharwal et al [8], in their study, also recorded a 100% positive result for aspiration smears and biopsy sections in the two cases of lymphomas studied by them. Mostserrat et al[20] observed that although bone marrow histological pattern and bone marrow aspiration are of value to estimate bone marrow lymphocytic infiltration in chronic lymphocytic leukemia but to predict the outcome of the disease, bone marrow biopsy is more reliable than aspiration.

Immune thrombocytopenic purpura (ITP) was diagnosed in 7 cases in BMA and 12 cases on BMB. Other studies showed 6.21%, 14.5%, 6.8% and 5% cases of ITP respectively in their studies.[4,10,21] 4 cases diagnosed as erythroid hyperplasia in the BMA was diagnosed as ITP on BMB.

Only one case of granulommatous inflammation of the marrow was diagnosed on BMA while 3 cases were diagnosed on BMB (fig. 4). This could mainly be because of focal involvement of the marrow by granulomas which is very difficult to be detected on aspirate smears. Other studies have also observed the detection of granulomas more on BMB sections in comparison to aspirate smears.[3, 21]

Infective pathology was seen in 6 cases out of which Malarial infection was diagnosed in 4 cases and leishmaniasis (fig. 5) was seen in two cases. Similar finding was seen in a study done by Santra et al.[22] A 100% correlation was seen in the BMA and BMB findings.

Out of the 9 cases diagnosed as normal marrow on BMA, 8 cases were confirmed the same on BMB. One case could not even be diagnosed on biopsy and further advised for flow cytometry as there was predominant lymphoid proliferation and the immunostains didn't helped to reach a definite diagnosis.

Marrow aspirate has been primarily utilized for cytological assessment. It is an important step to arrive at the confirmatory diagnosis of wide varieties of hematological disorders. Bone marrow examination also gives explanation for unexplained cytopenias and leukemia. It gives a more complete picture of the reaction of the hemopoietic tissue to anemia than can be gained from the peripheral blood smear alone.[4] Trephine biopsy; on the other hand, allow for studies of the marrow's overall cellularity, detection of focal lesions, and extent of infiltration by various pathologic entities.[23]

CONCLUSION

The study concludes that bone marrow aspiration cytology and trephine biopsy complement each other and should be performed simultaneously for complete bone marrow workup and evaluation. Though cellular morphology is better understood in marrow aspirates and is equally effective to biopsy in diagnosing anemias and leukemias, it is the histopathological study of trephine biopsy of bone marrow that gives well preserved marrow architecture with its all cellular and stromal components. So, trephine biopsy becomes mandatory in the diagnosis of aplastic anemia, myelofibrosis and granulommatous involvement yielding dry aspirate on bone marrow aspiration.

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