

Original Research Article

STUDY OF BONE MARROW BIOPSY IN HAEMATOLOGICAL DISORDERS

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Abstract

Bone marrow examination is very useful not only in the diagnosis of hematological disorders. Both bone marrow biopsy and aspiration findings were studied and findings are compared morphologically. The biopsy specimen is best for the architectural evaluation and its relation with pathologic marrow elements. Core biopsy is best for ancillary study like immunohistochemistry. The diagnoses of hematological disorders were mainly done by taking complete clinical history, careful physical examination, complete haemogram and bone marrow examination.

Keywords: Bonemarrow, Hematological diseases, Histopathology

Introduction

Since time immemorial, the diagnosis of haematological disorders were mainly done by using bone marrow aspiration. The available statistics show that the diagnosis of haematological disorders taking complete clinical history, careful physical examination, complete haemogram and Bone marrow examination by either aspiration (or) biopsy. Even though aspiration is diagnostic jamshidi introduced a biopsy needle that was easier to use and which provided similar intact biopsy specimens. The biopsy is more superior than aspiration.

Aim

1. To study the histology of Bone marrow in various haematological disorders.
2. To know the advantage of bone marrow trephine biopsy over the aspiration smear.
3. To study the cellularity of bone marrow with intact architecture in trephine biopsies and its comparison with aspiration smear.
4. To evaluate the diagnostic efficacy of trephine biopsy over the aspiration smear.

Materials and Methods

50 patients with haematological disorders who visited the Government General Hospital between March 2001 to Feb 2003 were included in the study. Before the biopsy procedure was done relevant clinical history, detailed clinical examination of the patient and complete haemogram examination were done for all patients. The patients were then subjected to bone marrow biopsy and bone marrow aspiration. The bone marrow biopsy specimens are fixed in 10% formaline overnight and decalcified in 5% formic acid. Biopsies are then routinely processed and 4-5µm thickness sections are cut and stained with hematoxylin and eosin. Perls Prussian blue reaction was done for Iron stores.

Results

Table I: Bone marrow aspiration/Biopsies

Bone marrow aspiration/Biopsies	Cases	Percentage
Total number of cases	50	
Total number of adequate aspiration	38	76
Total number of Inadequate aspiration including dry taps (6) and bloody aspiration (6)	12	24
Total number of adequate trephine biopsies	49	98
Total number of inadequate trephine biopsies	1	2
Case in which both adequate trephine biopsies and aspiration were obtained	37	74

Table II: Age & Sex distribution

Age Group	Total	Male	Female	Percentage
0-10	3	1	2	6%
11-20	11	4	7	22%
21-30	9	1	8	18%
31-40	12	0	12	24%
41-50	9	4	5	18%
51-60	3	1	2	6%
61-70	2	0	2	4%
71-80	1	1	0	2%
	50	12	38	100%

The maximum number of biopsies were performed as patients with the age group between 31-40 years and the male to female ratio was 1:3.

Table III: Cellularity on Biopsy

Cellularity	No. of Trepine	Percentage
Hypo	10	20.4%
Normo	20	40.8%
Hyper	19	38.8%
	49	100%

In 37 out of 50 cases both bone marrow trephine biopsies and aspirations were adequate for study.

However 30 out of 37 cases (81%) showed correlation between biopsy and aspiration regarding cellularity while 7 cases did not show correlation.

Table IV

S. No.	Cellularity on Bone marrow aspiration	Cellularity on Bone marrow biopsy	Diagnosis	No. of Cases
1.	Normo	Hypo	A plastic anaemia	1
2.	Hyper	Normo	Multiple myeloma	1
3.	Hypo	Hyper	Erythroid Hyperplasia	2
4.	Normo	Hyper	Storage disorders	1
5.	Hypo	Hyper	Pyrexia of unknown origin	2

In one case of a aplastic anaemia the appropriate smear showed normo cellularity, but the corresponding trephine biopsy section showed a hypocellular marrow. In one case of multiple myeloma the aspiration smear showed Hypercellularity but the biopsy section showed Normocellular marrow. In two cases of erythroid Hyperplasia the aspiration showed Hypocellularity but biopsy showed Hypercellularity. In one case of storage disorder the aspirate showed Normocellularity but the biopsy showed Hypercellularity. In two cases of PUO with hepatosplemegaly (Hyper cellular marrow with diffuse lymphocytic infiltration), the aspirate smeared showed Hypocellularity but the biopsy showed Hypercellularity.

Table V: Distribution of cases in the study

S. No.	Distribution of cases	Total cases	Percentage
1.	Non Malig hematological disorders	27	44%
2.	Malig hematological conditions	23	38%
3.	Myeloproliferative disorders	3	6%
4.	lymphoproliferative disorders	7	14%
5.	Plasma cell disorders	4	8%

Majority of cases were Non-malignant haematological conditions followed by malignant haematological conditions.

Table VI: Non Malignant haematological conditions

Cases	Total Cases	Percentage	Marrow aspiration	No. of marrow biopsy
Aplastic anemia	16	32%	10	16
Megaloblastic anemia	1	2%	1	1
Erythroid Hyperplasia (Hypersplenism)	8	16%	5	8
	27		16	27

Out of the 16 cases of aplastic anaemia bone marrow aspiration were obtained in 10 cases and failed in 6 cases out of 6 cases 4 were dry tap and 2 with blood tap.

Table VII: Malignant haematological conditions

Cases	Total Cases	Percentage	Marrow aspiration	No. of marrow biopsy
Myeloproliferative disorders				
AML	9		9	9
Lymphoproliferative disorders				
ALL	2	4%	2	2
CLL	1	2%	1	1
NHL	3	6%	2	1
HL	1	2%	0	4
Plasma cell disorders multiple myeloma	4	8%	3	4
	23		17%	20

In this study 23 cases of Malignant haematological cases on therapy were considered for biopsy.

In three cases i.e. one case of NHL, one case of HL, one case of Multiple Myeloma aspiration were dry tap because of packed marrow and fibrosis.

Table VIII: Reticulum content of bone marrow

S. No.	Cases	Total	Reticulum Content	
			Normal	Increased
1	Aplastic anaemia	18	17	1
2	Megaloblastic anaemia	4	4	0
3	Hypersplenism	8	8	0
4	Acute myeloid leukaemia	9	9	0
5	Acute lymphoblastic leukaemia	2	1	1
6	Chronic lymphatic leukaemia	1	1	0
7	Multiple myeloma	4	2	2
8	Non hodgkins lymphoma	3	3	0
9	Hodgkins lymphoma	49	42	7

In 42 out of 49 cases the reticulum content was normal. Increased reticulum content was noted 4 cases of aplastic anemia one case of acute lymphoblastic leukemia, and two cases of multiple myeloma.

Table IX: Bone marrow Iron stores

S. No.	Cases	Total	Iron Stores		
			Normal	Increased	Decreased
1.	Aplastic anaemia	17	12	2	3
2.	Megaloblastic anemia	4	4	0	0
3.	Hypersplenism	8	7	0	1
4.	Acute Myeloid leukemia	9	8	0	1
5.	Acute lymphoblastic leukemia	2	0	0	2
6.	Chronic lymphoblastic leukemia	1	0	0	1
7.	Multiple Myeloma	4	4	0	0
8.	Non-Hodgkin's Lymphoma	3	3	0	0
9.	Hodgkin's Lymphoma	1	1	0	0
	Total	49	39	2	8

Bone marrow Iron stores were normal in 39 out 49 cases. Increased in 2 out of 49 cases and decreased in 8 out of 49 cases. The bone marrow Iron stores were decreased in 3 cases of aplastic anemia.

Table X: Presentation of Pan cytopenia and leucoerythroblastic blood picture on bone marrow biopsy

Condition	Total cases	Malignant Hematological disorder	Non Malignant Hematological disorder
Pancytopenia	10	1	9
Leucoerythroblastic blood picture	1	1	0

Table XI: Correlation between Aspiration and Biopsy

Total cases	BM Aspiration	BM Biopsy	Inadequate material		Adequate material on	corr Bx & Asp	Not corr. Bx & Asp
			Asp	Bx	Bx & Asp		
50	38	49	12	1	37	33	4



Fig 1: Bone marrow biopsy Lymphoproliferative disorders

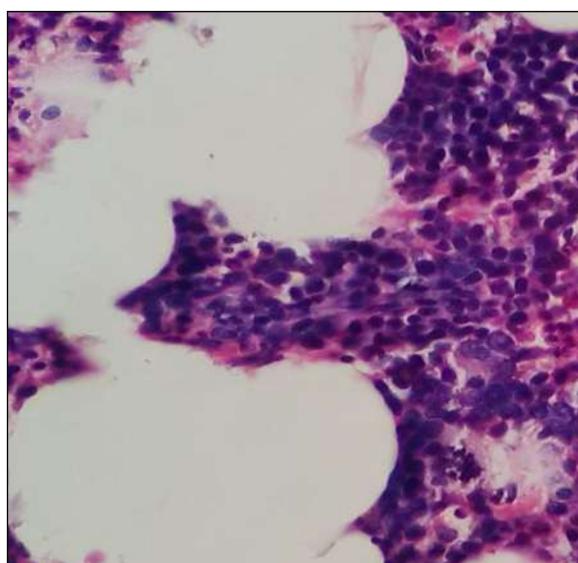


Fig 2: Bone marrow biopsy in NHL in NHL 100x(H&E) 400 x(H&E)



Fig 3: Bone marrow aspiration in *Multiple myeloma* 1000x (H&E)

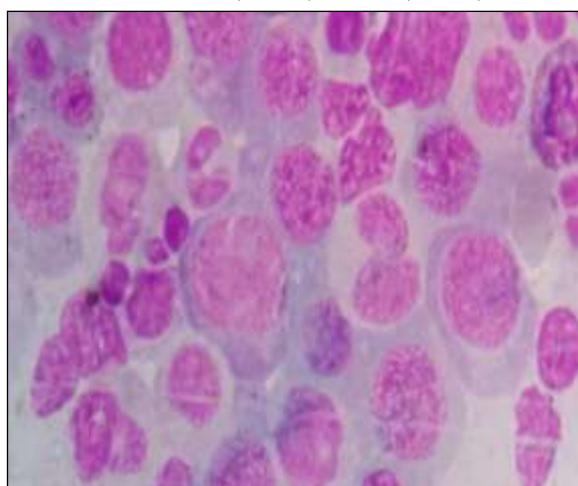


Fig 4: Bone marrow aspiration in *Megaloblastic anaemia* 1000x (H&E)

Discussion

Evaluation of Bone marrow is essential in many haematological disorders. A good marrow aspirate must have multiple fragments and adequate cell trails for proper evaluation. At times marrow aspirate is diluted, is a dry tap or is unsatisfactory. Moreover in certain diseases, marrow involvement is focal e.g.: granulomas, metastatic deposits, focal myelomas, Hodgkins disease associated with fibrosis, and therefore marrow aspiration fails to demonstrate the disease process to arrive at a diagnosis. Therefore a marrow biopsy is necessary which may be obtained surgically from iliac creast (or) a trephine biopsy under local anaesthesia.

In the present study 50 cases with haematological disorders were subjected to bone marrow aspiration and trephine biopsy. The maximum number of patients presented were between 21-50 years. The major clinical presentations were anaemia, bleeding diathesis, hepato splenomegaly. One case was presented with epilepsy, early onset cataract and stunted growth and on bone marrow biopsy, turned out to be a storage disorder. Male: Female ratio was 1:3 (12:38). Bone marrow often fails to be aspirated in aplastic anemias, packed marrow (Leukemias) and conditions associated with myelofibrosis (Hyun *et al.*, 1988 Neelam Verma 1993) The comparative study of Inadequate aspirations in various studies and present study is mentioned in the table below.

Comparison of inadequate aspiration in various studies and present study

Studies	Total Cases Studies	Adequate aspirations	Inadequate aspirations	% of Inadequate aspirations
Hyun <i>et al.</i> 1988	1357	1665	92	6.8%
Neelam Verma: 1993	535	342	283	36%
Present Study	50	38	12	24%

In the present study adequate biopsies were obtained in 38 cases. The chances of obtaining adequate biopsies are higher when compared to aspirates in cases of aplastic anemia and packed marrows. Some authors believe that a trephine biopsy is superior to aspirate smears in the assessment of cellularity (Krause, Hyum *et al.*). However others have found a good correlation between aspirate smears and trephine biopsies (Paul *et al.* 1989). In the present study 30/37 showed correlation between aspiration and biopsy with respect to cellularity i.e. 7 cases did not showed correlation. They constituted one case each of aplastic anemia and multiple myeloma. This variability could be due to tapping different areas of the bone marrow. Two cases of Erythroid Hyperplasia, one case of PUO with hepatosplenomegaly showed discrepancies in the cellularity. This could be explained due to packed marrow, which yields low cellularity on aspiration.

(Ref Hyunetal 1988^{Ref (1)}, Neelam Verma 1993^{Ref (2)})

The various morphological presentations were broadly divided in this study in to

- 1) Non-malignant.
- 2) Malignant.

The malignant were further subdivided in to

- a) Myeloproliferative

- b) Lympho proliferative disorders
 - c) Plasma cell disorders.
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- 1) Nonmalignant haematological disorders
 - a) Aplastic anemia
 - b) Megaloblastic anemia
 - c) Hyper splenism
 - 2) Malignant haematological disorders
 - a) Myeloproliferative disorders
 - i) AML - 9/50
 - b) Lymphoproliferative disorders
 - i) ALL - 2/50
 - ii) CLL - 1/50
 - iii) NHL - 3/50
 - iv) HL - 1/50
 - c) Plasma cell disorders
 - i) Multiple myeloma-4/50

In this study on peripheral smear examination there were 10/50 (20%) cases with pancytopenia and 1/50 (2%) with leucoerythroblastic picture. The bone marrow interpretation in these cases of pancytopenia was 6/10 (60%) cases with aplastic anaemia, 2/10 (20%) with Hypersplenism, and 1/10 (10%) with ALL. The case with leucoerythroblastic picture showed Hodgkin's lymphoma on bone marrow.

The total number of cases with adequate aspirations were 38/50 (76%), 12/50 (24%) cases did not yield any aspirate. 6/12 (50%) were drytap and 6/12 (50%) were blood aspirations. The number of adequate biopsies were 49/50 (98%) and only one did not yield adequate biopsy. So 37/50 (74%) were adequate on both aspiration and biopsy. Out of 37 cases available for correlation only 33/37 cases (89%) showed correlation between biopsy and aspiration. 4/37 (11%) did not correlate. They constituted one case of aplastic anaemia and two cases of hypersplenism. Bone marrow biopsy should be performed when ever bone marrow aspiration is indicated, because bone marrow biopsy is diagnostic in cases where aspiration is negative (or) equivocal. Also it is nearly impossible to predict in advance, which aspiration attempts will be technically difficult. The complications are nil and cost benefit analysis is in favour of combined approach. It is a safe outpatient procedure.

Conclusion

Bone marrow aspiration and trephine biopsies are complimentary to one another and the combined approach increases the diagnostic value. In this study the correlation between biopsy and aspiration was 89%. In cases of aplastic anemia and hyper cellular marrow, and bone metastasis as mentioned in literature, bone marrow biopsy proved to be superior than aspiration in this study, even though morphology is better appreciated on aspirate. Bone marrow biopsy should be performed when ever bone marrow aspiration is indicated, because bone marrow biopsy is diagnostic in cases where aspiration is negative or equivocal. The

complicated are nil and cost benefit analysis favour the combined approach. It is a safe outpatient procedure.

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