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Histolomorphological Patterns In 50 Bone Marrow Aspiration Failure Cases

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Abstract

The present study was carried out in the Department of Pathology, Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, to see the histmorphological patterns of trephine biopsy in bone marrow aspiration failure cases.

A total of 50 patients of aspiration failure cases were trephined to obtain bone marrow from posterior iliac crest during the period of two years from April, 2000 to March, 2002, attending the departments of haematology and medicine, BSMMU. In four cases (8%), trephine biopsy failed to show any marrow tissue and was discarded from the present study. The rest 46 cases (92%) with adequate biopsy material revealed 19 cases (41.30%) of acute leukemia, 13 cases (28.26%) of chronic myeloproliferative disorders, 07 cases (15.22%) of hypoplastic marrow, 02 cases (4.34%) of non-Hodgkin's lymphoma and one case (2.17%) of each of multiple myeloma, reactive marrow and metastatic carcinoma. Out of 46 cases, diagnosis could not be done in two cases (4.34%) due to poor preparation of biopsy material. In similar type of studies, Navone and Colombanol 6 reported 16%(35 out of 228) acute leukemia, 9.8%(44 out of 445) chronic myeloprliferatve disorders, 8.8%(29 out of 328) malignant lymphoma and hogkin's diseases, 4.8 %(10 out of 208) myelomas and 13.5%(10 out of 74) metastatic carcinomas in trephine biopsy of bone marrow aspiration failure cases. The discordance between these studies may be due to difference in their sample size. In the present study, two cases remained undiagnosed and five cases of acute leukemia could not be subcategorized into AML or ALL. It appears that as only H&E and reticulin stains were used in this study, those cases could not be diagnosed or subcategorized due to lack of other facilities. So it is recommended that facilities for plastic embedding, immunocytochemistry and use of enzyme and immunophenotyping should be developed in the department and used whenever necessary.

Introduction

Bone marrow examination has very important role in the diagnosis of a variety of haematological and non-haematological disease. It is well known that the blood picture does not always reflect accurately abnormalities that may exist in blood forming organs 1. Though cellular morphology is better understood in marrow aspirates, 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 anaemia, metabolic bone disease, myelofibrosis and granulomatous involvement 2. Sing et al 3 gave their opinion to consider and utilize the marrow examination to detect metastatic tumour when other techniques are negative or to establish a tissue diagnosis if suspicious lesions are encountered, particularly if a primary site is not known. They have also mentioned that bone marrow biopsy discloses the diagnosis in a higher percentage of cases than aspirate. Brynes et al 4 have stated that examination of bony trabeculae is important in the in the evaluation of metabolic disorders such as primary and secondary hyperparathyroidism, osteoporosis and paget's disease. They have also mentioned that the relationship of haemopoietic cells to bony trabeculae is helpful in distinguishing marrow invasion by lymphoma from benign lymphoid aggregates. According to Lee et al 5 trephine biopsy of bone marrow is the answer in the diagnosis of the diseases where there is repeated failure of marrow aspiration. It is to be noted that no study on trephine biopsy of bone marrow has been done yet in our country. This study was done to see the histomorphological patterns of trephine biopsy in aspiration failure cases.

Materials and methods

This study was done in the Department of Pathology, Bangabandhu Sheik Mujib Medical University (BSMMU),Shahbag, Dhaka during the period from April,2000 to March,2002. A total of 50 patients of different age and sex were selected from the departments of haematology and medicine of

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BSMMU, Dhaka. Clinically diagnosed patients of haematological and non-haematological disorders supported by relevant laboratory investigations were subjected to bone marrow aspiration and the cases in whom bone marrow aspiration failed repeatedly were selected for trephine biopsy.

The bone marrow biopsy was taken from either of the posterior iliac spines. Islam's trephine biopsy needle was used for this purpose. In the department of pathology, gross examination of the specimen was done. It was then placed in a bottle containing 10% buffered formalin and kept overnight for proper fixation. In the next morning, the specimen was washed in water for 30 to 60 minutes. Short decalcification of the specimen was done with 10% nitric acid for about one hour. Then it was washed for 60 to 90 minutes with several changes of water and submitted for tissue processing with paraffin impregnation. Routine paraffin section were stained with haematoxylin and eosin staining method and examined under light microscope. When necessary, tissue sections were also stained with some special stains (e.g. reticulin) for accurate diagnosis. Specimens containing at least five marrow spaces in any section were considered adequate for histopathological diagnosis.

Results and observations

Out of 50 cases, trephine biopsy failure occurred in four cases. Out of these four cases, in two cases bone marrow could not be trephine out, rather only cortical bone without marrow were obtained, and in one only marrow material without bone or bony trabeculae and yet in another, marrow spaces contained only adipose tissue but no haemopoietic element. Clinically out of these four cases, two were acute leukemia, one chronic leukemia and the other one was aplastic anaemia. Clinical diagnoses of the rest 46 cases are shown in Table 1.

Table-I

Clinical diagnoses of 46 cases where bone aspiration failed.

Clinical diagnosis	Total
Acute leukemia	19
Chronic myeloid leukemia	10
Chronic lymphocytic leukemia	01
Myelofibrosis	03
Hypoplastic anaemia	05
Kala-azar	03
Multiple myeloma	02
Lymphoma	01
Combined deficiency anaemia	02
Total	46

Each of the specimens of 46 trephine biopsies of bone marrow was 2 mm in diameter. Their length ranged from 0.3 to 1.6 cm. Of the 46 biopsies, on histological basis, acute leukemia was found in 19 cases which comprised 41.30% of the total. Chronic myeloproliferative disorders were found in 13 cases (28.26%), hypoplastic anaemia in 07 cases (15.22%), 02 cases (4.34%) of Non-Hodgkin's Lymphoma, 02 cases (4.34%) of undiagnosed lesion and one patient each (2.17%) of multiple myeloma, reactive marrow and metastatic carcinoma (poorly differentiated). Histological diagnosis of trephine biopsy of bone marrow of 46 cases of aspiration failure is shown in Table 2.

Table-II

Histopathological diagnosis of trephine biopsy of bone marrow of 46 cases of aspiration failure :

Histopathological diagnosis	No. of patients	Percentage
Acute leukemia (AL)	19	41.30
Chronic myeloproliferative disorders (CMPD)	13	28.26
Hypoplastic anaemia (HA)	07	15.22
Non-Hodgkin's lymphoma (NHL)	02	4.34
Multiple myeloma (MM)	01	2.17
Reactive marrow (RM)	01	2.17
Metastatic carcinoma (MC) poorly differentiated	01	2.17
Undiagnosed (UD)	02	4.34

Among 19 cases of acute leukemias, acute myeloblastic leukemia was in 08 cases (42.10%), acute lymphoblastic leukemia in 06 cases (31.58%) and acute leukemia (undifferentiated) in 05 cases (26.32%). Their distribution is shown in Table 3.

Table-III

Distribution of types of acute leukemias (19 cases)

Diagnosis	No. of Patients	Percentage
Acute Leukemia	19	100
Acute Myeloblasticleukemia(AML)	08	42.10
Acute Lymphoblastic Leukemia (ALL)	06	31.58
Acute Leukemia (undifferentiated)(AL-UD)	05	26.32

Among chronic myeloproliferative disorder group, myelofibrosis was found in 07 cases (53.85%) and chronic myeloid leukemia in 06 cases (46.15%) which is shown in Table 3.

Table-IV

Distribution of chronic myeloproliferative disorders.

Diagnosis	No. of patients	Percentage
Chronic myeloproliferative disorders	13	100
Myelofibrosis (MF)	07	53.85
Chronic myeloid leukemia (CML)	06	46.15

Table 4 shows clinicopathological correlation of 46 cases of haematological disorders in aspiration failure cases. It is evident from the table 4 that the clinical diagnosis of all the cases of myelofibrosis (n=3), hypoplastic anaeia (n=5) and lymphoma (n=1) show 100% concordance with histopathlogical diagnosis. Out of 19 cases of clinically diagnosed AL, histopathological diagnosis was AL in 17 cases (AML-7, ALL-5, AL-UD-5), HA in one and another one as MF. These findings show 89.5 % concordance with clinical diagnosis. Out of 10 cases of clinically CML, histopathological diagnosis was CML in six cases, AML in one and MF in the rest three cases which shows 60 % concordance. One case of clinically diagnosed chronic lymphocytic leukemia (CLL) was histologically lymphoma showing 0% concordance. Among the three cases of clinically diagnosed Kala-azar (KA), histolgically one was ALL, one HA and one reactive marrow showing 0% concordance. Out of two clinically diagnosed multiple myeloma, histologically one was MM and one was metastatic carcinoma showing 50% concordance. So it is evident that out of 46 cases, clinical and histopathological diagnoses in 33 cases were similar showing 71.74 % concordance.

Table-IV

Clinicopathological correlation of 46 cases where marrow aspiration failed

C/D	HISTOPAHTLOGICAL DIAGNOSIS										Cncd (%)
	Total	AL	CML	MF	HA	LYM.	MM	MC	RM	UD	
AL	19	17		01	01						87.5
CML	10	01	06	03							60.0
MF	03			03							100
CLL	01					01					0
HA	05				05						100
KA	03	01			01				01		0
MM	02						01	01			50
LYMP	01					01					100
CDA	02									UD	0
Total	46	19	06	07	07	02	01	01	01	02	

CDA= Combined deficiency anaemia, C/D = Clinical diagnosis, Cncd.(%) = Concordance of clinical diagnosis with histopathological diagnosis in percentage, HA = Hypoplastic anaemia, KA = Kala-azar, MM = Multiple myeloma, Lyp.= Lymphoma, MC = Metstatic carcinoma, MF = Myelofibrosis, RM = Reactive marrow, UD = Undiagnosed.

Histomorphological patterns in trephine biopsy of bone marrow of various haematological and non-haematological disorders:

Acute myeloid leukemia: Sections of all of the AML cases (eight patients) revealed hypercellular marrow with increased M:E ratio.The marrow shows predominantly myeloblasts. Erythropoiesis was depressed in seven cases and normal in one. Granulopiesis was depressed in three cases, active in three and hyperactive in two cases and all revealed shift to the left. Megakaryocytes were absent in four cases, scanty in two and normal in two cases.

Acute lymphoblastic leukemia: Sections of two cases were cellular but others were hypercellular. Majority of the cells were monomorphic consistent with lymphoblasts. All showed increased M: E ratio. Erythropoies is depressed in five cases but active in one case. Five showed depressed granulopoiesis but one was active. Five showed depressed granulopoiesis but one was hyperactive. Megakaryocytes were normal in one, scanty in two and nil in three cases.

Myelofibrosis : Sections show hypocellular marrow in six cases, hypercellular in one case but increased fibrosis in all cases. The fibrosis was mostly moderate and diffuse in all the cases. There was depressed haemopoiesis in hypocellular marrow but active haemopoiesis in hypercellular marrow. None of the case revealed any leukemic cell.

Chronic myeloid leukemia: Sections were hypercellular with increased M: E ratio. This cellularity is due to increase in granulocytes and it's precursors and megakaryocytes. Erythropoiesis was depressed in all. Fibrosis was normal in all cases except one where there was moderately increased reticulin fibrosis confirmed by Gomori's silver impregnation (reticulin stain) of the sections.

Hypoplastic anaemia: Sections of all the cases showed hypocellular marrow. The marrow spaces were occupied predominantly by adipose tissue with scattered lymphocytes and plasma cells. In one case, a few spaces contained dense collections of lymphocytes and plasma cells. Haemopoiesis of all three lineages were depressed.

Non-Hodgkins lymphoma: Sections show hypercellular marrow with increased M:E ratio in both the cases. In one case, haemopoiesis was depressed but in another, it was active. There was markedly increase number of mature lymphocytes with diffuse and focal distribution.

Reactive marrow: Sections showed normocellular marrow with normal and active haemopoiesis. Increased number of plasma cells, lymphocytes and histiocytes were seen.

Multiple myeloma : The sections show moderate cellular marrow. Marrow spaces contained increased number of plasma cells, some of which appeared immature. These cells were diffusely distributed. In this case, erythropoiesis was depressed but granulopoiesis was active and megakaryocytes were present.

Metastatic carcinoma: Sections revealed, in the marrow spaces, large atypical cells with hyperchromatic nuclei and scanty cytoplasm suggestive of a poorly differentiated metastatic carcinoma.

Discussion :

The purpose of this study was to see the histomorphological patterns of trephine biopsy of bone marrow in aspiration failure cases. The present study was carried out in the department of Pathology, Bangabandhu Sheik Mujib Medical University (BSMMU), Dhaka. The patients were selected from departments of haematology and medicine of the same institution. In this study, 50 cases of clinically diagnosed haematological and non-haematological diseases were included, where aspiration failure occurred. In four cases, trephine biopsy failure occurred. In the rest 46 cases, adequate material was obtained and their morphological features were studied. Laboratory investigations were also considered in this study.

Out of 46 cases, 19 cases were diagnosed histologically as acute leukemia. This comprised 41.30% of the total. Navone and Colombanol 6 reported 16% (35 out of 218) acute leukemia in aspiration failure cases. The discordance between two studies may be due to larger sample size of the later.

Out of 19 cases of histologically diagnosed acute leukemia, eight (43.10%) were acute myeloid leukemia, six (31.58%) were acute lymphoblastic leukemia and five cases (26.32%) were acute leukemia (undifferentiated). Categorizing these cases of Al (undifferentiated) into AML or ALL could not be done in our laboratory from the sections of trephine biopsy alone. For this purpose, immunohistochemistry and other tests were not available here. Burkhardt et al 7 reported 116 cases (88.55%) of acute myeloid leukemia and 15 cases (11.45%) of acute lymphoblastic leukemia out of 131 cases of acute leukemia. To be noted that Burkhardt et al 7 studied acute leukemia cases in combined bone marrow aspiration and trephine biopsy samples.

Out of 46 cases, 13 cases (28.26%) were of chronic myeloproliferative disorders. Navone et al 6 reported 9.8% cases (44 out of 445) of chronic myeloproliferative disorders in aspiration failure cases. This discordance may be due to its larger sample size. In a study of 850 cases, Burkhardt et al 9 found 186 cases (21.88%) of chronic myeloproliferative disorders among which CML was in 108 (58.06%) cases and myelofibrosis in 78 (41.94%) cases. In the present study, among 13 cases of myeloproliferative disorders in aspiration failure cases, 6 cases (46.15%) were diagnosed as chronic myeloid leukemia and 7 cases (53.85%) were diagnose as myelofibrosis.

In the present study, seven patients out of 46 were histopathologically diagnosed as hypoplastic anaemia. This comprised 15.22% of the total. Burkhardt et al 7reported 60 patients of aplastic anemia out of 441 patients of different diseases. This showed 13.60% of the total.

Two cases (4.34%) were diagnosed histopathologically as non-Hodgkin's lymphoma (NHL). Brunning et al 9 studied 343 trephine biopsies of lymphoma and other neoplastic diseases and found 50 cases (14.57%) of non-Hodgkin's lymphoma in bone marrow.

Out of 46 cases in this study, histologically, one case (2.17%)was diagnosed as multiple myeloma, one case (2.17%) reactive marrow and one case (2.17%) as metastatic carcinoma (poorly differentiated). Burkhardt et al (1982) reported 10 patients of multiple myeloma out of 8216 patients of diffrenet diseases. This showed 0.12% of the total. Navone et al (1984) reported 4.8% multiple myeloma in their study which was close to the present study. They showed 8.8% non-Hodgkin's and Hodgkin's lymphomas and 13.5% metastatic carcinomas. But Brunning et al9 reported out of 343 cases of lymphoma and other neoplastic diseases, 10 cases of nonhaematologic malignancy metastatic to bone marrow which comprised 2.91% of the total which showed concordance with present study.

Out of 46 cases in the present study, two cases with adequate material could not be diagnosed due to poor preparation of the biopsy material.

Summary and conclusion

The present study was carried out in the Department of Pathology, Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, to see the histmorphological patterns of trephine biopsy in bone marrow aspiration failure cases.

A total of 50 cases of aspiration failure cases were

trephined to obtain bone marrow from posterior iliac crest during the period of 24 months from April, 2000 to March, 2002, attending the departments of haematology and medicine, BSMMU. In four cases, trephine biopsy of bone marrow failure occurred in which no marrow element were found. The 46 cases with adequate biopsy material revealed histologically 41.30% acute leukemia, 28.26% chronic myeloproliferative disorders, 15.22% hypoplastic marrow, 4.34% non-Hodgkin's lymphoma and 2.17% each of multiple myeloma, reactive marrow and metastatic carcinoma. Out of 46 cases, diagnosis could not be done in two cases (4.34%) due to poor preparation of biopsy material. In a similar study, Navone et al (1984) reported 16% acute leukemia, 9.8% chronic myeloprliferatve disorders, 8.8% malignant lymphoma and hogkin's diseases, 4.8 % myelomas and 13.5% metastatic carcinomas in trephine biopsy of bone marrow aspiration failure cases. The discordance between these two studies may be due to difference in their sample size.

In the present study, two cases remained undiagnosed and five cases of acute leukemia could not be subcategorized into AML or ALL. It appears that as only H&E and reticulin stains were used in this study, those cases could not be diagnosed or subcategorized due to lack of other facilities. So it is recommended that facilities for plastic embedding, immunocytochemistry and use of enzyme and immunophenotyping should be developed in the department and used whenever necessary and also study of larger sample size is required for better evaluation.

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