Significance of Bone Marrow Histology in the Diagnosis of Acute Myeloid Leukemia

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Abstract

Background: Acute Myeloid Leukemia (AML) is a heterogeneous disease. The precise diagnosis requires a careful morphological examination of a well prepared bone marrow aspirate along with flow cytometry and genetic analysis wherever required. Traditionally, bone marrow biopsy has not been considered an essential diagnostic modality for AML. The aim of this study was to assess the diagnostic as well as prognostic significance of bone marrow histology in patient with acute myeloid leukemia.

Materials and Methods: Forty (40) patients of AML underwent a bone marrow examination including an aspirate and a trephine biopsy. Air dried films of peripheral blood and aspirates were fixed in methanol and stained with Giemsa. The following cytochemical stains were also applied: PAS, Myeloperoxidase, Non specific esterase, Chloracetate Esterase and Acid Phosphatase, and SBB. Bone marrow biopsy specimens were obtained from post superior iliac crest with a manual trephine and were processed in plastic after decalcification.

Results: In all the cases there were better diagnostic clues through histological examination of bone marrow particularly in assessing the cellularity, degree of fibrosis, extent of blast infiltration, percentage of inflammatory cells, dysplastic changes and residual haematopoiesis. All these features were better noted in histological examination of core biopsy.

Conclusion: The histological examination provided information additional to that provided by aspirate smears about the bone marrow changes in AML and suggested that some of the features may also have prognostic significance in addition to diagnostic importance.

Key Words: Acute myeloid leukemia, Bone marrow biopsy, bone marrow histology.

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Introduction

Despite the recent advances in field of molecular haematology and flow cytometry, bone marrow histology remains the cornerstone in the diagnosis of acute myeloid leukemia.[1] The histological studies not only give a better idea about the bone marrow cellularity but also carries significant information like percentage of inflammatory cells, presence of residual haematopoietic cells, dysplastic changes, extent of blast infiltration, and degree of fibrosis, which can predict the clinical outcome and the severity of symptoms in these leukemic patients.[2,3]

The standard approach to the diagnosis of acute leukemia has been based on the morphology and percentage of malignant haematopoietic cells in the peripheral blood and in an aspirated sample of bone marrow.[4] Aspirated bone marrow only provides a small volume sample which is diluted with sinusoidal blood and provides no information on the architectural changes occurring within the marrow cavity as a result of the leukemic process; addition to that, cells anchored firmly within the marrow or located focally may not be withdrawn on aspiration and thus can be excluded from examination. An adequate core biopsy sample permits a more accurate analysis of the degree of involvement of the marrow by the leukemic process and may provide additional information on the response of normal marrow elements to the malignant infiltrate. The study will assess the value of marrow core biopsy in complementing the diagnosis of acute myeloid leukemias on aspiration.[5]

Materials and Methods

Forty patients both male and female were included in the study. A thorough and methodical clinical history was taken. After informed consent was obtained, a marrow biopsy, an aspirate and a sample of peripheral blood were obtained from each patient. AML was diagnosed with clinical, morphological and cytochemical criteria according to FAB classification.

Air dried films of peripheral blood and aspirates were fixed in methanol and stained with Giemsa. The following cytochemical stains were also applied: PAS, Myeloperoxidase, Non specific esterase, chloracetate esterase and, and SBB. Bone marrow biopsy specimens were obtained from post superior iliac crest with a manual trephine and were processed in paraffin wax after decalcification. All the procedures of staining and processing of specimens were in accordance with the manual of practical hematology, Dacie and Lewis.[6]

Bone marrow cellularity was assessed by examining several individual marrow fragments in each case to establish the relative proportion of fat and marrow cells and the overall marrow cellularity was then expressed as an approximate percentage. Bone marrow cellularity in the histological sections was assessed in low power and the overall marrow cellularity was expressed as approximate percentage.

Results

The largest number of patients were in the M_2 and M_4 categories. When the cytomorphological details were compared, differences in marrow morphology were observed between bone marrow aspirate and bone marrow biopsy specimen. 4 of the 16 cases classified as FAB M_2 and 2 of the 4 cases classified as FAB M_5 showed some cells with morphological features of monoblasts and myeloblasts respectively in the sections (Table 1).

In most cases bone marrow cellularity in the sections was higher than that estimated in the aspirate smears. In 9 cases aspirate cellularity was less than 50%, while in the sections it was over 50% in 8 cases and over 95% in 4 of these 8 cases (Table 2).

A considerable difference in the extent of blast infiltration was also observed between aspirate smears and the biopsy sections (Table 3). In high proportion the extent of blast infiltration was much more in biopsy sections than in the aspirate smears.

The distribution pattern of megakaryocytes was affected and they were either widely scattered or loca-

Table 1: Cytomorphological classification based on aspirate and core biopsy specimens.

	M_1	M_2	M_3	M_4	M_5	M_6	Total (bone marrow aspirate)
M_1	1	1					2
M_2		12		4			16
M_3			2				2
M_4				14			14
M_5				2	2		4
M_6						2	2
Total (bone marrow biopsy)	1	13	2	20	2	2	40

Note: The numbers in the bold represent cases where there was concordance between bone marrow aspirate and biopsy specimen results.

Table 2: Comparison of bone marrow cellularity based on bone marrow aspirate and bone marrow biopsy specimen.

	10 < 25%	25 < 50%	50 < 75%	75 < 95%	95.100%	Total (bone marrow aspirate)
10 < 25%	0					
25 < 50%		1	3	1	4	9
50 < 75%			7	1	9	17
75 < 95%				4	10	14
95.100%				0	0	0
Total (bone marrow biosy)	0	1	10	6	23	40

Note: The numbers in the bold represent cases where there was concordance between bone marrow aspirate and biopsy specimen results.

Table 3: Comparison of extent of blast infiltration between bone marrow aspirate and bone marrow biopsy specimen.

	< 20%	20 < 40%	40 < 60%	60 < 80%	> 80%	Total (bone marrow aspirate)
< 20%	5	1	2	1	1	10
20 < 40%	1	1		1	2	5
40 < 60%	1	1	5	5		12
60 < 80%				1	8	9
> 80%					4	4
Total (bone marrow biopsy	7	3	7	8	15	40

Note: The numbers in the bold represent cases where there was concordance between bone marrow aspirate and biopsy specimen results.

lized in small isolated clusters, while they were often not found on the aspirate smears. Residual erythropoiesis, when present, was seen in small islands but was noticeably absent in the smears.

In 32 cases the marrow was infiltrated either alone or in combination with a variable number of inflammatory cells (lymphocytes, plasma cells, tissue mast cells, eosinophilic granuloscytes and macrophages). The presence and the number of such inflammatory cells could not be accurately assessed in the smears because of their patchy, compartmentalized, and non uniform distribution pattern.

Discussion

The results reported here clearly indicated that considerable additional and valuable information can be obtained in AML by examining sections of bone marrow biopsy specimens.

In general aspirate did not reflect the marrow cellularity accurately and in most cases it was considerably lower than that observed in the sections. In 9 cases (> 22%) it was less than 50%. Some of these cases could have been diagnosed as hypoplastic AML, if bone marrow biopsy had not been performed concurrently. This is important because intensive antileukemic therapy should be withheld for this group or that these patients can benefit from low dose cytosine arabinoside.

In most cases extent of blast infiltration was higher in sections than in aspirates. An accurate assessment of this is important because it provides a rough estimate of leukemic mass which in turn has some bearing on patient response to treatment, outcome and prognosis.

Moreover other important features that might affect the prognosis of the patient like the presence / absence of inflammatory cells (lymphocytes, plasma cells, tissue mast cells, eosinophilic granulocytes and macrophages) were better depicted on core biopsy specimens. Winfield D A and Polacarz SV in their article on the value of bone marrow histology in acute leukaemia, myelodysplastic syndromes and chronic myeloid leukaemia described similar advantages of obtaining an adequate core biopsy sample in addition to an aspirate sample.[7] Islam A, Frish B and Henderson ES also reported similar findings in their study on the role of bone marrow biopsy as a complementary approach to the diagnosis of AML.[8]

In general bone marrow aspirate samples are of insufficient quantity and hence not likely to be true representatives of the marrow. In addition, sampling errors inherent in the bone marrow aspirate technique remain a major problem. On the other hand, a large core biopsy overcomes these problems, and provides a more representative picture of the marrow. This technique has traditionally not been used in the AML diagnosis and classification. However with newer, improved methods of processing plastic embedded sections, excellent morphological details can be obtained.[9]

In conclusion, we strongly emphasize the need to obtain an adequate sample of bone marrow biopsy along with a bone marrow aspirate whenever the diagnosis of AML is suspected as the two approaches are complementary.

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