Original Article

Diagnostic importance of bone marrow examination in non-hematological disorders

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Abstract

Objective: To evaluate the frequency of involvement of bone marrow with non-haematologic disorders and to observe the significance of bone marrow examination in establishing primary diagnosis of the same.

Methods: It was a descriptive study that extended from January 2003 to September 2005. A total of 4569 bone marrow aspirate and trephines were reported during this period. Only the non-haematological disorders were analyzed for their clinical and laboratory parameter.

Results: During the study period, 63 patients (1.4%) were diagnosed to have non-haematological diseases detected primarily through bone marrow examination. The mean age of patients at time of procedure was 33 years (range 6 months to 89 years), with male to female ratio of 3.2:1. Anaemia was the most frequent clinical finding followed by splenomegaly and weight loss. In adults metastatic tumors were the commonest disorder, followed by chronic granulomatous disease/reaction. However in children, storage disorders were more prevalent followed by haemophagocytosis as the second commonest non-haaematological disease.

Conclusion: Metastatic solid tumors were the frequent non-hematologic disorder involving bone marrow in adult patients while storage diseases were most common among children. Hence, bone marrow examination is a useful laboratory tool in asserting the diagnosis of various non-haematological malignancies and other miscellaneous disorders (JPMA 57:123;2007).

Introduction

Although bone marrow biopsy is an uncomfortable procedure for the patient and should be performed only when there is a clear clinical indication[1] yet it is a useful technique not only in the diagnosis of different blood disorders but also for various systemic illnesses including pyrexia of unknown origin. Metastatic involvement with tumors[2], granulomatous diseases[3], storage disorder[4], haemophagocytic syndrome[5,6], histiocytoses[7] and Leishmaniasis[8,9] can be diagnosed through bone marrow examination. There have been documented reports on bone marrow involvement with rare metastatic tumours like glioblastoma[10], angiosarcoma[11], oligodendroglioma[12], Ewing's sarcoma[13], astrocytic glioma[14], malignant melanoma[15], osteosarcoma[16] and carcinoid tumor.[17] The clinical features of these may mimic some of the haematologic disorders[18], as the patients can present with cytopenias, lymphadenopathy and hepatosplenomegaly.

The present study was conducted to explore the role of this invasive technique in ascertaining the diagnosis of non-haematological disorders like metastatic tumours and granulomatous diseases as well as others. The result will also help a clinician in selecting cases for bone marrow biopsy for proper evaluation of their patients.

Material and Methods

We analyzed our bone marrow results over a period of 2.9 years from January 2003 to September 2005. A total of 4,569 bone marrow aspirate and trephines were performed during this period according to the techniques cited elsewhere.[1] The patients included those admitted in The Aga Khan University Hospital as well as outside referrals. The specimens were obtained through posterior iliac crest in all the patients. The smears prepared from concentrated marrow cells were routinely stained with Leishmann stain while biopsy specimens were decalcified and paraffin embedded blocks were stained with the usual haematoxylin and eosin (H&E) stain. Reticulin, Ziehl-Neelsen and appropriate marrow histochemical stains were used where considered necessary.

Of 4,569 bone marrow results that were reported during the study period, 1,843 (40.3%) were found to have haematologic disease which were excluded. Involvement of bone marrow with non-haematological disorders was reported in 79 (1.7%) cases of which 63 cases were considered for our study. Cases in which diagnosis was already known (13 cases) or where bone marrow biopsy material was not available for complete diagnosis (3 cases) were excluded. These sixty three cases were analyzed for their clinical manifestations and haemograms.

Results

During the study period, evaluation of bone marrow results and the medical records of those patients that revealed non-hematological disorders, we found involvement of bone marrow with non-hematological disorders in previously undiagnosed 63 patients. Patients ranged in age from 0.6 to 89, with the mean age of 33 years. There were 48 males and 15 females giving male to female ratio of 3.2:1. Anemia was found as single most common manifestation in these patients followed by enlargement of spleen, and history of weight loss. The white blood cells and platelet count showed a wide variation extending from sub-normal to above normal values (Table 1).

Metastatic tumors outnumbered any other systemic disorder (26 cases) in adults, followed by granulomatous disease (12 cases). The storage disorders were commonest non-haematological disorders in children (7 cases) while haemophagocytic syndrome was the second common disorder in the list (Table 2).

Leishmanniasis, and other miscellaneous disorders were found to have variable frequency (Table 2).

Table 1. Clinical and laboratory features in patients with bone marrow involvement (n=63).

Mean age at time of procedure	33 years (6 months -89 years)
Gender	48 Male and 15 Females
Clinical features	
Fever	10 (12.6%)
Weight loss	17 (27%)
Anaemia	45(71.4%)
Jaundice	1 (1.6%)
Lymphadenopathy	7 (11.1%)
Hepatomegaly	14 (22.2%)
Splenomegaly	17 (27%)
Haemogram	
Haemoglobin gm/dl	9.2 (2.4-14.5)
White cell count X109/L	8.2 (1.4-40)
Platelet count X109/L	145 (4-652)

Table 2. Frequency of bone marrow involvement in non-haematologic diseases and their relation to various age groups.

Disease	Number of cases n=63	Age <15 years n= 20	Age >15 years n= 43
Metastatic	26 (41.3%)	02	24
Chronic granulomatous disease.	18 (28.5%)	01	17
Storage disease	7 (11.1%)	07	0
Leishmaniasis	4 (6.3%)	03	01
Haemophagocytosis	4 (6.3%)	04	0
Histiocytosis	2 (3.2%)	02	0
Chronic non-granulomatous disease	2 (3.2%)	01	01

Table 3. Frequencies of various solid tumors in bone marrow with relative diagnostic value of aspirate and trephine specimens.

Tumour	Number of cases n=26	Gender		Positive bone marrow aspirate	Positive bone marrow trephines
		Male	Female		
Lung carcinoma	07 (26.9%)	7	0	05	07
Metastatic Adenocarcinoma	06 (23.1%)	4	2	01	06
Prostate	05 (19.2%)	05	0	01	05
Breast carcinoma	03 (11.5%)	0	03	0	03
Ewing's sarcoma	02 (7.7%)	1	1	01	02
Undifferentiated	03(11.5%)	2	1	01	03

The frequency of various solid tumors diagnosed through bone marrow examination as the primary modality with relative diagnostic value of aspirate and trephine in different non-haematological malignancies is shown in (Table 3).

On the basis of morphological features of bone trephine and immuno-histochemical stains, we found lung carcinoma as the commonest tumour in males while breast carcinoma was predominant in females. Among all neoplasms, lung carcinoma was detected equally well in both aspirate and trephine unlike other tumours where biopsy yielded superior results.

Discussion

Although bone marrow examination is a common procedure in the evaluation of patients with cancer and other non-haematologic disorders, its role and contribution have been questioned in recent years.[19]

This analysis was conducted in order to evaluate the frequency of involvement of bone marrow with non-haematologic disorders and to determine the value of bone marrow biopsy in establishing the diagnosis in previously undiagnosed patients.

No comparable data is available in this regard on regional basis. However, international statistics do support the role of bone marrow aspirate and biopsy in the diagnosis of different non-haematological diseases.[18,20,21]

In this study, anaemia was the most frequent finding. Various studies reveal an incidence of anaemia in neoplastic diseases from 55-90% of cases[18,19,22] but the same can not be compared for other diseases because of the non availability of equivalent data. The other clinical findings in order of frequency were splenomegaly and weight loss.

The patients who presented with cytopenias and hepatosplenomegaly were diagnosed to have either malignancy, storage disease or chronic granulomatous disease.

The common disorder in our study was metastatic tumours, followed by chronic granulomatous diseases in adults. However in paediatric group storage disorders and primary or secondary haemophagocytic syndrome were the commonest.

We found bone marrow aspirate to detect only 35% of all the tumours that were diagnosed on bone marrow biopsy. Thus, the demonstration of tumour metastases by bone marrow biopsy was far superior to the bone marrow aspirate in our study. Similar observations were made by others as well.[18,20] Nevertheless, trephine biopsy and bone marrow aspirate should be regarded as complementary investigation because either might show tumour cells when other procedure had failed to do so.[21]

The incidence of metastatic disease to bone marrow varies among different authors. Compared to study of Contreras et al[18], we encountered secondaries from lung cancer as the most frequent tumor diagnosed on bone marrow examination with metastatic adenocarcinoma as the close second. Our results showed Ewing sarcoma to be a rarity which is in sharp contrast to the work reported by Anner et al.[21] In very few cases (3%) the primary site remained undetermined despite appropriate immuno-histochemical stains.

Chronic granulomatous disease is the second common group in our adult patients. Granulomatous reactions can be seen in tuberculosis, sarcoidosis, fungal infection and Hodgkin's lymphoma. In our part of world as systemic tuberculosis is more prevalent, Ziehl-Neelsen staining was done in all cases to exclude tuberculosis. However, we found only 2 out of 18 such cases to be positive (11%) for acid fast bacilli. The correct evaluation of the patients that were diagnosed to have granulomas would require clinical correlation and further laboratory work up.

Lysosomal storage disorders and haemophagocytic syndromes had been reported to be often diagnosed mainly by bone marrow examination.[4] We diagnosed Gaucher's disease in six cases and one case of Niemann pick disease. We found that bone marrow examination is helpful in making primary diagnosis of storage diseases and haemophagocytic syndrome either primary or secondary; in majority of paediatric cases.

Conclusion

We conclude that bone marrow examination is a useful tool in diagnosing metastatic tumors, granulomatous diseases, storage disorders and many other non haematological diseases. It may provide an insight in to the diagnosis of a previously undiagnosed patient.

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