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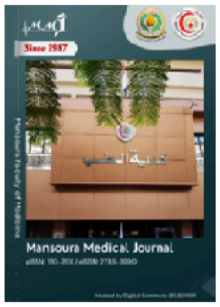

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BONE MARROW PATHOLOGY : EXPERIENCE OF KING ABDULAZIZ UNIVERSITY HOSPITAL IN THE WESTERN REGION OF SAUDI ARABIA

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BONE MARROW PATHOLOGY : EXPERIENCE OF KING ABDULAZIZ UNIVERSITY HOSPITAL IN THE WESTERN REGION OF SAUDI ARABIA

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ABSTRACT

Objectives :

To determine the indications and diagnosis encountered in bone marrow examination from 1998-2004 in a university set-up and referral hospital in Jeddah, Saudi Arabia and to compare our results to those reported in the local literatures.

Methods :

The bone marrow records from the hematology-pathology section of King Abdulaziz University Hospital were reviewed. The data collected include age, sex, main indication for performing bone marrow examination and primary bone marrow diagnosis.

Results :

There were a total of 1023 bone marrow specimens, 645 (63%) were from adults and 378 (37%) were from children. The M:F ratio was 1.7:1. The three most common indications were suspected leukemia and post-chemotherapy evaluation of bone marrow 20.9%, suspected myeloproliferative disorders 14.2% and pancytopenia 14%. The three most common specific diagnoses were acute leukemia 16.5%, aplastic anemia which includes aplasia secondary to chemotherapy for leukemia and lymphoma 14.3%, and chronic myeloid leukemia 8%.

Conclusion :

This study confirms that bone marrow examination is a very important investigation for establishing the diagnosis in haematological diseases, especially hematological neoplasms. The most common indication for this procedure in our hospital was to confirm and manage acute leukemia followed by myeloproliferative disorders. The most specific diagnosis made is acute leukemia.

Keywords : Bone marrow, Indications, Diagnosis.

INTRODUCTION

Bone marrow is one of the body's largest organs, representing 3.5 to 4.5% of the total body weight and averaging about 1500 grams in adults. The hematopoietic bone marrow is organized around the vasculature of the bone cavity. The optimal bone marrow examination requires both aspirate (BMA) and bone marrow trephine biopsy (BMB). BMA allows refined cytological examination (such as dysplastic changes, Auer rods, ring sideroblasts) as well as cytochemistry, flowcytometry, cytogenetic analysis and bone marrow cultures[1].

In the last 40 years, bone marrow trephine biopsy has become popular due to the availability of relatively simple biopsy needle [Jamshidi needle] [2].

BMB is an important procedure in the diagnosis and management of patients with acute leukemias, lymphoproliferative, myeloproliferative disorders, metastases, myelodysplasia and reactive disorders[3,4]. It is also useful in the diagnostic workup of fever of unknown origin (FUO). Revealing infections such as tuberculosis, Mycobacterium avium-intracellular (MAI), histoplasmosis, leishmaniasis and other disseminated fungal infections. Finally, it may be useful in establishing the diagnosis of storage disease [5].

AIM :

This study was carried out to identify the most frequent indications and pathological diagnosis encountered in bone marrow examination from 1998-2004 in a teaching and referral hospital in Jeddah, Saudi Arabia. Our results will be compared to those reported in the local literature.

MATERIALS AND METHODS

The bone marrow records from the hematology/pathology sections of King Abdulaziz University Hospital,

Jeddah (KAUH) during the period from 1998-2004 were reviewed. The following data were collected, age, sex, clinical indications, pathological diagnosis and the adequacy of the bone marrow samples for diagnosis. All data were recorded in a structured form. The adult's age was considered above 14 years. Bone marrow smears are stained with Hematoxylin and Eosin (H&E), Perl's (iron) and reticulin. For certain indications in order to confirm the diagnosis, special stain and immunohistochemistry were applied.

STATISTICAL ANALYSIS

All results were fed to SPSS version 10.

RESULTS

A total of 1203 bone marrow examinations were carried out during the study period. Six hundred forty five (63%) samples were obtained from adults while 378 (37%) were from children. Males represented 635 (62%) while 388 (38%) were from females. The mean age for adults was 44.3, age range (15-100) and for children 4.9 years, age range (4 days - 14).

We found that the main indications for bone marrow examination were in descending orders of frequency: diagnosis and management of acute leukemia 326 (31.9%), suspected myeloproliferative disorders 145 (14.2%), pancytopenia 144 (14%), staging for lymphoma 138 (13.5%), excluding malignant metastases 65 (6.4%), isolated thrombocytopenia 62 (6.8%), anemia 60 (6.9%) and other miscellaneous indications like fever of unknown origin, suspected multiple myeloma, histocytosis and glycogen storage disease. As shown in table 1. Out of the 1023 bone marrow samples 112 (10.9%) were inadequate for evaluation while nine hundred eleven bone marrow specimens were subjected for diagnostic evaluation, 326 (35.8%) of the marrows had no pathology.

The most common diagnoses encountered are summarized in Table 2.

Acute leukemia was the commonest 150 (16.5%). Acute lymphoblastic leukemia (ALL) accounted for 100 (11%) bone marrow specimens and 50 (5.5%) were acute myeloid leukemia (AML). Sixty seven were adults (38 ALL, 29 AML) while 83 cases were children (62 ALL, 21 AML).

Table 1. Distribution of bone marrow indications

Indications	No. of specimens	Percent (%)
Suspected acute leukemia and post-chemotherapy evaluation	214	20.9
Suspected myeloproliferative disorder	145	14.2
Pancytopenia	144	14
Staging for lymphoma	138	13.5
Suspected malignant infiltration	65	6.4
Isolated thrombocytopenia	62	6.8
Anemia	60	6
Fever of unknown origin	52	5
Suspected multiple myeloma	24	2.3
Histocytosis	5	0.5
Glycogen storage disease	2	0.2

Table 2. Distribution of specific diseases diagnosed on bone marrow examination

Diseases	Number of specimens	%
Acute leukemia	150	16.5
Aplastic anemia	131	14.3
Chronic myeloid leukemia	73	8
Malignant lymphoma	53	5.8
Primary myelofibrosis	35	3.8
Myelodysplastic syndrome	20	2.2
Megaloblastic anemia	20	2.2
Anemia of chronic disease	20	2.2
Multiple myeloma	15	1.6
Metastatic nonhematopoietic malignancy	14	1.5
Essential thrombocythemia	11	1.2
Polycythemia rubra vera	10	1.1
Iron deficiency anemia	10	1.1
Granulomas	9	1
Leishmaniasis	6	0.7
Histocytosis	4	0.4
Storage disease	4	0.4

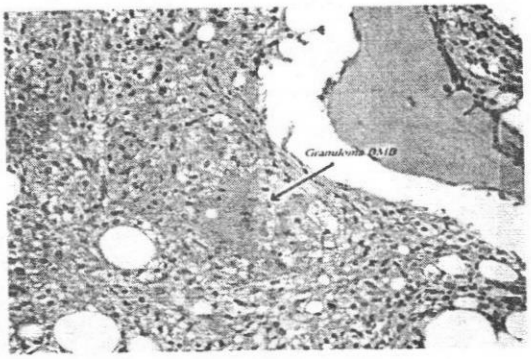

Figure 1 : Bone marrow biopsy of a patient with granuloma.

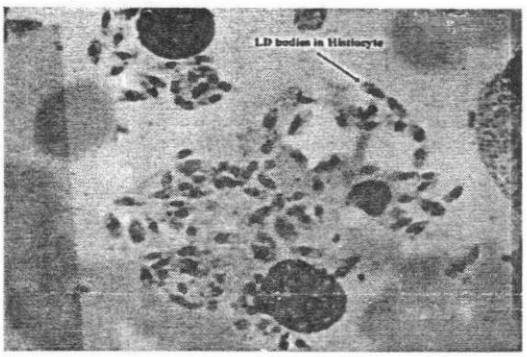

Figure 2 : Bone marrow aspiration of a patient with Leishmaniasis.

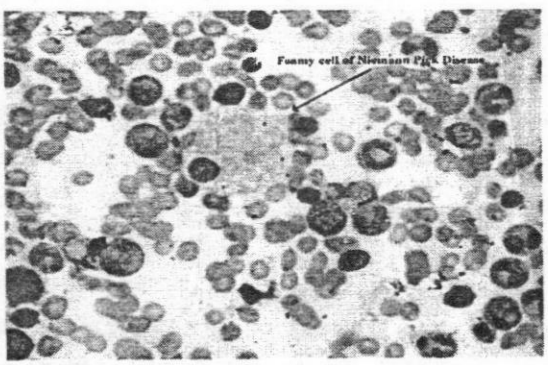

Figure 3 : Bone marrow aspiration of a patient with foamy cell.

DISCUSSION

Bone marrow examination is an established procedure in the evaluation of many malignant and benign diseases. It may also be necessary and important in establishing the final diagnosis. The indications for bone marrow examination are variable and are usually based on the clinical picture and/or laboratory abnormalities diagnosed by blood count or peripheral blood smear- or both[1].

In this study, the most common indication for bone marrow examination was the diagnosis and post-chemotherapy evaluation of acute leukemia, on the other hand the most common encountered diagnosis was acute leukemia (16.5%), a common malignancy in both children and adults in the Kingdom of Saudi Arabia (KSA)[6,7]. Aplastic anemia was the 2nd most common disease diagnosed in 131 (14.3%). The causes of which were so diverse, especially post-chemotherapy induced hypocellularity, seen in cases of leukemia and lymphoma. De novo marrow aplastic anemia is generally a rare disease, therefore it was less commonly seen in 26 (2.9%) of bone marrow specimens. Out of 145 specimens referred for suspected chronic myeloproliferative disorders 129 (14.1%), showed features consistent with myeloproliferative disorders (35 primary myelofibrosis, 11 essential thrombocythemia, 10 polycythemia rubra vera and 73 chronic myeloid leukemia). This indicates that other parameters were probably evaluated before bone marrow examination was performed.[8]

The percentage of indication for bone marrow examination in myeloproliferative disorder in this study is much higher than the two studies from KSA which were 9.4% and 1% respectively.[8,9] The cause for this difference is probably the special interest of the hematologist in our hospital to this group of disorders. Pancytopenia without qualitative abnormality, was important indication for bone marrow assessment (14%), the causes of which include bone marrow aplasia, acute leukemia, myelofibrosis, megaloblastic anemia, non-hematopoietic malignancy and more than half of those patients had, in addition, a clinical picture suggestive of hypersplenism which was supported

by bone marrow findings. [10]

The role of bone marrow examination in lymphoma can be reviewed as follows, staging of an already identified tumor, evaluation of residual hemopoiesis, patient follow-up and detection of residual disease after treatment. [11,12] Bone marrow involvement by lymphoma cells denote stage VI disease. In this study, another common indication for bone marrow examination was staging for lymphoma (13.5%) which is another common malignancy in the KSA.[7] Fifty three (5.8%) cases were positive for bone marrow infiltration by lymphoma, only 4 of them were Hodgkin's lymphoma. Factors that contribute to the frequency of bone marrow involvement in malignant lymphoma, are the sample size and whether the biopsy is unilateral or bilateral.[13,14]

Many lymphomas infiltrate the bone marrow in focal pattern of distribution, and the lesion may be missed if the volume of biopsy is inadequate. It is known that performing bilateral iliac crest marrow biopsies increases the yield of marrow involvement.[15] In our study cases for evaluation of lymphoma had unilateral biopsies with rare exceptions having bilateral biopsy.

Solid tumors arising elsewhere in the body, such as carcinoma or sarcoma may metastasize to the bone marrow. Patients having any of these solid tumors may undergo bone marrow studies when the initial diagnosis is established for evaluation of the degree of tumor spread and/or clinical staging of the patient's disease.[16] In this study another encountered indication for bone marrow examination was to exclude malignancy 65 (6.4%), only 14 (1.5%) of these were positive.

Bone marrow evaluation for cases of anemia is not a frontline investigation. They can be diagnosed usually by examination of the peripheral blood in conjunction with the clinical finding and other laboratory studies. In this study anemia was the indication in 6%. It showed various causes, the most common one's were megaloblastic anaemia and anemia of chronic disorder. Isolated thrombocytopenia was also a common indication for bone marrow examination ac-

counted for 6.8%. This is in contrast with two studies from KSA in which isolated thrombocytopenia was the 2nd most common indication (9.9-11%).[8,9] This difference probably because in our institution not all cases of idiopathic thrombocytopenic purpura (ITP), are subjected to bone marrow examination. It is limited to those patients with atypical features of ITP both clinically and hematologically or those patients going to be treated with corticosteroid.[17,18] Fever of unknown origin was an indication in 52 cases (5%). Granulomatous inflammation (figure 1) was found in 9 specimens (1%) and 6 specimens (0.7%) were positive for Leishmaniasis[5] (figure 2). In 2.3% of the bone marrow specimens, the indication was suspected multiple myeloma, positive samples accounted for 1.6%. This finding is similar to another study from the KSA[8] where multiple myeloma was diagnosed in 1.8% of the cases. Other miscellaneous diagnosis of bone marrow examination include Langerhan cell Histocytosis and glycogen storage disease (figure 3).

In 10.9% of the bone marrow specimens, the samples were inadequate. The inadequacy was either in the form of a diluted bone marrow aspiration, or a crushed, cortical or inadequate size of the biopsy samples. The reason behind this high failure rates was mostly due to lack of experience of the physician as well as the trainees performing the procedure in our teaching hospital despite supervision while performing the procedure. In the study by Al-Gwaiz from KSA, out of 3494 bone marrow samples, 160 (4.5%)[8] were inadequate for evaluation, which is much less compared to our result. However, in another study from King Fahd Hospital of the University of Al-Khobar (KFHU), they reported 9.7% failure rate.[9], which is close to our results. The indications for bone marrow examination in this study were almost similar to another study from the KSA[9] were the most frequent indications for this procedure were evaluation of bone marrow in acute leukemia (32.9%). The second most common indication in our study was myeloproliferative disorders, but in the other study it was for suspected lymphoma (15.2%). The frequencies of acute leukemia, malignant lymphoma and chronic myeloid leukemia,

were relatively similar in both studies being a common diagnoses.

CONCLUSION

Bone marrow assessment is a very important tool in diagnosis and management of hematological disorders. Evaluation of bone marrows for suspected leukemia and post-chemotherapy effects followed by myeloproliferative disorders appears to be the most common indications in this study. The most specific diagnosis made is acute leukemia.

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