

Comparative Evaluation between Bone Marrow Aspirate and Biopsy Morphologic Findings, Experience At King Hussein Medical Center

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ABSTRACT

Objective: To assess the matching between bone marrow aspirate and bone marrow biopsy findings done simultaneously in patients with clinical indications of bone marrow examination, to stand on the diagnostic efficacy of each in various bone marrow diseases.

Methods: This study was conducted at King Hussein Medical Center, Haematology and Oncology Department in collaboration with Hematopathology Division of the Laboratory Department. The Pathology reports of both bone marrow aspirate and biopsy done simultaneously on 500 cases in the period between January and December 2012 were retrospectively reviewed.

Results: About 76.2% of the cases showed positive correlation between the bone marrow Aspirate and biopsy findings. The highest correlation was noted in diffuse bone marrow diseases, and hematological malignancies; including acute myeloid leukemia (92.8%), idiopathic thrombocytopenic purpura (91%), and chronic myeloid leukemia (90.9%), poor correlation was observed in infiltrative bone marrow diseases including idiopathic myelofibrosis was 0%, lymphoma involvement 14.2%, and bone marrow metastasis 18.2%. The diagnostic accuracy was 76.2% for aspirates and 98.8% for biopsy.

Conclusion: This study shows that bone marrow aspirate is of diagnostic value mostly in diffuse bone marrow diseases and is of limited value in infiltrative bone marrow diseases where biopsy is mandatory. In general, there was a good correlation between the aspirate and biopsy findings.

Key words: Bone marrow aspiration, Bone marrow biopsy, Comparative, Correlation.

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Introduction

Bone marrow examination is an important diagnostic procedure; it is useful in establishing diagnosis of various hematological and non hematological diseases. It is the process^(1,2) of

obtaining the soft liquid tissue (aspirate) and solid trephine piece (biopsy) of bone marrow for laboratory analysis and diagnosis.

Bone marrow aspirate is particularly useful in assessment of marrow cellularity and is

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considered diagnostic in certain diseases including idiopathic thrombocytopenic purpura (ITP), hematological malignancies, and in typing of anemias.⁽³⁾ Biopsies on the other hand, are of paramount importance in diagnosing certain conditions including aplastic anaemia and myelofibrosis and in defining pattern of involvement of marrow spaces especially in lymphoma and solid tumors,⁽⁴⁾ and granulomatous diseases.

The aim of our study is to assess the correlation between bone marrow aspirate and biopsy in various hematological diseases so that efficient procedure is defined for more rapid diagnosis.

Methods

This is a retrospective review that was conducted at King Hussein Medical Center where random 500 bone marrow aspirates were compared with the simultaneously done 500 bone marrow biopsies, between January and December 2012. Only adult patients (18 years of age and older) were included. Bone marrow aspiration and biopsy were performed at the Oncology clinic for both in-patients and out-patients. All patients were provided an explanation of the purpose of the investigation and how the procedure will be carried out and oral consent is usually considered sufficient. The posterior iliac crest⁽⁵⁾ is the usual site for the procedure in our hospital. The procedure is performed by an hematology/oncology fellow. Technical expertise⁽²⁾ is needed to obtain adequate sample. Jamshidi needle or disposable bone marrow needle are most commonly used to draw the aspirate and biopsy, the collected amount for both are operator dependent, the average amount for aspirate was in the range 0.5-1 ml, and 0.5-1cm biopsy length are needed.

Aspirate smears are routinely stained by Geimsa stain while biopsy sections are stained by hematoxylin and eosin stain. This study was approved by the research ethics committee at KHMC.

Results

A total of random 500 reports of bone marrow aspirates were compared to simultaneously done bone marrow biopsy reports.

The age range was between 18 to 91 years, the male to female ratio was 1.34:1. The most

common indication for bone marrow examination in our study was reviewing the diagnosis and monitoring patients already diagnosed and managed for major hematological malignancies to look for therapy effect, anemia, pancytopenia, and bone marrow staging. Other indications as listed in Table I.

The diagnostic findings of bone marrow aspirate, biopsy, and percentage of correlation, respectively, for different diseases are summarised in Table II. The most commonly correlated diagnosis were for AML (26, 28, 92.8%), ITP (61, 67, 91%), CML (20, 22, 90.9%), while the poorest correlations were IM (idiopathic myelofibrosis) (0, 34, 0%), Lymphoma involvement (3, 21, 14.2%), and metastasis (2, 11, 18.2%) Table II summarise these findings.

Out of the 500 cases, aspirate was diagnostic in 381 cases (76.2%) while biopsy was diagnostic in 459 cases (98.8%), the sensitivity for aspirate and biopsy were respectively 78.3%, 99.1%, specificity 96.2%, 97.1%, positive predictive value 99%, 99% , and negative predictive value 57%, 96%. The majority (76.2%) of the cases showed positive correlation between the bone marrow aspirate and biopsy findings.

Discussion

Bone marrow examination (aspiration and biopsy) remains a corner stone in the diagnosis of various hematological and non hematological diseases. The correlation between both procedures is important to determine the most diagnostic method in various hematological diseases.

The final interpretation requires the integration of peripheral blood,⁽⁶⁾ bone marrow aspirate and biopsy findings, together with other ancillary tests such as immunophenotyping, cytogenetic and molecular genetics results in the context of clinical history and clinical picture which can lead to a definitive diagnosis. The pathology report for bone marrow aspirate generally takes less than one day, but about 2-3 days for biopsy.

Our findings are similar to what is mentioned in the literature. In this study there was a 76.2% positive correlation between aspirate and biopsy, this is similar to the study published in Pakistan by Khan *et al.*⁽⁷⁾ where positive correlation was 73.8%, as well as a study done in India by

Table I: Indications for Bone Marrow study

Indication	No.	%
Review & follow up of hematological malignancies	116	23.2
Anemia	112	22.4
Pancytopenia	66	13.1
Bone marrow staggng	52	10.4
Thromocytopenia	34	6.9
Hepatosplenomegaly & lymphadenopathy	30	6.0
Leuckocytosis	24	4.8
Osteolytic lesion	16	3.2
B-symptoms	15	3.1
↑Red cell mass	15	3.1
Thrombocytosis	12	2.3
Hemolysis	3	0.6
Miscellaneous	5	1
Total	500	

Table II: Cases diagnosed on Bone Marrow Aspirate and Biopsy and percentage of correlation

Diagnosis	+ve BMA	+ve BMBx	Percentage of correlation
AML (Acute myeloid leukemia)	26	28	92.8 %
ITP (Idiopathic thrombocytopenic purura)	61	67	91.0 %
CML(chronic myeloid leukemia)	20	22	90.9 %
Nutritional & Megaoblastic anemia	35	39	89.7 %
ALL (Acute lymphocytic leukemia)	17	19	89.5 %
Hematological malignancy Relapse	30	34	88.2 %
MM (Multiple Myeloma)	14	16	87.5 %
CLL (Chronic Lymphocytic Leuckemia)	13	15	86.7 %
PRV (polycythemia rupra vera)	12	14	85.7 %
ET (Essential thrombocythemia)	5	6	83.3 %
Hematological malignancy Remission	24	29	82.7 %
MDS (Myelodysplastic Syndrome)	13	16	81.3 %
Aplastic Anemia	4	14	28.0 %
Metastasis	2	11	18.2 %
Lymphoma	3	21	14.2 %
IM (Idiopathic Myelofibrosis)	0	5	0.0 %
Normal	149	103	69.1 % of normal Aspirate are true normal, 30.9 % are false normal.
Dry Tab	26	-	
In adequate sample	31	41*	
Others	16 * not diagnosed, to be correlated with bone bx result.	-	
Total	500	500	
Diagnosed	381	459	
Non diagnosed	119	41	
+ve Matching between Aspirate and Biopsy = $381 / 500 = 76.2 \%$			

*Some needs flow cytometry and cytogenetics for diagnosis

Table III: Diagnostic Efficacy of Bone Marrow Aspirate.

Sensitivity	Specificity	Positive predictive value	Negative predictive value
78.3 %	96.2 %	99 %	57 %

Table IV: Diagnostic Efficacy of Bone Marrow Biopsy .

Sensitivity	Specificity	Positive predictive value	Negative predictive value
99.1 %	97.1 %	99 %	96 %

Chandra *et al.*⁽⁸⁾ where the correlation was 78% .

The highest correlation was noted in diffuse bone marrow diseases including: acute myeloid leukemia (92.8%), idiopathic thrombocytopenic purpura (91%), and chronic myeloid leukemia

(90.9%), this was observed by Khan *et al.*⁽⁷⁾ Chandra *et al.*⁽⁸⁾ and Goyal *et al.*⁽⁹⁾ Poor correlation was observed in infiltrative bone marrow diseases: including idiopathic myelofibrosis (IM) was 0%, lymphoma

involvement 14.2%, metastasis from distant site 18.2%, and aplastic anemia 19%, similar results were reported by Khan *et al.*⁽⁷⁾ Chandra *et al.*⁽⁸⁾ and Goyal *et al.*⁽⁹⁾

In contrast, bone marrow aspirate has good predictive value and reliable in hematological malignancies, immune thrombocytopenia, and anemias. It has very limited and poor diagnostic in metastatic solid tumor, lymphoma involvement, aplastic anemia and myelofibrosis where biopsy is the standard diagnostic procedure.

One hundred forty nine patients were reported to have normal bone marrow aspirate, of them 103 have been proven to be normal (true negative) by correlation with biopsy (69.1%), the other 46 were really considered false negative, most of them were diagnosed by biopsy as lymphoma involvement, metastasis, aplastic anemia and myelofibrosis, this again proves poor diagnostic efficacy of aspirate for these infiltrative bone marrow diseases, these findings were correlated with the Chandra *et al.*⁽⁸⁾ where the correlated normality between aspiration and biopsy was 72.5%.

Seventy three (14.6%) of patients were undiagnosed by bone marrow aspiration, 31 (6.2%) were hemodiluted and inadequate sample, 26 (5.2%) were dry aspirates, and 16 patients have no diagnosis and need bone marrow biopsy correlation, few others were in need for further flow cytometry and cytogenetics. Humphries⁽¹⁰⁾ has reported the frequency of dry aspirate to be 3.9%.

The only limitation for diagnostic efficacy of bone marrow biopsy was inadequate samples in 41 patients (8.2%). Rehman *et al.*⁽¹¹⁾ reported inadequate specimens in 2007, 2008, and 2009 to be 4.9%, 10.5% and 3.3% respectively, very few cases need further flow cytometry and cytogenetics for the purposes of diagnosis.

The present study shows the diagnostic efficacy of both bone marrow aspirate and biopsy to be 76.2% and 98.8% respectively. Khan *et al.*⁽⁷⁾ have reported the diagnostic efficacy of bone marrow aspiration 73.8 %, and 99% for biopsy, Chandra *et al.*⁽⁸⁾ have reported them 77.5% and 99.2% respectively, sensitivity, specificity, positive predictive value and negative predictive value are shown in Table III and IV.

Monitoring hematological malignancies for therapy response was the most common indication for bone marrow examination in our study. Other indications are shown in Table I. These indications were to some extent comparable to Bashawri *et al.*⁽¹²⁾ indications for bone marrow examination.

Limitations of the study

We excluded patients who were less than 18 years old. The high percentage of non diagnosed aspirate and hemodiluted biopsies or inadequate samples, which depend on nature of underlying disease and experience of physician obtaining the specimen, may effect the diagnostic efficacy of both. The result of flow cytometry, cytogenetics, and immunohistochemistry were not included in our study.

Conclusion

Bone marrow aspirate is a complementary diagnostic test, it has good predictive value reaching that of biopsy in diffuse bone marrow diseases like: AML, ITP, CML, nutritional and megaloblastic anemia, ALL, hematological malignancy relapse, MM, CLL, PRV, ET, hematological malignancy remission, MDs. On the other hand, aspiration has very limited predictive value in infiltrative bone marrow diseases like: lymphoma, solid tumor metastasis, myelofibrosis, aplastic anemia, unexplained leucoerythroblastic blood film, where biopsy is mandatory.

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