

COMPARATIVE ANALYSIS OF DIAGNOSTIC VALUE OF SIMULTANEOUS USE OF BONE MARROW ASPIRATION AND BIOPSY IN ROUTINE HAEMATOLOGY PRACTICE: AN INSTITUTIONAL EXPERIENCE

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ABSTRACT

BACKGROUND

Bone marrow aspirations and simultaneous use of bone marrow biopsies are important diagnostic procedures done in various haematological and non-haematological disorders. A comparative study of both the procedures done simultaneously was retrospectively reviewed in 50 cases with clinical correlation with BMA and BMB results. The advantage of each method is analysed.

The objectives of the study were to assess the diagnostic value of the BMA and BMB and role of both the procedures to reach final diagnosis when done simultaneously and its correlation with clinical data.

MATERIALS AND METHODS

BMA and BMB were performed on 50 patients. Criteria of inclusion included the main indications for performing this procedure, the availability of full medical records and patient consent. The patients had a male to female sex ratio of 1.8:1 and a wide age range from 5 years to 76 years.

RESULTS

In the present study, the main indications for bone marrow examination were categorized. Out of 50 cases studied, in 33 cases, a strong positive correlation between BMA and BMB was noted. However, it was found that in the cases of aplastic anaemia, different phases of myeloproliferative neoplasm (MPN), multiple myeloma, metastatic diseases, tubercular granulomas and haemato-lymphoid neoplasm, involvement of the marrow was detected better in bone marrow biopsies. Many of BMB aided with special stains and IHC came with better outcome.

CONCLUSION

The study concludes that preparations of aspirate and trephine biopsy are easy, rapid and complementary to each other in majority of the lesions. The advantage of both the procedures done together enabled us to study the cytomorphology of the cells along with the pattern of distribution of the cells depending on the cases, hence help in making the diagnosis accurately.

KEYWORDS

Bone marrow aspiration, Bone marrow trephine biopsy, Bone marrow examination.

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BACKGROUND

Bone marrow aspirations and bone marrow biopsies are very useful diagnostic procedures for the diagnosis of haematological and non-haematological malignancies, typing of anaemia, evaluation of pyrexia of unknown origin, rule out infective diseases, staging of marrow as well as assessing the reticulin content of the marrow in myelofibrosis, metastatic diseases, Bone marrow is involved in variety of haematological and non-haematological disorders. The haematological disorders include acute leukaemia, myeloproliferative neoplasm (MPN), haemato-

lymphoid neoplasm, nutritional deficiency diseases and any metastatic diseases as well. These procedures are also valuable for follow up of patients undergoing chemotherapy, Study of Minimal residual disease, bone marrow transplantation and other forms of medical treatment.^{1,2} Involvement of marrow by metastatic tumour, have an effect on clinical treatment and prognosis. Similarly, involvement of the marrow by granulomatous lesion especially tuberculous granulomas may be easily identified in bone marrow biopsies. Moreover, in cases where malignancies are not clinically suspected, bone marrow aspirations and biopsies have been useful in detecting non-hematologic malignancies.

When both the procedures are performed simultaneously, they are complementary to each other there is more material to study the morphology and the pattern of distribution of the cells.³ This study was conducted in our institute to evaluate the complementary role of both the procedures done simultaneously and to see the advantages and disadvantages of these procedures.

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Hence, we attempted to correlate both these parameters to arrive at a more conclusive final diagnosis.

Aims and Objectives

This study was aimed to assess the diagnostic value of the BMA and BMB and role of both the procedures to reach final diagnosis when done simultaneously and its correlation with clinical data.

MATERIALS AND METHODS

The study has been conducted for bone marrow examination on 50 cases presenting with anaemia, fever and organomegaly examined in the department of pathology of our institution from Jan 2014 to Dec 2017.

The patients had a male to female sex ratio of 1.8:1 and a wide range of age from 5 years to 76 years.

It includes both indoor and outdoor patients, who were suspected of having their bone marrow involvement by any haematological or non-haematological disorders. The relevant history and bio-data of patients was recorded and informed consent was taken.

Patients were investigated for complete blood count, coagulation profile, reticulocyte count and peripheral blood film (PBF) examination prior to the procedure as routine measures. BMA and BMB were done simultaneously for these patients.

In patients of thrombocytopenia, five minutes of firm pressure was applied at the end of the procedure. However, as a precaution, the patients were kept in lying down position on his/her back for a further 10–15 minutes to apply more prolonged pressure.

BMA was performed by Salah’s marrow puncture needle; smears prepared were stained with Leishman stain. Prussian blue for iron demonstration was done in selected cases and iron grading was done.³ BMB was taken by Jamshidi biopsy needle and specimens were fixed in 10% formalin fixative, decalcified in 10% formic acid–5% formaldehyde and processed with paraffin-wax embedding. Sections, 4µm thick, were cut and were stained by Haematoxylin and Eosin (H&E) stain.

The staining for reticulin fibers with Gomori’s Silver impregnation method was done in selected cases and grading was done.⁴ Bone marrow biopsy and aspiration findings were analysed in context of clinical signs, symptoms, other laboratory investigations and diagnosis reached.

RESULTS

Total cases studied were categorized further on the basis of peripheral blood features and accepted indications were summarized (Table 1). The results were analysed as per the extent of correlation between BMA and BMB.

Out of the 50 cases studied, in 23 cases both the procedures were comparable (Figure 1). BMA was reported as suggestive of aplastic anaemia in nine cases but BMB revealed hypo cellular marrow only in three cases where as aplastic anaemia in rest of the six cases (Table 2).

Accepted Indications	No. Cases	%
Pancytopenia	20	40
Anaemia	14	28
Acute Leukaemia	09	18
Chronic Leukaemia	04	08
Leucoerythroblastic Blood picture	01	02
Thrombocytopenia	02	4

Table 1

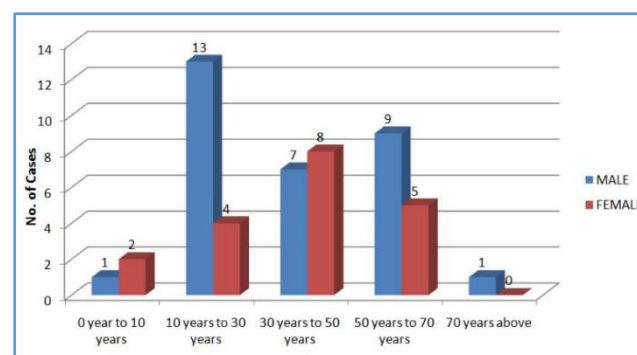


Figure 1

PBF	BMA	BMB	No. of Cases	%
AML	AML	AML	05	10
ALL	ALL	ALL	03	06
Pancytopenia	AML	AML	02	04
Pancytopenia	ALL	ALL	02	04
Anaemia	Anaemia	Anaemia	13	26
		Total	25	

Table 2. Showing Cases with Similar Findings on Bone Marrow Aspiration and Bone Marrow Biopsy *Peripheral Blood Film, †Bone Marrow Aspiration, #Bone Marrow Biopsy, §Acute Myeloid Leukaemia, || Acute Lymphoblastic Leukaemia

PBF	BMA	BMB	No. Cases	%
Pancytopenia	Hypocellular	Aplastic anaemia	05	10
Pancytopenia	Hypocellular	Hypocellular	03	06
		Total	08	16

Table 3. Showing Cases Where Findings on Bone Marrow Aspiration were Suggestive Only. *Peripheral Blood Film, †Bone Marrow Aspiration, #Bone Marrow Biopsy

PBF	BMA	BMB	No. Cases	%
Pancytopenia	Blood Tap	Hypocellular	03	06
Pancytopenia	Dry Tap	Hypercellular	03	06
Leukoerythroblastic Blood Picture	Dry Tap	Epithelioid Cells	01	02
Anaemia	Normocellular marrow	Focal collection plasma cells	01	02
		Total	08	16

Table 4. Showing Cases Where Diagnosis Was Possible Only on Bone Marrow Biopsy
*Peripheral Blood Film, †Bone Marrow Aspiration, ‡Bone Marrow B

PBF	BMA	BMB	No. Cases	%
CML	Bloody Tap	Prefibrotic Phase MPN	03	06
Anaemia	Dry tap	Myelofibrosis with myelosclerosis	02	04
Pancytopenia	MPN	MPN with MF (Prefibrotic Phase)	02	04
Pancytopenia	Blood tap	MPN with MF	01	02
Pancytopenia	Dry tap	MPN with MF	01	02
Pancytopenia	CLL	Diffuse Involvement	02	04
Anaemia	NHL (>40 % lymphoblast)	Nodular involvement	01	02
Pancytopenia	NHL (>90%)	Diffuse involvement	01	02
Thrombocytopenia	Megakaryocytosis	Megakaryocytosis	01	02
	Total		14	28

Table 5. Showing Cases where Patterns of Involvement were Seen on Biopsy*Chronic Myeloid Leukaemia, †Myeloproliferative Neoplasm, ‡Myelofibrosis, §Chronic lymphocytic leukaemia, || Non-Hodgkin's Lymphoma

DISCUSSION

The bone marrow examination is valuable investigation in haematology practice. BMA and BMB both are important procedures for the diagnosis of haematological and non-haematological conditions. These procedures are also useful for follow up of the patients undergoing chemotherapy.^{5,6}

In the present study 25 out of total 50 cases showed comparable results between BMA and BMB. Out of these 25 cases, indication for bone marrow examination was anaemia in 14 cases and both BMA and BMB examination revealed erythroid hyperplasia with either micronormoblastic or megaloblastic proliferation. These observations were nearly similar to the findings seen in a study conducted by Ch Toi P et al.,⁷ But iron stained sections of BMB showed discrepancies in iron content from that of BMA smears. Stuart-Smith SE et al., have also shown in a study that aspirate smears reflect bone marrow iron stores more reliably than decalcified trephine biopsy sections.⁸ Rest of the 9 out of these 25 cases were diagnosed as acute leukaemia by peripheral blood film examination in all, except two cases, where it was confirmed on bone marrow examination. Younus U and associates emphasized that although BMA confirms the diagnosis of acute leukaemia, bone marrow biopsy specimen complements the peripheral blood and aspirate findings in providing additional information of cellular distribution, its pattern of infiltration for the diagnosis and especially aids in prognosis of acute leukaemia.⁹ Also various immunomarkers, yield diagnostic value of for use on paraffin wax embedded sections in the diagnosis of acute leukemia in sections from bone marrow biopsy specimens.¹⁰ In 9 out of total 50 cases, BMA smear interpretation was suggestive of aplastic anaemia, whereas BMB revealed hypocellular marrow with focal hyper cellular areas in 3 cases. Rest of the 5 cases were ultimately confirmed as aplastic anaemia.

As BMB gives the qualitative and quantitative assessment of cellularity, therefore confirms the diagnosis and overcomes the limitation of BMA.^{8,11} Due to variability of cellularity from one intertrabecular space to the next, a case which was wrongly diagnosed as Aplastic anaemia on BMA was turned out to be of hypocellular marrow with patchy hypercellular areas on thorough examination of BMB. Thus, the use of the biopsy avoids misinterpretation of cellularity by smears.¹² An important limitation of bone marrow obtained by aspirate is the admixing of marrow and sinusoidal blood, which may not allow for reliable estimates of marrow cellularity.

Also it is necessary that finding of a 'dry tap' should never be dismissed as being due to faulty technique and always needs a bone marrow biopsy for further evaluation.¹³

In the present study, out of total 50 cases, 5 cases were reported as bloody tap/dry tap on BMA. Which were turned out to be hypocellular / hypercellular marrow on BMB. Also, one case of leukoerythroblastic blood picture, on repeated BMA attempts was found to be of dry tap. BMB showed myelofibrosis. One case was of granuloma on aspirate which was further confirmed on BMB with discrete granulomas. The latter case was confirmed by PCR as positive for tuberculosis. Ch Toi P et al., have mentioned that 80% cases of granulomatous lesions were diagnosed by BMB alone.⁷ Also the role of BMB for detection of minimal residual disease after treatment in case of multiple myeloma and leukaemia are very useful.¹⁴ We have encountered six cases of MPN's out of which diagnosis was possible to be made from PBF and BMA in 2 cases only rest four cases were confirmed on BMB. Role of trephine biopsy is not only in differentiation of MPN but also to assess the overall marrow cellularity, histotopography, morphology of megakaryocytes as well as blasts, and degree of Myelofibrosis.

Rest of the four non-diagnostic aspirates in patients who had grade-3 marrow fibrosis highlights the importance of trephine biopsy.¹⁵ It is confirmed that BMA does not have much role in diagnosis of primary myelofibrosis because diffuse osteomyelosclerosis, intrasinusoidal haematopoiesis, megakaryocyte morphology and its distribution and vascular proliferation as seen in present study, which is characteristic of primary myelofibrosis, can be confirmed and graded on BMB only. Also, reticulin stain which gives accurate platform for grading of fibrosis to get done is possible on BMB only.¹⁶

There were two cases of NHL in present study where BM biopsy renders information which cannot be determined from aspiration such as spatial distribution and extent of infiltrates, overall cellularity and fibrosis. This also implies that trephine biopsy may be more useful in post chemotherapy patients to assess the residual tumour cell burden and degree of chemotherapy response.¹⁷

There was one case of Chronic Lymphocytic Leukaemia (CLL) with diffuse involvement of marrow on biopsy section while aspiration showed only that marrow is involved. Bone marrow examination in case of CLL should always include a trephine biopsy because bone marrow aspirate gives very little information beyond that already available from examination of blood. Pattern of marrow involvement by leukemic cells could be only analysed by trephine biopsy whether it is chronic or acute leukaemia. Also, trephine biopsy permits an accurate assessment of extent of infiltration and gives information of prognostic importance.¹⁸

In one case of thrombocytopenia in present study BMA and BMB findings were consistent to each other. But an additional finding on BMB was normal arrangement of megakaryocytes which were seen with only increased in number on BMA.¹⁹

Hence, it was observed from the above discussion that bone marrow evaluation is an important and effective tool in diagnosing and evaluating haematological and non-haematological disorders. Complete evaluation of bone marrow samples includes a brief patient history, haematological profile, BMA smears and biopsy sections.²⁰ A correlation of bone marrow aspiration and biopsy showed that both the procedure were complementary to each other. The BMA generally provides an excellent cytomorphological details which enables haematopathologist in recognising the abnormal hematopoietic cells or the non-native cells in case of non-haematological disorders. Whereas, a bone marrow trephine biopsy demonstrates the topographic arrangement of hematopoietic cells within the marrow framework and hence gives a more representative view of the cellularity of the marrow and allows infiltration to be recognized clearly. BMB examination has definite edge over BMA in the detection of minimal residual diseases, staging of lymphoma and for the diagnosis of acute leukaemia in relapse cases which are otherwise clinically silent.

CONCLUSION

The present study showed that BMA and BMB are easy, rapid, cost-effective and more or less are of equal value in various haematological and non-haematological disorders of

bone marrow. Although, methods are complementary on correlation but in some cases one or the other of these methods is more conclusive and also have important diagnostic value even by using basic standard fixation and embedding procedures, with the aspiration smears being primarily useful for cytological diagnosis and biopsy sections mainly helpful to identify histological features like architectural patterns, grading of fibrosis, pattern of infiltration with lymphomas and granulomatous conditions. Both of the procedures should be done simultaneously as they play important role in providing findings, which are mandatory for making final diagnosis.

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