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Comparison of Bone Marrow Aspiration Cytology, Touch Imprint Cytology and Bone Marrow Biopsy for Bone Marrow Evaluation at a Tertiary Health Care Institute

Girish Taori[1], Archana Ukey[2]* and Preeti Bajaj[3]

[1]PG Resident, Department of Pathology, MVP's Dr. Vasantrao Pawar Medical College, Hospital and Research Centre, Nashik - 422003, Maharashtra, India; dr.girishtaori@gmail.com
[2]Associate Professor, Department of Pathology, Dr. Vasantrao Pawar Medical College, Hospital and Research Centre, Nashik - 422003, Maharashtra, India; archu12241@gmail.com
[3]Professor and Head, Department of Pathology, Dr. Vasantrao Pawar Medical College, Hospital and Research Centre, Nashik - 422003, Maharashtra, India; dr.prbajaj@gmail.com

Abstract

Introduction: Bone marrow examination is an important investigation in haematology which involves Bone Marrow Aspiration (BMA), Bone Marrow Imprint (BMI) and Bone Marrow Biopsy (BMB). **Aim: C**orrelation of findings of bone marrow aspiration and imprint smears with biopsy in hematological disorders. **Materials and Methods:** It was a prospective study to correlate bone marrow examination findings by BMA, BMI and BMB of 111 patients in which bone marrow biopsy was done and correlated with aspirate and imprint smears. For aspiration Salah's needle and for biopsy Jamshidi needle were used. Correlation of hematological and histopathological findings was done. **Results:** Megaloblastic anaemia was the commonest diagnosis followed by acute leukemia, nutritional anaemia, chronic leukemia, multiple myeloma, leukemia/lymphoma syndrome, and essential thrombocythemia. In case of dry aspirate or diluted marrow biopsy was useful to diagnose aplastic anemia, and secondary myelofibrosis associated with acute and chronic leukemia, multiple myeloma, leukemia/lymphoma syndrome and myelomonocytic leukemia. Aspirate and imprint smears were better for cellular morphology. **Conclusion:** Aspiration and imprint smears give better morphological details/cytologic diagnosis. In dry tap or diluted marrow, biopsy was more helpful in identifying architectural pattern, cellularity and fibrosis whereas imprint smears were more helpful for cellular morphology. BMA, BMI and BMB are complimentary to each other.

Keywords: Anaemia, Bone Marrow Aspiration (BMA), Bone Marrow Imprint (BMI) and Bone Marrow Biopsy (BMB), Haematology, Leukemia

1. Introduction

Bone marrow is one of the most widely distributed organs in the body which contains hematopoetic cells as red marrow and adipose tissue as yellow marrow. It produces cellular components of blood like red cells, white cells and platelets[1].

Bone Marrow Aspiration Cytology (BMA), Bone Marrow Biopsy (BMB) and Bone Marrow Imprint (BMI) (TOUCH IMPRINT) cytology are the methods to examine bone marrow.

Cytological picture is given by BMA and BMI however cellularity is less in BMI while cytological picture and architecture is better studied by BMB.

For studying marrow cellularity examination of core biopsy is the gold standard[2].

Bone marrow examination is useful investigation in diagnosis and staging of several haematological diseases, for assessment of overall bone marrow cellularity and morphology, even for diagnosing, non haematological disorders and unexplained abnormalities of any peripheral blood cell type[3].

*Author for Correspondence

In the present study results of BMA, BMI and BMB are compared as only BMA may be insufficient in some cases.

Though peripheral blood gives information of haematological diseases, many times study of haematopoesis with BMA and BMB is also required[4].

Core needle biopsy was started in late 1950[5]. BMA is simple, minimally invasive technique but has lower sensitivity in diagnosing solid tumour metastasis and lymphoma as compared to BMB[6]. BMB is older technique, more reliable to study pattern of marrow involvement[7] and cellularity of marrow than BMA.

In case of dry or bloody tap, trephine biopsy gives information on architecture, cellularity, fibrosis and pattern of distribution of abnormal infiltrates[8,9] and BMI smears may be helpful in diagnosing the underlying disease process, thus beneficial to patient in getting early treatment even before the histopathological report of core biopsy is ready for study.

Confirmation of clinically suspected disease or diagnosis of previously unsuspected diseases can be done by bone marrow studies.

2. Aims and Objectives

1. To study the bone marrow aspiration, bone marrow imprint and bone marrow biopsy profiles among patient undergoing bone marrow evaluation.
2. To study the validity of BMA as compared to BMB in bone marrow evaluation.
3. To study the validity of BMI as compared to BMB in bone marrow evaluation.
4. To compare the results of our studies with other studies.

3. Materials and Methods

1. Study design: - Validity of diagnostic test.
2. Study setting: - Department of Pathology, Dr. Vasantrao Pawar Medical College Hospital and Tertiary care centre.
3. Duration of the study:- Period of two years and five months from August 2016 to December 2018.

The present study was done from August 2016 to December 2018 where BMA, BMI and BMB of 111 cases of inpatients and outpatients departments of Tertiary Health Care Institute were performed. Clinical history, physical examination of patient along with complete hematological and other relevant investigations was done and proforma filled.

3.1 Inclusion and Exclusion Criteria

3.1.1 Inclusion Criteria

Indication of bone marrow examination with due informed consent of patients admitted to or attending OPD in Tertiary Health Care Institute. Indication included: Red cell disorders, Leukocytic disorders, Megakaryocytic and platelet disorders, Myeloproliferative disorders, Myelodysplastic syndromes, Paraproteinemias, Pyrexia of unknown origin, Suspected lysosomal or other storage disorders, Iron store assessment, Metastasis, Unexplained hepatomegaly and/or splenomegaly.

3.1.2 Exclusion Criteria Included

Hemorrhagic disorders, skin infection or recent radiation, therapy at sampling site, bone disorders such as osteogenesis imperfecta,inadequate bone marrow biopsy, pregnancy.

To know the necessity of BMB and BMI and correlate the results of BMA with BMI and BMB, all three procedures were performed in all cases.

4. Procedure of Bone Marrow Examination[2,10]

Clinical history was taken, PBSs taken at the time of doing BMA and BMB, stained with Romanowsky stains and examined.

4.1 BMA/BMI Smears

- Smears with marrow particles were examined under low power for cellularity, megakaryocytes and presence of metastatic carcinoma cells if any. The area in the cell trail of the particle where dilution was not present and cell morphology was best appreciated was selected and differential count done by counting at least 500 nucleated cells other than erythroid precursors using oil immersion.
- M: E ratio was then calculated.

4.2 BMB

Overall cellularity, architecture, megakaryocyte number with distribution, abnormalities of the bone, focal lesions such as granulomas, infiltrates of metastatic tumor or lymphoma were studied. On high power hemopoietic cells and marrow stromal elements were studied.

4.3 Following Points were Considered for Comparative Study

Technique used, adequacy of material obtained, architecture, cytomorphology and cellularity, use of the study in diagnosis of different disorders.

4.4 Results

The age of patients ranged from age 1 to 80 years with median age of 40 years. In this study of 111 cases, 56 cases were males and 55 were females. The male to female ratio was 1.01:1.

The most common presenting complaint of patients was fever (67.56%) followed by bone pain (27.93%). Splenomegaly was the most common clinical finding (60.36%) followed by hepatomegaly (16.09).

In the present study, 48 cases (43.24%) were of pancytopenia. The most common cause of pancytopenia was megaloblastic anaemia (24 cases).

The commonest hematological disorder was megaloblastic anaemia (25.20%) followed by acute leukemia (18.01%).

In this study111 cases were classified into 12 groups according to haematological investigations and other investigations as listed in (Table 1 and 2).

Table 1. Bone marrow biopsy diagnosis of 111 cases

Sr. No.	Diagnosis	No. of cases	Percentages (%)
1.	Megaloblastic Anaemia (MA)	28	25.22
2.	Microcytic Hypochromic Anaemia (MCHC)	1	0.90
3.	Dimorphic Anaemia (DA)	15	13.51
4.	Aplastic Anaemia (AA)	7	6.30
5.	Idiopathic Thrombocytopenic Purpura (ITP)	7	6.30
6.	Plasma Cell Dyscrasias (MGUS, PCM)	6	5.40
7.	Chronic Myeloid Leukemia (CML)	8	7.20
8.	Lymphoproliferative Disorders (CLL, NHL, LPD)	4	3.60
9.	Acute Leukemia (AML, ALL, AL)	20	18.01
10.	Normal Bone Marrow (NOC)	11	9.91
11.	Metastasis to BM (METS)	1	0.90
12.	Miscellaneous (IMF, GRANULOMATOUS, PV)	3	2.70
	Total	**111**	**100**

Table 2. Clinical presentation (percentage) of different haematological diseases in 111 cases

Sr. No.	Signs and Symptoms	No. of Cases	Percentage of Cases
1.	Fever	74	66.67
2.	Bone Pain	31	27.93
3.	H/O Bleeding	16	14.41
4.	Splenomegaly	67	60.36
5.	Hepatomegaly	39	35.14
6.	Jaundice	15	13.51
7.	Lymphadenopathy	17	15.32

Maximum patients presented with complain of fever followed by bone pain. Splenomegaly was the most common clinical finding.

Diagnosis of total 111 cases based on BMA, BMI and BMB are listed in (Table 3).

Table 3. Diagnosis of cases based on BMA, BMI and BMB

Sr. No.	Diagnosis (Total)	BMA	BMI	BMB
1.	Megaloblastic Anaemia (MA) (28)	26	28	28
2.	Microcytic Hypochromic Anaemia (MCHC) (1)	1	1	1
3.	Dimorphic Anaemia (DA) (15)	15	15	15
4.	Aplastic Anaemia (AA) (7)	0	0	7
5.	Idiopathic Thrombocytopenic Purpura (ITP) (7)	7	7	7
6.	Plasma Cell Dyscrasia (MGUS, PCM) (6)	5	6	6
7.	Chronic Myeloid Leukemia (CML) (8)	6	8	8
8.	Lymphoproliferative Disorders (CLL, NHL, LPD) (4)	1	1	4
9.	Acute Leukemia (AML, ALL, AL) (20)	15	20	20
10.	Normocellular/Normal Bone Marrow (NOC) (11)	11	11	11
11.	Metastasis to BM (METS) (1)	0	0	1
12.	Miscellaneous (IMF, GRANULOMATOUS, PV) (3)	1	0	3
	Total (111)	**88**	**97**	**111**
	Percentages %	**79.28**	**87.39**	**100**

In the present study 88 cases (79.28%) diagnosed on bone marrow aspiration while 97 cases (87.39%) were diagnosed on imprint smears whereas all 111 cases diagnosed on bone marrow biopsy (Table 4 and 5).

Table 4. Validity of bone marrow aspiration

Validity of Bone Marrow Aspiration in the Bone Marrow Evaluation as Compared to Bone Marrow Biopsy as Gold Standard				
		BMB		Total
		Positive	Negative	
BMA	Positive	88	0	88
	Negative	12	11	23
Total		**100**	**11**	**111**
Computed Probability Value of Different Statistics Test				
Test Statistics	**Formula**	**Value**		
Sensitivity	TP/(TP+FN)	0.88		
Specificity	TN/(FP+TN)	1		
Prevalence	(TP+FN)/N	0.9		
Diagnostic Accuracy	(TP+TN)/N	0.89		
Positive Predictive Value	TP/(TP+FP)	1		
Negative Predictive Value	TN/(FN+TN)	0.48		

The Computed Probability Value of Different Statistical Tests observed in our study where BMA was compared with BMB by assuming BMB as a gold standard was as follows:

- Sensitivity of BMA was 88%
- Specificity of BMA was 100%
- Prevalence of BMA was 90%
- Diagnostic Accuracy of BMA was 89%
- Positive Predictive Value of BMA was 100%
- Negative Predictive Value of BMA was 48%

Table 5. Validity of bone marrow imprint

Validity of Bone Marrow Imprint in the Bone Marrow Evaluation as Compared to Bone Marrow Biopsy as Gold Standard				
		BMB		Total
		Positive	Negative	
BMI	Positive	97	0	97
	Negative	3	11	14
Total		**100**	**11**	**111**
Computed Probability Value of Different Statistics Test				
Test Statistics	**Formula**	**Value**		
Sensitivity	TP/(TP+FN)	0.97		
Specificity	TN/(FP+TN)	1		
Prevalence	(TP+FN)/N	0.9		
Diagnostic Accuracy	(TP+TN)/N	0.97		
Positive Predictive Value	TP/(TP+FP)	1		
Negative Predictive Value	TN/(FN+TN)	0.79		

The Computed Probability Value of Different Statistical Tests observed in our study where BMI was compared with BMB by assuming BMB as a gold standard was as follows:

- Sensitivity of BMI was 97%
- Specificity of BMI was 100%
- Prevalence of BMI was 90%
- Diagnostic Accuracy of BMI was 97%
- Positive Predictive Value of BMI was 100%
- Negative Predictive Value of BMI was 79%

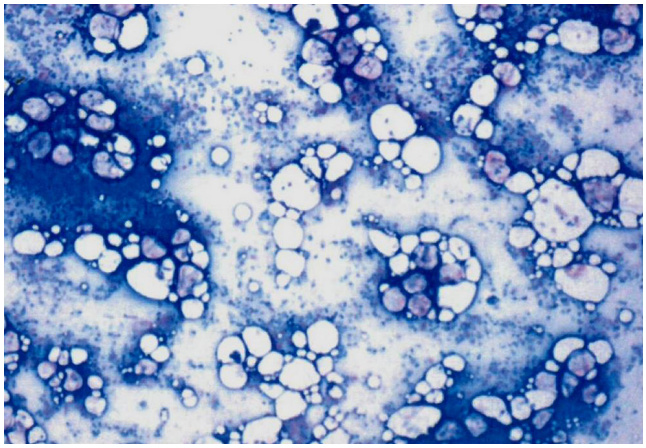

Figure 1. BMA showing hypocellular marrow in AA (10X).

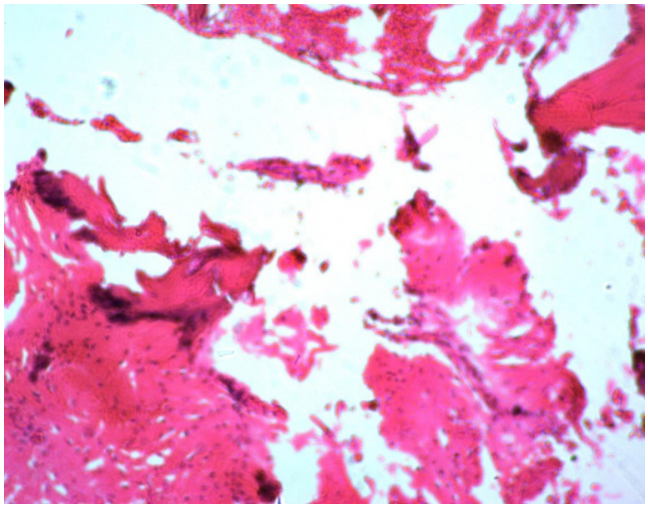

Figure 2. BMB showing metastasis from adenocarcinoma of the prostate (10X).

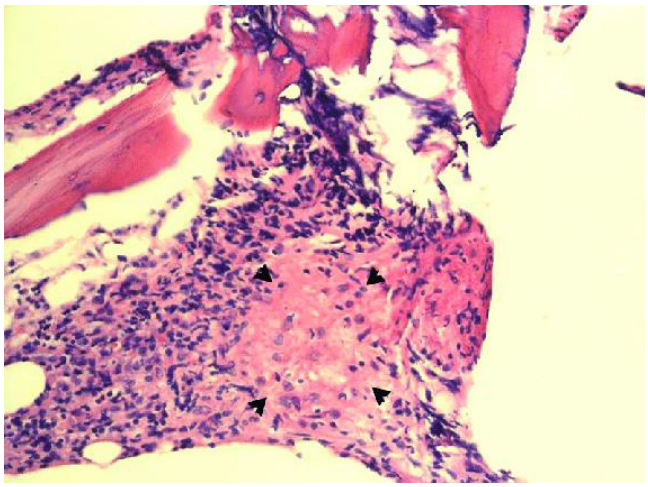

Figure 3. Photomicrograph of BMB showing granuloma (10X).

5. Discussion

In the present study 15 cases of nutritional anaemia showed erythroid hyperplasia with either micro normoblastic or megaloblastic maturation in both BMA and BMB. Similarly, 50 cases of anemia showed positive correlation between BMA and BMB in the study done by Kaur et al[11].

All seven cases (6.30%) which were hypocellular on BMA and BMI were diagnosed as aplastic anaemia on BMB (figure 1). Findings are similar to the study by Kaur et al.[11] according to whom misinterpretation of cellularity by smears can be avoided by BMB.

Out of 20 cases of acute leukemia, 2 were diluted marrow, 15 were diagnosed on BMA, 3 cases had dry tap which may be due to the tightly packed marrow by leukemic cells which was also observed in the study by Chandra and Chandra[12].

Out of 8 cases of chronic leukemia, 6 cases showed correlation between BMA and BMB, 2 cases were dry tap on aspiration, biopsy showed myelofibrosis. Our findings were similar to other studies[9,12].

Our study included 4 cases of lymphoproliferative disorders out of which 3 were diagnosed on BMB. Sabharwal et al.[5] and Kaur et al.[11] had same finding in their study.

All six cases (5.40%) of dry tap on aspiration were diagnosed on BMB, out of which 3 were AML, 2 were CML, 1 was myelofibrosis. A single case of metastasis from adenocarcinoma of the prostate was seen in this study (Figure 2).

A single case which was normocellular on BMA and BMI was diagnosed as granulomatous lesion on BMB. Our finding was similar to study by Chandra[12] (figure 3).

Eleven cases (9.91%) showed normal bone marrow on all three procedures BMA, BMI, BMB.

Chandra et al.[12] compared the diagnostic accuracy of all three methods of bone marrow examination i.e. BMA, BMI and BMB and stated that biopsy remains to be the gold standard. They observed that diagnostic accuracy of BMI (83.7%) was higher than BMA (77.5%). Similarly, Aboul-Nasr et al.[13] also observed in their study that diagnostic accuracy of BMI (99.4%) was higher than BMA (84.4%). Gong et al.[14] in their study have documented diagnostic accuracy of BMI (94.5%) and BMA (89.8%).

The comparative study of BMA, BMI and BMB is more reliable, rapid, and efficient method in the diagnosis of haematological disorders. Diagnostic accuracy of BMB was highest (100%) but of BMI was (97%) considerably higher than BMA (89%). Hence BMB remains gold standard. Our observation was similar to other international studies.

6. Conclusion

From the comparative study of different bone marrow procedures BMA, BMI and BMB, it was concluded that BMA is a easy and smooth procedure causing very little discomfort to the patient. Cytomorphological study is best done by BMA smears.

However, it has limited predictive value in infiltrative bone marrow diseases like lymphoma, solid tumor, metastasis, myelofibrosis and aplastic anaemia where BMB and BMI are helpful.

BMI is rapid and reliable diagnostic tool. It gives better information regarding cellularity compared to BMA if imprint smears prepared meticulously by gentle rolling. BMI is also helpful in early diagnosis of critically ill patients, where BMB trephine section processing is time consuming.

BMB is a reliable mode of accurate determination of cellularity and topography. BMB remains gold standard to diagnose dry tap on BMA.

To conclude, BMA and BMB along with BMI are complimentary to each other. Hence all the three modalities are performed in single setting for betterment of the patients to reach at accurate diagnosis.

7. References

1. Bain BJ, Clark DM, Wilkins BS. The normal bone marrow. In: Bain BJ, Clark DM, Wilkins BS, editors. Bone Marrow Pathology. 4th ed. Singapore: Wiley-Blackwell; 2010. p. 1-51.
2. Bain BJ. Bone marrow trephine biopsy. J. Clin. Pathol. Oct 2001; 54(10):737-42. https://doi.org/10.1136/jcp.54.10.737. PMid: 11577117, PMCid: PMC1731298.
3. Bearden JD, Ratkin GA, Colyman. Comparison of the diagnostic value of bone marrow biopsy and aspiration in neoplastic disease. J. Clin. Pathol. 1974; 27:738-40. https://doi.org/10.1136/jcp.27.9.738. PMid: 4426982, PMCid: PMC475459.
4. Toi PCh, Varghese RG, Rai R. Comparative evaluation of simultaneous bone marrow aspiration and bone marrow biopsy: An institutional experience. Indian J. Hematol. Blood Transfus. 2010; 26:41-44.
5. Sabharwal BD, Malhotra V, Aruna S, Grewal R. Comparative evaluation of bone marrow aspirate particle smears, imprints and biopsy sections. J. Postgrad Med. 1990; 36(4):194-98.
6. Antonino Musolino, Annamaria Guazzi, Rita Nizzoli, Michele Panebianco, Cristina Mancini and Andrea Ardizzoni. Accuracy and relative value of bone marrow aspiration in the detection of lymphoid infiltration in non-Hodgkin lymphoma. Tumori. 2010; 96:24-27. https://doi.org/10.1177/030089161009600104. PMid: 20437853.
7. Hamid GA, Hanbala N. Comparison of bone marrow aspiration and bone marrow biopsy in neoplastic diseases. Gulf J. Oncology. Jul 2009; (6):41-44.
8. Mahajan V, Kaushal V, Thakur S, Kaushik R. A comparative-study of bone marrow aspiration and bone marrow biopsy in haematological and non haematological disorders - An institutional experience. JIACM. 2013; 14(2):133-35. https://doi.org/10.7788/figurationen.2013.14.2.133.
9. Tripathy S, Dudani S. Comparative evaluation of simultaneous bone marrow aspiration and trephine biopsy-Experience from routine clinical practice. Ind. J. Clin. Pract. 2013; 24(5):446-50.
10. Bain BJ. Bone marrow trephine biopsy. J. Clin. Pathol. 2001 Sep; 54(9):657-63. https://doi.org/10.1136/jcp.54.9.657. PMid: 11533068, PMCid: PMC1731527.
11. Kaur M, Rana A, Kapoor S, Puri A. Diagnostic value of bone [6] marrow aspiration and biopsy in routine haematological practice. J. Clin. Diagn. Res. 2014; 8(8):13-16.
12. Smita Chandra, Harish Chandra. Comparison of bone marrow BMA cytology, BMI cytology and BMB for bone marrow evaluation. Hematology Reports. 2011; 3:e22.
13. Aboul-Nasr R, Estey EH, Kantarjian HM, Freireich EJ, Andreeff M, Johnson BJ, Albitar M. Comparison of touch imprints with BMA smears for evaluating bone marrow specimens. American Journal of Clinical Pathology. 1999; 111(6):753-58. https://doi.org/10.1093/ajcp/111.6.753. PMid: 10361510.
14. Gong X, Lu X, Wu X, et al. Role of bone marrow imprints in haematological diagnosis: A detailed study of 3781 cases. Cytopathology. Apr 2012; 23(2):86-95.

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