



COMPARATIVE EVALUATION OF BONE MARROW ASPIRATION AND TREPHINE BIOPSY IN PANCYTOPENIA IN VARIOUS HEMATOLOGICAL DISEASES

Pathology

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ABSTRACT

Bone marrow examination is an important tool for the diagnosis of various hematological disorders. It involves the use of bone marrow aspiration (BMA) and bone marrow biopsy (BMB). **Objectives:** To compare concordance and discordance rate between bone marrow aspiration and trephine biopsy findings in making etiological diagnosis in pancytopenia patients. **Material And Methods:** A cross sectional prospective study was conducted in department of pathology MAMC, Agroha on 36 cases of pancytopenia to compare the findings of bone marrow aspiration and bone marrow biopsy. **Results:** The overall concordance and discordance rate between BMA and BMB was 63.8% and 36.2% respectively. **Conclusion:** It was concluded in our study that BMA and BMB are important, useful complementary diagnostic procedures which gives a higher diagnostic yield when performed simultaneously.

KEYWORDS

pancytopenia, Bone marrow aspiration, Bone marrow biopsy, concordance.

INTRODUCTION

The term pancytopenia means reduction in all the three major elements of blood; hence it is the simultaneous presence of anemia, leucopenia and thrombocytopenia(1). It is not a disease entity but a triad of findings that may result from various disease processes primarily or secondarily involving the bone marrow(2). Pancytopenia exist when Hb <13gm/dl for male, Hb <12gm/dl for female. WBC count <4x10⁹/L for male and female. Platelets <150x10⁹/L for male and female (3).

Bone marrow examination is a useful and cost effective diagnostic procedure in hematological practice for the diagnosis of both neoplastic and non-neoplastic hematological diseases(4). Bone marrow examination not only helps in final diagnosis but can also help in indicating the approach to diagnosis based on various parameters like cellularity (hypocellular or hypercellular), blasts (for leukemia), abnormal cells (lymphoma, plasma cells, carcinoma cells, histiocytes), organisms (fungus, parasite), dysplastic changes in cells (myelodysplastic syndrome) or megaloblastic maturation(5).

Bone marrow aspiration alone is usually sufficient to diagnose nutritional anemia, most of the acute leukemia and immune thrombocytopenia. Aspiration is useful in making out better individual cell morphology, whereas biopsy is useful in bone marrow architectural pattern and distribution. Correlation with bone marrow biopsy is important in cases where aspirate is hemodiluted or in hypocellular marrow. Trephine biopsy does provide important diagnostic information in patients with granulomatous disease, myelofibrosis and bone marrow infiltration (6).

MATERIAL AND METHODS

The present study was a hospital based cross sectional study which was carried out in the department of Pathology at Maharaja Agrasen Medical College Agroha, Hisar. Thirty six cases of pancytopenia were included.

The inclusion criteria for this study were:

1. Patients with age more than 18 years, Hb <13gm/dl for male and <12gm/dl for female
2. WBC count <4x10⁹/L for male and female
3. Platelets <150x10⁹/L for male and female
4. Patients willing to give consent for bone marrow aspiration and

biopsy (7).

The exclusion criteria were:

1. Patients with age less than 18 years
2. Patients who had already been diagnosed with pancytopenia
3. Patients who did not give consent for bone marrow aspiration and biopsy.

A complete profile of the patient which included Age, Sex, and clinical features were recorded. Patients were investigated for complete blood count and peripheral blood film examination. Only those patients were included in the study in which both bone marrow aspiration and trephine biopsy were performed. Posterior superior iliac supine was the preferred site. Bone marrow aspiration and trephine bone marrow biopsy was done using Salah's needle and Jamshidi needle respectively. Bone marrow aspirate was transferred to set of slides, films prepared, dried and fixed in methanol for 15 minutes and later stained with Leishman stain. Cytochemical stains such as myeloperoxidase (MPO), periodic acid Schiff (PAS) were done whenever necessary. Prussian blue staining was done in cases of anemia. Fixation of biopsy was done using 10% formalin and surface decalcification was done using 5% ethylene diamine tetra acidic acid. Then the tissue was processed as routine histological processing and stained with hematoxylin and eosin stain.

RESULTS

Mean age of the study population was 41.97±17.66 years with age range of 18-80 years. Male outnumbered female patients i.e. 21 (58.34%) male and 15 (41.66%) female with male to female ratio 1.4:1.

Bone marrow aspiration was found to be satisfactory for evaluation in 32 (88.9%) and in rest 4 (11.1%) cases, it was unsatisfactory.

Cellularity of bone marrow was assessed taking in consideration the age of the patient.

Aspirated smears were found to be hypercellular in 28 (75%) cases, normocellular in 5 (13.9%) cases and in 3 (11.1%), cellularity couldn't be assessed as it was either dry tap or marrow diluted with blood.

Majority of cases 19(52.77%) had macrocytic RBC picture followed by dimorphic blood picture in 10 (27.77%) cases, normocytic normochromic picture in 5 (13.88%) cases and microcytic hypochromic blood picture in 2 (5.55%) cases.

In present study, commonest cause of pancytopenia was megaloblastic anemia in 52.8% cases followed by dimorphic in 16.7% cases, acute leukemia in 8.3% cases, iron deficiency anemia and multiple myeloma contributed 5.5% each. Aplastic anemia, tuberculosis and myelodysplastic syndrome (MDS) each contributed 2.8%.

The concordance and discordance rate between BMA and BMB findings in making etiological diagnosis of pancytopenia in various hematological diseases are depicted in table-1.

Table 1: Correlation Of Diagnosis Established On BMA + BMB

TYPE OF CASES	TOTAL	BMA + BMB CONCORDANCE	BMA ALONE DISCORDANCE	BMB ALONE DISCORDANCE
MEGALOBLASTIC ANEMIA	19	14 (73.7%)	5 (26.3%)	0
DIMORPHIC ANEMIA	6	4 (66.7%)	2 (33.3%)	0
MICRO NORMOBLASTIC ANEMIA	2	1 (50%)	1 (50%)	0
ACUTE LEUKEMIA	3	2 (66.7%)	0	1 (33.3%)
MULTIPLE MYELOMA	2	1 (50%)	0	1 (50%)
APLASTIC ANEMIA	1	0	0	1 (100%)
TB	1	0	0	1 (100%)
MDS	1	0	0	1 (100%)
HYPERSPLENISM	1	1 (100%)	0	0
TOTAL	36	23 (63.8%)	8 (22.2%)	5 (14%)

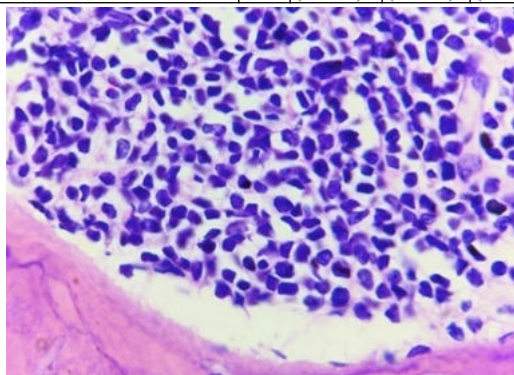


Figure 1: BMB Showing sheet of lymphoblasts in ALL (H&E, 1000x)

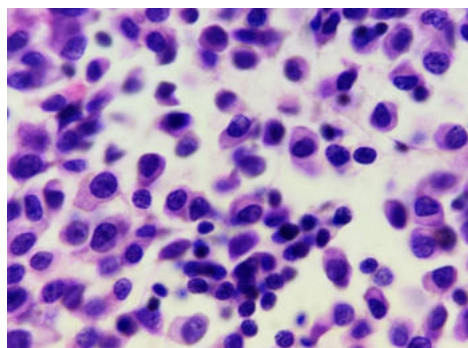


Figure 2: Bone marrow biopsy showing sheet of plasma cells in multiple myeloma case (H&E, 1000x)

DISCUSSION

Bone marrow aspiration was diagnostic in all 19 (100%) cases of megaloblastic anemia whereas bone marrow biopsy was diagnostic in 14 (73.70%) cases of megaloblastic anemia and showed erythroid hyperplasia in rest 5 (26.30%) cases. The concordance and discordance rate between BMA and BMB in diagnosis of megaloblastic anemia was 73.7% and 26.3% respectively. BMA was diagnostic in all six cases of dimorphic anemia whereas bone marrow biopsy was diagnostic in 4 cases (66.7%) and showed erythroid hyperplasia in rest 2 (33.3%) cases. The concordance and discordance rate between BMA and BMB in diagnosis of dimorphic anemia was 66.7% and 33.3% respectively. Two cases of micronormoblastic anemia were diagnosed on BMA but BMB was diagnostic in one case and in other one case diagnosis of erythroid hyperplasia was made. The concordance and discordance rate between BMA and BMB in diagnosis of micronormoblastic anemia was 50% each. Overall in our study, 100% cases of nutritional anemia were diagnosed on BMA. These findings were similar to study conducted by Mehra et al in which BMA alone was diagnostic in 94.7% cases of nutritional anemia(8). In present study concordance between BMA and BMB in cases of nutritional anemia was seen in 70.27% cases. Similar results were seen by Verma et al in which they found 78.94% concordance between BMA and BMB in cases of nutritional anemia(9).

Out of three cases of acute leukemia concordance between BMA and BMB was seen in 2 cases. BMB was diagnostic in one discordant case as it was dry tap on aspiration which could be explained due to tightly packed marrow by leukemic cells. Aspirated smears in 2 cases of acute leukemia showed >20% myeloblasts. In one case auer rods were noted on bone marrow aspirate smears and in another, MPO positivity was seen in more than 3% of myeloid series cells and were labeled as acute myeloid leukemia (AML). One case diagnosed on bone marrow biopsy showed lymphoblasts >20% (figure 1) and was labeled as acute lymphoblastic leukemia (ALL). The concordance and discordance rate between BMA and BMB in acute leukemia was calculated as 66.7% and 33.3% respectively. Our study was comparable to study conducted by Mehra et al in which concordance and discordance rate between BMA and BMB in leukemia cases was 62.5% and 37.5% respectively(8). Our study was also similar to study conducted by Verma et al in which concordance and discordance rate between BMA and BMB in leukemia cases was 60% and 40% respectively(9). The results were in contrast to study conducted by Patro et al, they diagnosed 34 cases of acute leukemia, 30 were diagnosed on BMA and BMB both and 4 cases were diagnosed only on BMB. The concordance rate calculated was 88.23% and discordance was 11.77%.¹⁰ This may be attributed to less number of leukemia cases in present study.

There were two cases of multiple myeloma in our study. BMA and BMB showed concordance in one case. In another case, aspiration was inconclusive as it showed scattered plasma cells, whereas BMB showed sheets of plasma cells (figure 2). Bone marrow biopsy is recommended in multiple myeloma even if an adequate aspirate is obtained, since it is needed as a baseline to assess post treatment response when no adequate aspirate is obtained. These cases were labeled as multiple myeloma after correlating bone marrow biopsy features, radiological and biochemical evaluation. The concordance and discordance rate between BMA and BMB in multiple myeloma cases was 50% each. The results were in contrast to study conducted by Patro et al, in which they diagnosed 8 cases of multiple myeloma, 6 were diagnosed on BMA and BMB both and 2 cases were diagnosed only on BMB. The concordance and discordance rate calculated was 75% and 25% respectively(10). This may be attributed to less number of multiple myeloma cases in present study.

Bone marrow aspiration was inconclusive in cases of aplastic anemia and tuberculosis as in case of aplastic anemia, aspirate was dry tap and in tuberculosis, it was bloody tap. Bone marrow biopsy showed markedly reduced cellularity and presence of mature lymphocytes and plasma cells in aplastic anemia. In case of tuberculosis, focal epithelioid granuloma along with caseous necrosis was noted on bone marrow biopsy.

Both cases showed 100% BMB discordance. The results of our study were similar to study conducted by Mehra et al in which total of 2 cases were diagnosed as aplastic anemia on bone marrow biopsy which was given as hypocellular marrow on aspiration and showed 100% BMB discordance. Trephine biopsy gives the qualitative and quantitative assessment of cellularity, therefore, is confirmatory in the diagnosis of aplastic anemia(8).

Only one case of MDS was diagnosed in our study on bone marrow biopsy and showed BMB discordance. Aspirate was diluted with blood and bone marrow biopsy detected features of hypercellularity, trilineage dysplasia and dysmegakaryopoiesis, abnormal localization of myeloid precursors. The results were in contrast to study conducted by Mehra et al, they diagnosed 2 cases of MDS and both were diagnosed on BMA and BMB(8). The concordance rate calculated was 100%. The results of our study were also in contrast to study done by Verma et al which showed 83.33% concordance between BMA and BMB(9). This may be attributed to less number of MDS cases in our study. The literature has mentioned that biopsy may sometimes be more helpful in the assessment of cellularity and findings of dysmegakaryopoiesis and abnormal localization of myeloid precursors as stated by Khonglah et al(11).

Only one case of hypersplenism was diagnosed and showed 100% concordance with both aspiration and biopsy showing normocellular marrow. Patient presented with pancytopenia, moderate splenomegaly and features of portal hypertension in the form of hemorrhoids. BMA and BMB showed normocellular bone marrow. The results of our study were similar to study conducted by Patro et al in which 100% concordance with BMA and BMB was observed in hypersplenism cases(10).

The overall concordance and discordance rate between BMA and BMB was 63.8% and 36.2% respectively. Our results were in concordance with Verma et al in which they calculated concordance rate between BMA and BMB in 46 out of 72 (63.90%) cases(9).

CONCLUSION

Bone marrow examination is an important and useful investigation for the study of various hematological disorders. The superiority of one method over the other depends upon the specific disease process. It is deduced in our study that BMA is superior to BMB in diagnosis of nutritional anemia cases as morphology of individual cell is better appreciated. Bone marrow biopsy is mandatory for diagnosis in cases with dry tap or diluted marrow on aspiration. Bone marrow biopsy is better tool for assessment of cellularity, architectural pattern, and pattern of marrow infiltration and for detection of focal lesion, if any. In our study, BMB was more helpful in diagnosing aplastic anemia, multiple myeloma, MDS, acute leukemia and granulomatous lesion like TB. So, bone marrow aspiration and bone marrow biopsy are complementary to each other and both should be performed simultaneously for complete marrow work and evaluation.

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