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Original Article

Evaluation of sensitivity and specificity of bone marrow trephine biopsy tests in an Indian teaching hospital

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ABSTRACT

Introduction: Bone marrow aspiration (BMA) and bone marrow biopsy (BMB) is an indispensable diagnostic tool for evaluating haematological and non-haematological disorders and patient follow-up in present era. We have compared the advantages of trephine biopsy over bone marrow aspiration in these patients.

Aim and objective: To evaluate sensitivity and specificity of trephine biopsy test for haematological and non haematological disorder patients in comparison to bone marrow aspiration test.

Materials and method: In this 1 year prospective study (June 2014–May 2015), we evaluated the haematological and non-haematological disorder patients by BMA and BMB (aided with I.H.C. when ever needed). The sensitivity and specificity of the tests were calculated.

Results: Among, final 504 hemotological/non haematological disorder patients, 416 cases were diagnosed (+ve) in BMA test, where as it was 494 in BMB test and with chi^2 test it was highly significant as p = 0.0001. It was concluded that True positive cases were 416, True negative were 9 cases, false negative 78 cases and false positive was in one case only. The sensitivity and specificity of bone marrow trephine biopsy test was 84% and 90% respectively.

Conclusion: BMB (aided with I.H.C) is a gold standard test for detecting different haematological and non hamatological disorders. In our study the sensitivity and specificity of BMB test was 84% and 90% respectively. When performed in association with BMA in the same sitting, significantly augments the chances of reaching a correct diagnosis.

1. Introduction

Bone marrow examination includes pathological examination of bone marrow aspiration (BMA) and bone marrow biopsy (BMB) specimens. Peripheral blood gives much of information regarding haematological disorders but many a times, "the assessment of haematopoesis with BMA and BMB" are highly required. BMA and BMB are an invaluable diagnostic tool for both haematological and non-haematological disorders. It is also routinely used for follow up of patients undergoing chemotherapy for hematolymphoid malignancies.[1] Marrow samples can be obtained from various sites. BMA and trephine BMB are commonly done from posterior superior iliac spine and iliac crest. BMA can be done from sternum with patient lying on his back, and pillow under the shoulder. Ideally it should not be done from sternum, because of risk of damaging vital organs. BMA can also be done from tibia in children up to 2 years of age.

BMA is the best tool for studying morphology, differential count and M:E ratio. It can be used for flowcytometry, cytogenetics as well as procedures like Polymerase chain reaction. whereas trephine BMB gives information regarding cellularity, architecture and focal lesions. Moreover, trephine biopsy is mandatory for staging of lymphomas.[2] Rarely marrow examination provides the only clue regarding occult malignancies.[3]

BMB is not only the 'clue' for infiltration, but also provides pattern of involvement.[4] In earlier days surgical trephine biopsy was in practice. With introduction of needle trephine biopsy in late 1950s, things have become much simpler and minimally invasive.[4] However, trephine biopsy, unlike aspiration, demands more technical skills and is time consuming as well as a painful procedure.

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Interpretation depends on numerous factors like quality of tissue section and availability of ancillary techniques like immunohistochemistry, special staining and good coordination between hematopathologists and histopathologists.[5] Bone marrow procedures help in confirming the clinical diagnosis as well as some new diagnosis, which were not suspected previously. Few studies have analyzed the diagnostic accuracy of marrow aspirates with trephine biopsies.[1,6–8] Here, we compare these two tests i.e. BMB and BMA, to evaluate the sensitivity and specificity of BMB in haematological and non-haematological patients in the same sitting.

2. Material and methods

This single centre prospective study was carried out, by the Department of Pathology (Lab Hematology), Department of Hemato-oncology and Stem cell transplantation, Medicine and Paediatrics in IMS & SUM Hospital from June 2014 to May 2015. This study was done for bone marrow examination on patients presenting with anemia, history of thrombocytopenia, leukopenia, pancytopenia, marked leucocytosis, bleeding/disseminated intravascular coagulation, fever and organomegaly. Both indoor and outdoor patients, showing features, raising suspicion of involvement of bone marrow by non haematological/haematological disorders were included. Relevant history, informed consent and other bio-datas were noted. Patients were investigated for routine complete blood count (CBC), peripheral blood smear comment (PSC), reticulocyte count, coagulation profile (prothrombin time, activated partial thromboplastin time, thrombin time, fibrinogen). Then BMA and trephine BMB were done for these patients at the same sitting. A total of 595 (570 + 25) cases of BMA along with trephine BMB were carried out. Out of which 25 tests were inadequate for assessment, hence excluded from the study. Adequacy of biopsy was based on the presence of at least 5–6 intertrabecular spaces. So the cohort comprised of 570 cases. Among them 66 cases were post induction marrows for assessment of remission. So, these 66 cases were excluded from this study. Finally, for comparison of trephine BMB with BMA tests a total of 504 cases were studied.

The clinical indications, physical findings and peripheral smear findings of patients were compiled. Under local anesthesia (2% xylocaine, 2% lignocaine) infiltration of periosteal region, the BMA and BMB were done from posterior superior iliac spine, by using jamshidi needle. Patient is made to lie on their side (lateral decubitus position). A Bone marrow aspiration needle was inserted through the skin with pressure until it abuts the bone. The needle was advanced through the bony cortex and in the marrow cavity with twisting motion of the hand and wrist of the clinician. After the needle tip reaches the marrow cavity, a syringe was attached to the back of the jamshidi needle and aspiration done. A twisting motion is performed during the aspiration to avoid excess content of blood in the sample. For BMA procedure, Jamshidi needle (13 G for children, 11 G for adults) and Illinois needle size 18 were used. Subsequently 0.25–0.5 ml aspirate was withdrawn using a 2 ml plastic syringe and smears were prepared immediately. Trephine BMB was done using Jamshidi biopsy needle and at the same incision but approximately 0.5–1.0 cm away from aspiration site to avoid getting a haemorrhagic biopsy. In patients of thrombocytopenia, 5 minof firm pressure was applied at the end of the procedure. At the same time patients were asked to lie down on their back for further 10–15 min for prolonged pressure. Aspiration smears were stained with Giemsa stain after being fixed in alcohol. Prussion blue stain for iron store assessment and grading was done routinely. Biopsy specimen was fixed using 10% buffered formalin and decalcified using 10% formic acid for 24 h and processed by preparing paraffin wax embedding sections. Histological sections were made approximately 1–2 μm thick. Haematoxylin and eosin (H&E) stain was used and reticulin fibres were stained with Gomori's silver impregnation method routinely. Immuno histo chemistry (IHC) was done as and when required.

3. Results

Both BMA and trephine BMB tests were performed on all 504 cases of haematological and non-haematological patients. In BMA, 416 cases were diagnosed (positive) whereas in trephine BMB, it was 494 cases (Table 1). The chi-square statistic is 68.7673 and p-value is 0.0001. This result is significant at $p \leq 0.05$.

The 504 new cases were divided into 3 age group categories. 4 cases were below 1 yrs of age, 91 cases belonged to 1–14 yrs age group and 410 cases were above 14 yrs of age (Fig. 1). The cases were divided into groups according to the final diagnosis, after assessing the peripheral smears, bone marrow aspiration and trephine biopsy.

Acute leukemia was the largest group comprising of 128 cases. Bone marrow aspiration was in agreement with trephine biopsy in 110 cases but was inadequate in 18 cases which had tightly packed marrow with blasts on biopsy. Aplastic anemia was the next single largest group with 45 cases. Biopsy in aplastic anemia is of utmost importance for definitive diagnosis. 6 cases showed diluted/non diagnostic aspirates which were diagnosed on only trephine biopsy (Figs. 2 and 3). One case diagnosed in aspiration as hypoplastic marrow suggestive of aplastic anemia, showed focal increase in immature precursors and diagnosis was revised to hypoplastic myelodysplastic syndrome (MDS) in biopsy.

Out of 52 Myeloproliferative neoplasm cases of MPN, 42 cases were of CML, 2 cases of Essential thrombocythemia (ET), 1 case of Polycythemia vera (PV), 3 cases of Chronic Eosinophilic Leukemia/Hypereosinophilic syndrome (CEL/HES) and 4 cases were of Myelofibrosis. Poor aspiration material was found in 9 cases of CML. Fibrosis was increased in 7 cases. All 4 cases of Myelofibrosis showed dry tap, trephine showed marked fibrosis and atypical bizarre megakaryocytes (Fig. 4a–c).

A total 41 cases of lymphoma were analyzed, of which 8 cases were Hodgkin's lymphoma, and 33 cases were NHL. Out of 33 cases of NHL, few cases showed occasional atypical cell in marrow aspirate (but not diagnostic of marrow infiltration by lymphoma). In BMB, four cases of low grade B cell lymphoma (Fig. 5a and b), 1 case of Follicular lymphoma were detected. One case of Burkitt lymphoma diagnosed on IHC and unfortunately 02 cases could not be typed. None of the Hodgkins lymphoma showed marrow infiltration in aspiration. Among the total, Chronic lymphocytic leukemia (CLL/SLL) comprised of 16 cases. All cases of CCL/SLL were diagnosed in BMA. Among 42 cases of multiple myeloma (plasma cell dyscrasia) 41 cases were detected in BMA. One case of aspiration showed hypercellular marrow with poor cell trails showing occasional plasma cells and biopsy was diagnosed to be of multiple myeloma with marked plasmacytosis. Six cases of metastasis were encountered in biopsy out of which 2 (33.3%) were missed in aspiration.

Out of four cases, two cases showed granulomas in both aspiration and biopsy. Whereas two cases showed granulomas in biopsy only (missed in aspiration). Out of 25 cases of MDS, aspiration and biopsy correlated in 20 cases, in rest 5 cases, diagnosis was done in biopsy only. In Immune Thrombocytopenic purpura (ITP), there were 100% concordance between aspiration and biopsy. Out of 5 cases of Pure Red Cell Aplasia (PRCA), trephine biopsy of one case showed presence of paratrabecular collection of lymphoid cells pointing towards the possibility of lymphoma as a probable cause of PRCA (Secondary PRCA). However, the patient was lost to follow

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