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Assessment of hematological diseases by bone marrow examination in patients in Patna medical college and hospital

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Abstract
Bone marrow aspiration (BMA) examination is one of the most frequent and relatively safe invasive procedures. Though an invasive procedure it can be easily performed even in the presence of thrombocytopenia with little or no risk of bleeding. .Biopsy of bone marrow is an adjunct to the study of haematological disorders which are quite frequent in all age groups. The spectrum of haematological disorders is relatively different in the developing world than the developed countries. Commonly it is done for the evaluation of unexplained cytopenias and malignant conditions like leukemia. Bone marrow examination is also at times done for the diagnosis or staging of a neoplasm and storage disorders.
The present study was planned in the Department of Pathology, Patna Medical College and Hospital, Patna from April 2018 to sept 2018. Total 50 cases of the Haematological disorders were enrolled in the present study. Patients were explained about the procedure. In each case a det ailed history along with systemic, general and local examination and routine haematological investigation was carried out prior to bone marrow examinations.
Bone marrow examination is necessary to diagnose, prognosis, and/ or evaluate therapeutic response for a variety of hematologic and non-hematologic problems. The procedure remains a veritable tool in the diagnoses and management of a wide range of haematological and some non-haematological diseases. Bone marrow aspiration & bone marrow biopsy are diagnostic procedures used routinely nowadays, easy procedure does not require sophisticated equipment's.

Keywords: bone marrow aspiration, Leukemia, Megaloblastic anemia, hematological diseases, etc

1. Introduction
Bone marrow examination refers to the pathologic analysis of samples of bone marrow obtained by bone marrow biopsy (often called trephine biopsy) and bone marrow aspiration. Bone marrow examination is used in the diagnosis of a number of conditions, including leukemia, multiple myeloma, lymphoma, anemia, and pancytopenia. The bone marrow produces the cellular elements of the blood, including platelets, red blood cells and white blood cells. While much information can be gleaned by testing the blood itself (drawn from a vein by phlebotomy), it is sometimes necessary to examine the source of the blood cells in the bone marrow to obtain more information on hematopoiesis; this is the role of bone marrow aspiration and biopsy.
Bone marrow samples can be obtained by aspiration and trephine biopsy. Sometimes, a bone marrow examination will include both an aspirate and a biopsy. The aspirate yields semi-liquid bone marrow, which can be examined by a pathologist under a light microscope and analysed by flow cytometry, chromosome analysis, or polymerase chain reaction (PCR). Frequently, a trephine biopsy is also obtained, which yields a narrow, cylindrically shaped solid piece of bone marrow, 2 mm wide and 2 cm long (80 μL), which is examined microscopically (sometimes with the aid of immunohistochemistry) for cellularity and infiltrative processes. An aspiration, using a 20 mL syringe, yields approximately 300 μL of bone marrow [1]. A volume greater than 300 μL is not recommended, since it may dilute the sample with peripheral blood [1].
Bone marrow aspiration and trephine biopsy are usually performed on the back of the hipbone, or posterior iliac crest. An aspirate can also be obtained from the sternum (breastbone). For the sternal aspirate, the patient lies on their back, with a pillow under the shoulder to raise the chest. A trephine biopsy should never be performed on the sternum, due to the risk of injury to blood vessels, lungs or the heart. Bone marrow aspiration may also be performed on the tibial (shinbone) site in children up to 2 years of age while spinous process aspiration is frequently done in a lumbar puncture position and on the L3-L4 vertebrae.
Anesthesia is used to reduce surface pain at the spot where the needle is inserted. Pain may result from the procedure's insult to the marrow, which cannot be anesthetized, as well as short periods of pain from the anesthetic process itself. The experience is not uniform; different patients report different levels of pain, and some do not report any pain at certain expected points [2].
A bone marrow biopsy may be done in a health care provider's office or in a hospital. Informed consent for the procedure is typically required. The patient is asked to lie on their abdomen (prone position) or on their side (lateral decubitus position). The skin is cleansed, and a local anesthetic such as lidocaine or procaine is injected to numb the area. Patients may also be pretreated with analgesics and/or anti-anxiety medications, although this is not a routine practice.
Typically, the aspirate is performed first. An aspirate needle is inserted through the skin using manual pressure and force until it abuts the bone. Then, with a twisting motion of clinician's hand and wrist, the needle is advanced through the bony cortex (the hard outer layer of the bone) and into

the marrow cavity. Once the needle is in the marrow cavity, a syringe is attached and used to aspirate ("suck out") liquid bone marrow. A twisting motion is performed during the aspiration to avoid excess content of blood in the sample, which might be the case if an excessively large sample from one single point is taken. Subsequently, the biopsy is performed if indicated. A different, larger trephine needle is inserted and anchored in the bony cortex. The needle is then advanced with a twisting motion and rotated to obtain a solid piece of bone marrow. This piece is then removed along with the needle. The entire procedure, once preparation is complete, typically takes 10–15 minutes. If several samples are taken, the needle is removed between the samples to avoid blood coagulation.

After the procedure is complete, the patient is typically asked to lie flat for 5–10 minutes to provide pressure over the procedure site. After that, assuming no bleeding is observed, the patient can get up and go about their normal activities. Paracetamol (aka acetaminophen) or other simple analgesics can be used to ease soreness, which is common for 2–3 days after the procedure. Any worsening pain, redness, fever, bleeding or swelling may suggest a complication. Patients are also advised to avoid washing the procedure site for at least 24 hours after the procedure is completed.

There are few contraindications to bone marrow examination. It is important to note that thrombocytopenia or bleeding disorders are not contraindications as long as the procedure is performed by a skilled clinician [3]. Bone marrow aspiration and biopsy can be safely performed even in the setting of extreme thrombocytopenia (low platelet count). If there is a skin or soft tissue infection over the hip, a different site should be chosen for bone marrow examination.

While mild soreness lasting 12–24 hours is common after a bone marrow examination, serious complications are extremely rare. In a large review, an estimated 55,000 bone marrow examinations were performed, with 26 serious adverse events (0.05%), including one fatality [4]. The same author collected data on over 19,000 bone marrow examinations performed in the United Kingdom in 2003, and found 16 adverse events (0.08% of total procedures), the most common of which was bleeding. In this report, complications, while rare, were serious in individual cases [5].

Currently, inspection of bone marrow is considered one of the most valuable diagnostic tools for evaluating hematologic disorders [6]. Indications have included diagnosis, staging, and therapeutic monitoring for lymphoproliferative disorders such as chronic lymphocytic leukemia CLL), Hodgkin and non-Hodgkin lymphoma, hairy cell leukemia, myeloproliferative disorders, myelodysplastic syndrome and multiple myeloma. Furthermore, evaluation of cytopenia [7], thrombocytosis, leukocytosis, anemia, and iron status can be performed. Bone marrow inspection is also done to rule out inflitrative infectious diseases such as fungal infections, tuberculosis, and other granulomatoses.

The application of bone marrow analysis has grown to incorporate other, nonhematologic, conditions. For example, in the investigation for fever of unknown origin (FUO), specifically in those patients with AIDS [8], the marrow may reveal the presence of microorganismsn that can cause infections such as tuberculosis, Mycobacterium avium-intracellulare (MAI; also referred to as Mycobacterium avium complex [MAC]) infections, histoplasmosis, leishmaniasis, and other disseminated fungal infections.

Furthermore, the diagnosis of storage diseases (eg, Niemann-Pick disease and Gaucher disease [9]), as well as the assessment for metastatic carcinoma and granulomatous diseases (eg, sarcoidosis) can be performed. Bone marrow analysis may reveal toxic effects of certain offending medications or substances (eg, alcohol) or nutritional deficiencies (eg, deficiencies of copper/zinc or vitamin B12/folate).

Bone marrow analysis can also be performed in patients with idiopathic thrombocytopenic purpura (ITP), incidental elevated serum paraprotein levels, iron deficiency anemia, polycythemia vera, essential thrombocytosis, or infectious mononucleosis; but these conditions are often more appropriately diagnosed by routine laboratory evaluation. [10] Thrombocytopenia is not in itself a contraindication for bone marrow aspiration and biopsy.

Bone marrow aspiration (BMA) examination is one of the most frequent and relatively safe invasive procedures. Though an invasive procedure it can be easily performed even in the presence of thrombocytopenia with little or no risk of bleeding. .Biopsy of bone marrow is an adjunct to the study of haematological disorders which are quite frequent in all age groups. The spectrum of haematological disorders is relatively different in the developing world than the developed countries. Commonly it is done for the evaluation of unexplained cytopenias and malignant conditions like leukemia. Bone marrow examination is also at times done for the diagnosis or staging of a neoplasm and storage disorders.

Methodology

The present study was planned in the Department of Pathology, Patna Medical College and Hospital, Patna April 2018 to Sept 2018. Total 50 cases of the Haematological disorders were enrolled in the present study. Patients were explained about the procedure. In each case a detailed history along with systemic, general and local examination and routine haematological investigation was carried out prior to bone marrow examinations.

The procedure of Bone marrow aspiration was done after giving 2% xylocaine as local anesthesia either from sternum or from posterior iliac spine. Leishman stained peripheral blood and bone marrow smears were studied. Bone marrow trephine biopsy was performed as an adjuvant when the bone marrow aspiration yields a bloody tap or dry tap. Bone marrow examination was done on Leishman stained bone marrow aspiration smears and on Hematoxylin and eosin stained bone marrow trephine biopsy sections.

They were informed about possible complications but also assured for safety, simplicity and usefulness of the procedure. All the patients were informed consents. The aim and the objective of the present study were conveyed to them. Approval of the institutional ethical committee was taken prior to conduct of this study.

Following was the inclusion and exclusion criteria for the present study.

Inclusion Criteria: All cases that were referred for bone marrow examination and also for staging of lymphomas and metastasis.

Exclusion Criteria: Children below 10 year of age were excluded

Results & Discussion

Haematological disorders include a wide range of diseases ranging from reactive hyperplasia to haematological malignancies. Bone Marrow Aspiration plays a very important role not only in determining the cause of disease but also help in establishing a definitive diagnosis. It's a relatively safe procedure which can be performed on an outpatient basis.

The spectrum of haematological disorders both in children and adults is very wide. Bone marrow examination is a useful test in reaching the final diagnosis. Bone marrow trephine biopsy is an important adjunct to aspiration in arriving at an etiological diagnosis. BMA is one of the most common and safe procedure done routinely in medical practice. Rarely infection, excessive bleeding or embolism has been reported after bone marrow biopsy [11].

The spectrum of hematological disorders is very wide. Examination of the bone marrow is one of the most important diagnostic pillar in diagnosing hematological disorders. Bone marrow aspiration and trephine biopsy are the two procedures done for the diagnosis of hematological and non-hematological disorders. "Frequently it is a combination of clues gathered from examination of several different preparations that leads to a correct diagnosis [12].

Table 1: Age & Sex Distribution

Sex	Number of Cases
Males	28
Females	22
Age Group	
10 – 20 years	8
21 – 30 years	9
31 – 40 years	9
40 – 50 years	7
51 – 60 years	11
Above 60 years	6
Total	50

Table 2: Various haematological disorders

Disorders	Number of Cases
Erythroid hyperplasia	17
Megaloblastic anemia	5
Dimorphic anemia	1
Anemia of chronic disease	0
Hypoplastic marrow	1
Acute leukemias	3
Chronic leukemias	5
Multiple myeloma	2
Myelofibrosis	1
ITP	2
Metastasis	1
Staging	2
Normal study	6
Remission	2
Inadequate	1
Infective pathology	1
Total	50

Kumar et al. [13] stated in his study bone marrow aspiration and biopsy should be performed simultaneously in pancytopenic patients when the diagnosis is elusive.

The commonest cause for pancytopenia was megaloblastic anemia (54%), followed by aplastic anemia (25.6%). The study results are similar with Gayatri et al. 13 (74.04%, 18.26%) According to recent studies by Chandra et al. [14] 2011, Parajuli et al. [15] and Khan et al. [16] 2014 erythroid hyperplasia is the predominant diagnosis which were comparable to our study. The finding of a dry tap should never be dismissed as being due to faulty technique and always needs a bone marrow biopsy. Trephine biopsy is necessary for making a diagnosis due to incomplete information provided by aspiration.

Because of the lack of laboratory resources, we could not find out the etiology of megaloblastic anemia. Serum cobalamin level and red cell folate level were advised to confirm the diagnosis of megaloblastic anemia. Although iron deficiency anemia is the most common nutritional deficiency worldwide, almost all cases are diagnosed on the basis of peripheral blood findings and/or biochemical findings. Bone marrow examination is usually not done in these cases. That is the reason why iron deficiency anemia was not featured in the list of diagnoses in our study. Similar finding was observed by other national and international studies [17]. However, Momami et al from Jordan found iron deficiency anemia as the third most common disorder [18].

In the study of Atla et al, 19% cases had aplastic anemia. [19] Some other studies had lower incidence of the disease. It was seen in only 5.3% cases in a study done by Pudasaini et al. [15] The frequency was even lower in a study carried out in Jordan by Momani et al; only one case was found in that study. [18] Although aplastic anemia is an autoimmune disease, its incidence is equal in both sexes [20].

An important limitation of marrow examination obtained by aspirate is the admixing of marrow and sinusoidal blood, which may not allow for reliable estimates of marrow cellularity. This evaluation is of particular importance in the hyper cellular marrow which yields a "dry tap" or only dilutes sinusoidal blood. Thus, the use of the biopsy avoids misinterpretation of cellularity by smears in patients in whom the biopsy confirmed a normal, hypo cellular or hyper cellular marrow.

The decision to perform a marrow aspiration alone or in combination with marrow biopsy depends on the diagnosis being considered. In nutritional anemias, most hematologic malignancies and immune thrombocytopenia, marrow aspiration alone is sufficient, but for detection of disorders with focal marrow involvement biopsies are must [21].

Conclusion

Bone marrow examination is necessary to diagnose, prognosis, and/ or evaluate therapeutic response for a variety of hematologic and non-hematologic problems. The procedure remains a veritable tool in the diagnoses and management of a wide range of haematological and some non-haematological diseases. Bone marrow aspiration & bone marrow biopsy are diagnostic procedures used routinely nowadays, easy procedure does not require sophisticated equipment's.

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