ROLE OF BONE MARROW ASPIRATION IN DIAGNOSIS OF HAEMATOLOGICAL DISORDER

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ABSTRACT

BACKGROUND

The bone marrow examination is an essential investigation for the diagnosis of disorders of the blood and bone marrow. This simple and relatively safe procedure is important, particularly in resource poor centres since access to adjuvant diagnostic techniques are often lacking or absent.

MATERIALS AND METHODS

189 patients of all age groups were studied for haematological and non-haematological disorders by bone marrow aspiration in the Department of Pathology, MGM Medical College during the period of 2014 to 2016.

RESULTS

Majority of the patients who had bone marrow aspiration were aged 0-15 years. The male-to-female ratio was 1:1.03. Most (97%) of the marrow aspirate examined had definitive pathologic features, while 14 (7%) were normal marrow elements. Out of 189 cases of bone marrow aspiration, acute leukaemia was the most common haematological disease diagnosed using this procedure. Acute lymphoblastic leukaemia was more common than acute myeloid leukaemia. Aplastic anaemia was seen in 16% cases. Megaloblastic anaemia occurred more commonly than other anaemias. Megaloblastic anaemia was seen in 13 cases (7%) and microcytic anaemia was seen in 5 cases (3%). There were 10 cases (5%) of Idiopathic Thrombocypenic Purpura. Myelodysplastic syndrome and multiple myeloma was seen in 7% and 2% cases respectively. Storage disorder was seen in 3 cases (2%), out of this 02 cases were Gaucher's disease and one case was Niemann-Pick's disease.

CONCLUSION

Bone marrow examination is an important step to arrive at the confirmatory diagnosis of many haematological disorders. This procedure remains a veritable tool in the diagnosis and management of a wide range of haematological diseases, especially in a resource poor centre.

KEYWORDS

Bone Marrow Aspiration (BMA), Acute Leukaemia, Aplastic Anaemia, Pancytopenia, Pure Red Cell Aplasia (PRCA), Acute Lymphoblastic Leukaemia (ALL), Acute Myeloid Leukaemia (AML).

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BACKGROUND

Bone Marrow Aspiration (BMA) is the most frequent and safe invasive procedures done routinely in the hospitals for the diagnosis and management of haematological disorder.[1-3] There is very little or no risk of bleeding and we can do safely this procedure in cases of severe thrombocytopenia.[2] Bone marrow aspiration is primarily utilised for cytological assessment with analysis directed towards morphology and obtaining a differential cell count. Bone marrow examination also gives explanation for unexplained cytopenias and leukaemia.[2] It gives a more complete picture of the reaction of the haemopoietic tissue to anaemia than can be gained from Peripheral Blood Smear (PBS) alone.[1]

Diseases affecting the bone marrow may be primary or a secondary spread to the marrow. In both cases, the normal marrow cellular architecture is distorted. Anaemia is a common presentation in most of these diseases, whether haematological or otherwise. A detailed description of the morphology of the marrow elements may provide sufficient explanation for unexplained cytopaenias, leukaemia and other haematological disorders including metastases to the bone marrow.[4]

AIMS AND OBJECTIVES

The aim of the study is to evaluate the cytological pattern of various haematological disorders reported in bone marrow aspiration.

Design of study- Prospective study.

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MATERIALS AND METHODS

A prospective study of 189 bone marrow aspirates was conducted in the Department of Pathology. It comprises all the bone marrow aspiration performed during the period of 2014 to 2016 on patients admitted to teaching hospital. The clinical details, complete blood counts and other relevant laboratory investigations were obtained. Then data was manually collected and subsequently analysed.

Inclusion and Exclusion Criteria

Aspirates of inadequate material or dry tap were excluded from the study.

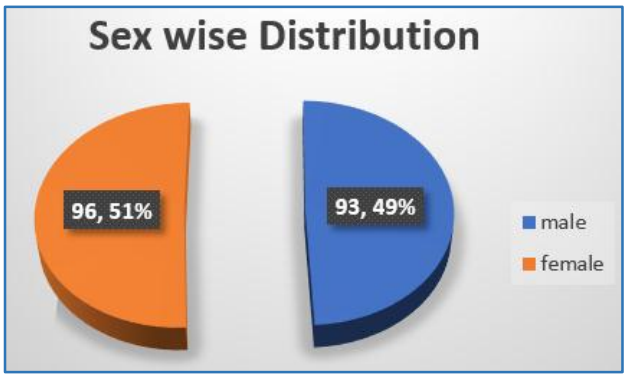
Patients were explained about the procedure. They were informed about possible complications, but also assured for safety, simplicity and usefulness of the procedure and written consent was taken from relative or patient himself.

Procedure

Bone marrow aspiration is performed on the tibial (shinbone) site in children up to 2 years of age. In patients above 2 years of age, procedure is performed on the posterior iliac crest. For the bone marrow aspiration from the posterior iliac crest, the patient is placed in the lateral decubitus position with the top leg flexed and the lower leg straight. In all the cases the site is prepared, cleaned with an antiseptic (usually Betadine) scrub and draped, exposing only the procedure area. The skin and the area down to the periosteum are infiltrated with a local anaesthetic (eg, 2% lignocaine). Approximately, 5 cc of 2% lignocaine is used. The bone marrow aspiration needle with a stylet in place is inserted. Once the needle contacts the bone, it is advanced by rotating clockwise and counterclockwise slowly until the cortical bone is penetrated and the marrow cavity is entered. Usually, a sudden change is noted when the marrow cavity has been entered. Once within the marrow cavity the stylet is removed and using a 10-cc syringe, approximately 0.5cc of bone marrow is aspirated for pathology slides. Slides are made and fixed with methanol after drying. The marrow aspiration needle is removed, and pressure is applied to the site with gauze until bleeding has stopped. After the procedure, several layers of gauze are applied to the site with an Elastoplast on top to immobilise the gauze, and the patient is instructed to check the site frequently, to report any bleeding and to keep it dry. The dressing is removed 48 hours later. Bone marrow aspiration slides are stained with Leishman stain and Field stain.

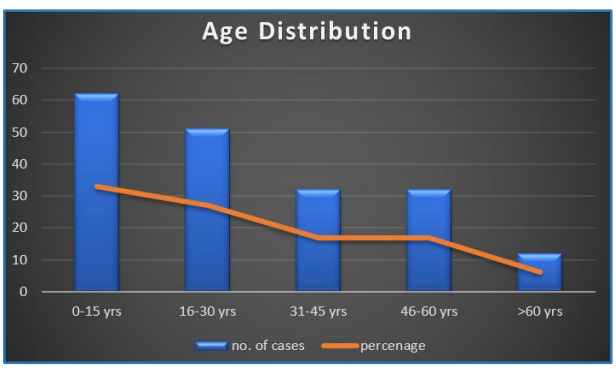
RESULTS

A total number of 189 patients were included in this study aged between 2 months and 74 years. The mean age was 37 years; 93 (49%) were males and 96 (51%) were females with (M:F=1:1.03). Graph 1 shows sex distribution of patients.



Graph 1. Sex Wise Distribution

Out of 189 patients, 62 cases (33%) of haematological disorder who underwent BMA was in the age group of 0-15 years. Graph 2 shows the age distribution of the patients.



Graph 2. Age Distribution

Ninety-seven percent (175) of the marrow aspirate had pathological features, while 7% (14) were normal marrow aspirate (Table 1).

Bone Marrow Feature	Frequency (%)
Pathological Marrow	175 (97%)
Normal Marrow	14 (7%)
Total	**189 (100%)**

Table 1. Proportion of Normal and Abnormal Bone Marrow Features

We distribute the cases according to cellularity; most of the bone marrow was hypercellular. We did come across normocellular marrows as well (Table 2).

Sl. No.	Cellularity	Number of Cases	Percentage
1.	Hypercellular	114	60%
2.	Normocellular	31	17%
3.	Hypocellular	44	23%
Total		**189**	**100%**

Table 2. Bone Marrow Cellularity

The spectrum of haematological disorders commonly diagnosed with BMA cytology are summarised in (Table 3). Acute leukaemia was the most common disease diagnosed with this procedure. Acute lymphoblastic leukaemia

occurred more commonly than acute myeloid leukaemia (Table 3). Acute lymphoblastic leukaemia was seen in 25 cases (13.2%) (Figure 1). Acute myeloid leukaemia was diagnosed in 21 cases (11.1%) (Figure 2). Aplastic anaemia detected in 30 (15.8%) cases (Figure 3). In all cases, all 3 lineages of cell were suppressed. BMA findings were correlated with PBS, which also showed pancytopenia. However, bone marrow biopsy was not done in these cases. Erythroid hyperplasia was seen in 09 cases (Figure 4). In these cases, there were no other significant findings. Megaloblastic anaemia (6.9%) was more common than microcytic anaemia (2.6%). Only 02 cases show dimorphic anaemia. Myelodysplastic Syndrome (MDS) was diagnosed in cases with increased erythroid series of cells with megaloblastic changes and dyserythropoiesis and dysmegakaryopoiesis (Figure 5A, B).

There were 4 cases of multiple myeloma where >20% of the nucleated cells were plasma cells. Binucleated and immature plasma cells were also seen. Though the diagnosis was given as multiple myeloma, biochemical, radiological and clinical correlation was recommended in each case. Chronic myeloid leukaemia and chronic lymphoid leukaemia were diagnosed in 14 cases (7.5%) and 3 cases (1.6%) respectively. Non-Hodgkin lymphoma was diagnosed in 06 cases (3.2%). ITP was diagnosed in 10 cases, all the patients were female. Storage disorder were diagnosed in 03 cases, out of which 02 cases shows Gaucher's cells diagnosed as Gaucher's disease, one case was diagnosed as Niemann-Pick's disease. Pure Red Cell Aplasia (PRCA) was diagnosed in 06 cases and it is a disease of children detected in less than 15 years of age (Figure 6).

Cause	Number of Cases	Percentage
Megaloblastic anaemia	13	6.9%
Microcytic anaemia	5	2.6%
Hypoplastic anaemia	30	15.8%
Dimorphic anaemia	2	1.1%
Acute leukaemia (Acute lymphoblastic leukaemia (25 cases13.2%) acute myeloid leukaemia (21 cases11.1%))	46	24.3%
Chronic leukaemia Chronic myeloid leukaemia (14 cases 7.5%) Chronic lymphoid leukaemia (3 cases, 1.6%)	17	9%
Myelodysplastic syndrome	13	6.9%
Non-Hodgkin lymphoma	6	3.2%
Multiple myeloma	4	2.1%
Haemophagocytic syndrome	1	0.5%
Storage disorder	3	1.6%
Hypersplenism	4	2.1%
ITP	10	5.3%
Erythroid hyperplasia	9	4.8%
PRCA	6	3.2%
Polycythaemia	1	0.5%
Bone marrow suppression chemotherapy induced	4	2.1%
Chronic granulomatous disorder	1	0.5%
Normal marrow	14	7%
Total Cases	**189**	**100%**

Table 3. Spectrum of Haematological Disorders Diagnosed by BMA

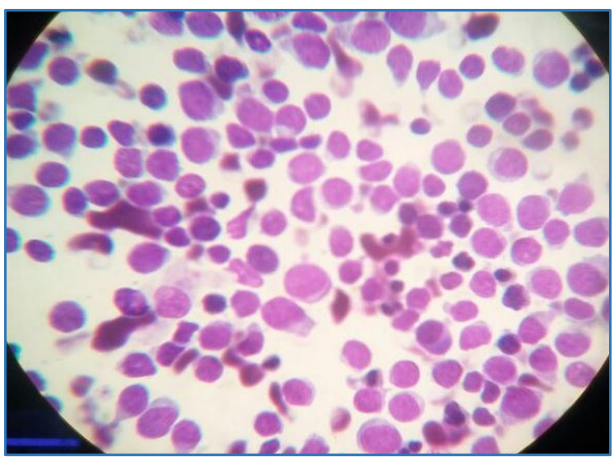


Figure 1. Bone Marrow Aspirate showing Lymphoblasts in ALL (100x)

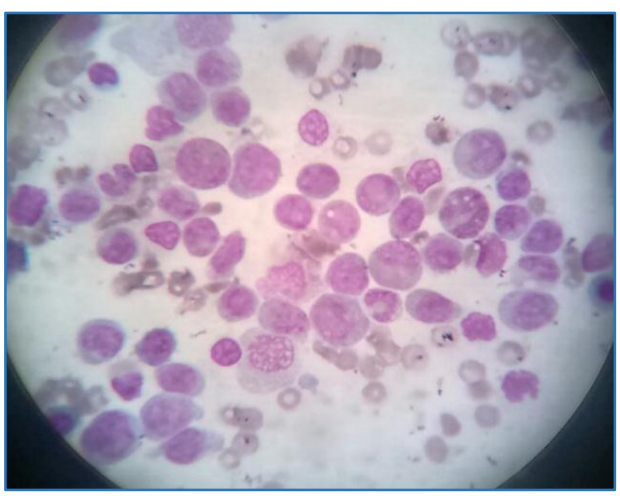


Figure 2. Myeloblast in AML (100x)

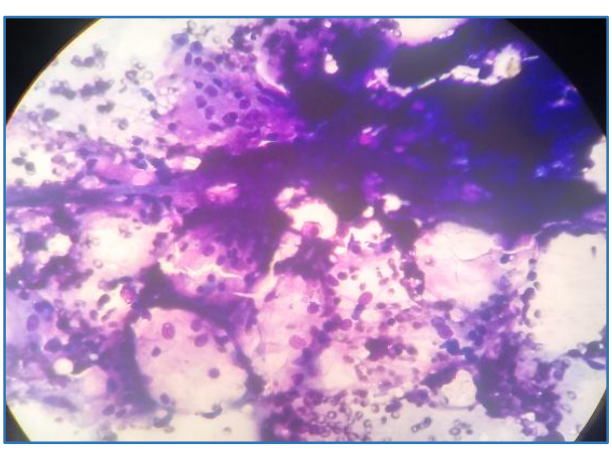


Figure 3.Case of Aplastic Anaemia, Bone Marrow Aspirate showing Increased Fat Cells (100x)

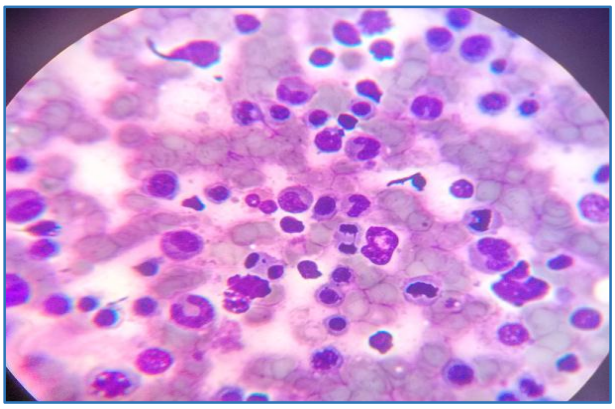


Figure 4. Bone Marrow Aspirate showing Erythroid Hyperplasia (100x)

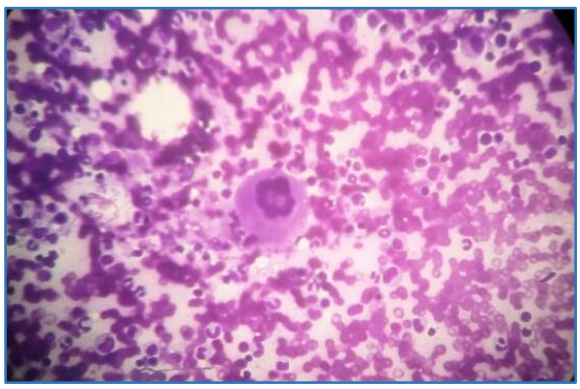


Figure 5A

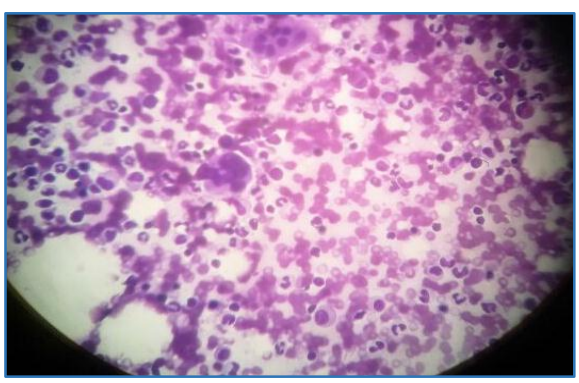


Figure 5B

Figure 5A, 5B. Case of MDS, Bone Marrow Aspirate showing Hypercellular Marrow with Dysmegakaryopoiesis (100x)

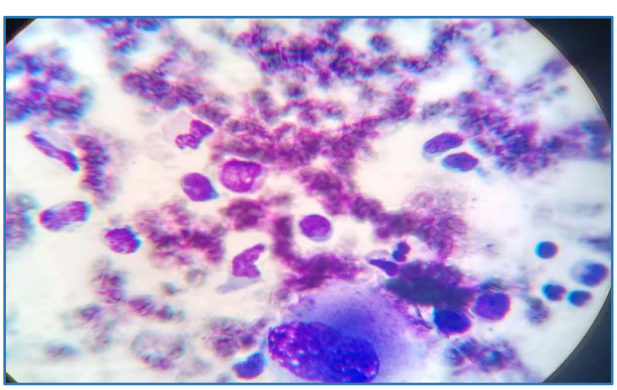


Figure 6. Case of PRCA, Bone Marrow Aspirate showing Markedly Reduced Erythroid Series (100x)

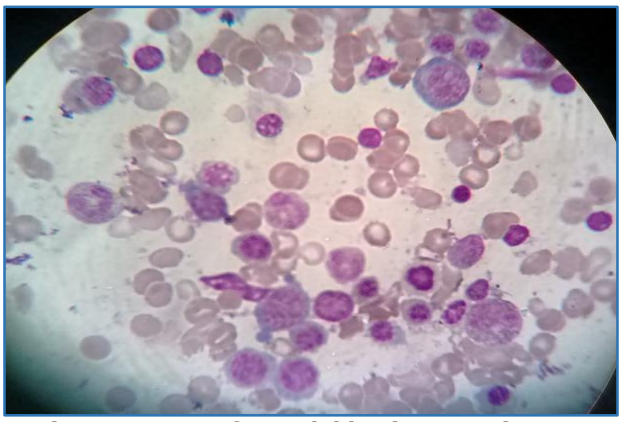


Figure 7. Case of Megaloblastic Anaemia, Bone Marrow Aspirate showing Megaloblast with Sieve-like Nucleus (100x)

DISCUSSION

The present study sought to determine the diagnostic value of BMA cytology examination in a resource poor centre. This study like other studies have shown that BMA cytology can be carried out in all age group. The age range (2 months to 74 years) as well as the sex ratio of subjects undergoing BMA evaluation is similar to that reported in other studies.[5-7]

The diagnostic efficacy of BMA cytology in making or arriving at a definitive diagnosis in this study is quite high (97%) and comparable to those of similar studies Egesie et al.[1] Using this procedure we were able to identify the causes of haematological disorders in majority (97%) of the cases.[4] Thus, this suggests that BMA is an important diagnostic tool, especially in resource poor centers. However, in 14 (7%) cases of suspected haematological diseases, no pathology was found on examination of the bone marrow aspirate. Higher values of 14.4% and 38% respectively have been reported by Damulak et al and Bashawri et al.[8,9] This observation shows that some non-haematological conditions may present with haematological manifestations, thus suggesting some limitations of this procedure.

This study has shown that the acute leukaemia (24.3%) were the most frequently diagnosed haematological malignancy from BMA examination in our centre. Out of this, 25 cases (13.2%) were Acute Lymphoblastic Leukaemia (ALL) and 21 cases (11.1%) were Acute Myeloid Leukaemia (AML). Of the AML subtypes, AML-M2 was the most common followed by AML-M3. This finding is at variance with the observation from a similar study, in which AML being more common than ALL.[1,6,10]

Other malignancies reported in this study, in descending order of occurrence include chronic myeloid leukaemia, MDS, non-Hodgkin's lymphomas, multiple myeloma and chronic lymphoid leukaemia.

All the cases of suspected lymphoma (6 cases) were diagnosed with BMA examination; however, bone marrow examination appears not to be a routine practice in staging of lymphoma in our centre. This finding is at variance with the observation from a similar study in which bone marrow

examination, especially bone marrow biopsy was a frequent practice in the staging of lymphomas.[9]Bone Marrow Biopsy (BMB) provides a more reliable index of marrow cellularity, infiltration, fibrosis and granulomas.

The incidence of multiple myeloma in this study (2.1%), is lower than that reported by Egesie et al,[1] Kibria et al[2], Laishram et al.[3] and However, the incidence of MDS (6.9%) was relatively higher than those reported in other studies.[2,6,10]

Furthermore, evaluation of anaemia showed that megaloblastic anaemia occurred more commonly than microcytic anaemia. This contrasts the findings from other studies in which IDA has been reported to be the most common cause of nutritional anaemia globally.[11] Thus, bone marrow examination could be used effectively in most cases to determine the cause of anaemia. This finding also differ from study that reported by Egesie et al.[1]

CONCLUSION

The procedure remains a veritable tool in the diagnoses and management of a wide range of haematological and some non-haematological diseases, especially in a resource poor centre.

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