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Bone Marrow Aspiration: The Indications and the Diagnostic Value

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BACKGROUND/AIMS
Bone marrow aspiration (BMA) is a common and useful investigation tool in clinical practice that helps gather information about both hematological and nonhematological disorders. Against this backdrop, the aim of this work was to identify the main indications for BMA tertiary hospital and to determine the common diagnoses encountered.

MATERIAL and METHODS
This was a prospective laboratory-based study conducted in a tertiary hospital, from December 2015 to August 2017. BMA was carried out in 204 cases of suspected hematologic disorders. The information extracted was inclusive of the main indications for performing the procedure, the age groups involved, as well as the most common diagnoses established. In addition, a specially designed form was used for this purpose, after which the data were analyzed using the Statistical Package for the Social Sciences computer program.

RESULTS
Two hundred and four cases of BMA were performed and analyzed. The most patients (30.4%) were aged 15-30 years, of which 62.7% were males and 37.3% were females. This resulted in a male-to-female ratio of 1.7:1.0. The most frequent indications were found to be pancytopenia (48.1%), suspected leukemia (26.5%), and unexplained splenomegaly (8.3%). Hypersplenism was the most common diagnosis (20.1%) followed by visceral leishmaniasis (15.2%) of the cases. 16 (7.8%) of the aspirates revealed a normally functioning marrow.

CONCLUSION
BMA assumes importance in the context of establishing the diagnosis in several medical conditions. The most common indication for this procedure was pancytopenia, while the most common finding was hypersplenism.

Keywords: Bone marrow aspiration, diagnostic role, hematological disorders

INTRODUCTION

Bone marrow aspiration (BMA) is a cytologic preparation of bone marrow cells obtained by aspirating of marrow mostly from the posterior iliac crest. Notably, it is indicated in patients with suspected hematological diseases whose diagnosis remains unclear after examination of the peripheral blood with complete blood count (CBC) and peripheral smear examination. This procedure may be necessary for the diagnosis and management of hematological as well as, to some extent, nonhematological disorders, for staging, prognostication, and evaluation of therapeutic response.[1]

BMA is one of the most commonly-used, cost-effective, and safe invasive procedures; it is associated with minimal complications after precautions are taken into consideration.[2] Megaloblastic anemia and acute myeloid leukemia were the most common hematological disorders reported in the study conducted by Atla et al.[3] Correspondingly, the study carried out by Sreedevi et al.,[4] the most common hematological disorder was erythroid hyperplasia, followed by idiopathic thrombocytopenic purpura. Meanwhile Pudasaini et al.[5] stated in their study that the most common hematological disorder was erythroid hyperplasia, followed by megaloblastic anemia and acute leukemia.

The aim of the current study was to identify the spectrum of diseases diagnosed by BMA at Referral Teaching Hospital, Asmara, Eritrea.

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MATERIAL and METHODS

This prospective laboratory-based study was carried out in a tertiary hospital, over a period of 21 months from December 2015 to August 2017.

All the patients came for BMA with results of CBC performed as a routine test. A brief medical history was taken from all of them. Along with revised CBC and indication, the general condition of the patients (including examination of liver, spleen, and lymph node groups) were checked, patient consent was taken, and his/her comfort was ensured; patients were instructed to lie down on their left side flexing the right knee joint and extend the left leg, whereas BMA was performed from the posterior superior iliac spine under aseptic condition using Klima BMA needle. In order to avoid dilution of the yield by peripheral blood, only approximately 0.5 mL bone marrow was aspirated from each patient and deliberately kept in ethylenediamine tetra-acetic acid anticoagulated.

For the purpose of assessing the adequacy of the sample, smears were made for staining and examination, it was concluded. Four cases out of 208 cases were accounted for by "dry tap," which represents about 1.9% of the total; these samples were excluded from this study.

Data Collection and Analysis

The information obtained included the demographic data, the primary indications for performing bone marrow examination as well as the most common diagnoses established. A special form was designed for this purpose in which data were displayed.

Thereafter, data generated were coded, validated, and analyzed using Statistical Package for the Social Sciences (SPSS) version 22 (IBM SPSS Corp.; Armonk, NY, USA). A Pearson chi-squared test was used to assess the significance between proportions; to that end, *P*-value below .05 was considered to be statistically significant. The main variables evaluated included age, sex, an indication of BMA, as well as final conclusion/diagnosis.

Main Points

- Bone marrow aspiration assumes important in the context of revealing the diagnosis in several medical conditions.
- In males, the most common diagnosis was hypersplenism followed by Visceral Leishmaniasis. the most common hematological neoplasm was acute leukemia and chronic lymphoid leukemia followed by chronic myeloid leukemia.
- In females, acute leukemia was the common diagnosis followed by hypersplenism.
- Pancytopenia was observed to be the most common clinical indication encountered.
- Visceral Leishmaniasis was the common cause of pancytopenia in children, followed by hypersplenism. In adults, this was hypersplenism, followed by Megaloblastic anemia.
- The second common indication was suspected leukemia.
- The need to rule out the underlying causes of hypersplenism by conducting further investigations to detect the root cause of hyperactive spleen.

TABLE I. Age and Sex Distribution of BMA Cases

Age-group	Sex = n (%)		N = 204 (%)
	Male	Female	
<15	34 (60.8)	22 (39.2)	56 (27.45)
15-30	34 (54.8)	28 (45.2)	62 (30.39)
31-45	26 (70.3)	11 (29.7)	37 (18.14)
>45	34 (69.4)	15 (30.6)	49 (24.02)
Total	128 (62.7)	76 (37.3)	204 (100)

Bone Marrow Aspiration Films Preparation and Staining Method

BMA smears are made by placing a drop of bone marrow on a slide and using a smear preparation technique. The film is then air dried and flooded with the Leishman's stain. After 2 minutes, the volume of water is doubled and the film stained for 5-7 minutes. Afterwards, it is washed in a stream of buffered water until it acquires a pinkish tinge (up to 2 minutes).

After the back of the slide has been wiped clean, it is then left (set upright) to dry.[6] The slides were observed for the quality, fragments, and stain. Preparation of smears and staining was undertaken by the same person in order to avoid errors caused by a change in performer. The slides were examined by the author, a hematopathologist under a light microscope.

Bone Marrow Aspiration Examination Findings

The bone marrow fragments were first examined on a lower power to determine the cellularity and megakaryoblasts/cytes. Then on high power, an examination is undertaken for red blood cells precursors, white blood cells precursors, the myeloid/erythroid ration (ME ratio), and the maturity of cells were examined: for example, blasts may make equal or more than 20% of the type of white blood cells in cases of acute lymphocytic leukemia and acute myelocytic leukemia, plasma cells, parasites, as well as any other types of cells. Write report and suggest further investigations if needed.[2]

Ethical Approval

The research proposal was reviewed by the Ethical Committee of the research unit in the ministry of health, and ethical clearance was approved by the National Health Laboratory, Asmara, Eritrea (registration number: 34/19 and the approval date is 08/06/2019).

RESULTS

A total of 204 cases were included in this study. The age of the patients ranged from 9 months to 80 years with a mean age of 29.5 years, and males being the most common gender (1.6:1.0) are shown in Table I. Of the 204 cases, (30.4%) were between 15 and 30 years. The smallest patient was a 9-month-old baby as shown in Table I.

Hypercellular marrow was reported in 175 (85.8%) of the cases with 10 (4.9%) cases of hypocellular marrow are shown in Table 2.

The clinical indications for the BMA included pancytopenia (48.1%), suspected leukemia (26.5%), unexplained splenomegaly

TABLE 2. The Cellularity of the Bone Marrow Aspiration

Cellularity of the marrow	No. of patients	Percentage (%)
Hypercellular	175	85.8
Normocellular	20	9.8
Hypocellular	9	4.4
Total	204	100

TABLE 3. Clinical Indications of Bone Marrow Aspiration

Indication	No. of patients	Percentage (%)
Pancytopenia	98	48.1
Suspected leukemia	54	26.5
Unexplained splenomegaly	17	8.3
Unexplained fever	14	6.9
Thrombocytopenia	9	4.4
Anemia	6	2.9
Suspected malignancy	6	2.9
Total	204	100

(08.3%), unexplained fever (06.9%), and suspected malignancy (2.9%) are shown in Table 3.

In 188 (92.2%) of these cases, BMA provided either the diagnosis or diagnostic clues concerning the disease process, while 16 (7.8%) of the aspirates revealed a normally functioning marrow.

The most frequent diagnoses made included hypersplenism 20.1%, visceral leishmaniasis 9.8%, acute leukemia 9.8%, megaloblastic anemia 8.3%, chronic myeloid leukemia 8.3%, chronic lymphoid leukemia 7.4%, bone marrow hypoplasia 4.9%, idiopathic thrombocytopenic purpura 4.4%, hemolytic anemia 3.9%, iron deficiency anemia 1.5%, multiple myeloma 1.0%, and polycythemia 1.0%. Meanwhile there was one case (0.5%) for each of the following conditions: Gaucher's disease, secondary malignancy, and essential thrombocythemia are shown in Table 4.

DISCUSSION

In this study, we described briefly the basic concepts of BMA, in addition to our findings of the clinical indications and the final diagnoses within a 21-month period in Asmara city.

Two hundred and four cases were involved in this study. This number is lower than the expectations, particularly when considering population of 896,000 living in the Asmara locality. However, since BMA service was not previously available in this city, the few numbers of requests are not unexpected, due to the fact that the physicians need some time to be aware of the services available upon their request.

Some authors are of the view that BMA has deteriorated as a diagnostic tool in clinical practice.[7] This might be true in certain settings where other alternative diagnostic procedures exist. However, BMA is still essential and of great importance in most developing countries for establishing the diagnosis of many conditions. A difference was observed between males and females who underwent BMA during the study period. Notably, 128 (62.7%) were male and 76 (37.3%) were female; the male to female ratio was 1:1.6.

In our study, in males, the most common diagnosis was hypersplenism 40 cases (31.3%), followed by visceral leishmaniasis 23 cases (17.9%). Meanwhile the most common hematological neoplasm was acute leukemia and chronic lymphoid leukemia nine cases (7%) for each, followed by chronic myeloid leukemia eight cases (6.3%).

In our study, in females, the most common diagnosis was acute leukemia 11 cases (14.5%), followed by hypersplenism 10 cases (13.2%). Males are affected by hypersplenism more than females in many studies.[8,9] The exact cause can't be identified. In our society, females may be presented less than males to tertiary care facilities, and usually after serious illnesses like leukemia, as shown in our study.

Importantly, the most common age group that underwent the procedure was in the 15-30 age group. This finding suggests that the rate of suspected hematological disorders is high in the youngest population. Pancytopenia was observed to be the most common clinical indication encountered (48%). This is similar to the study conducted by Ahmed et al.[10] However, pancytopenia was the third most common indication in a study done by Bashawri.[11]

The study found visceral leishmaniasis to be the most common cause of pancytopenia in children, followed by hypersplenism. In adults, this was hypersplenism, followed by megaloblastic anemia. According to our study, the second common indication was suspected leukemia (26.5%), which is consistent with the finding of Pudasaini et al.[5] and Bashawri.[11]

We found that most of the BMA was hypercellular (60.17%), which is comparable to the observations of Marwah et al.[12] It is attributed to compensatory trilineage hyperplasia seen in the BMA due to peripheral pooling of blood cells within the enlarged spleen. Of importance is also the fact that hypersplenism was found to be the most common diagnosis in our study, which is similar to the results of Sreedevi et al.[4]

Erythroid hyperplasia emerges as the most common BMA finding in the study conducted by Pudasaini et al.[5] In our laboratory, visceral leishmaniasis (kalazar) was the second most common diagnosis encountered, as evidenced in 31 (15.2%) of the cases. However, all of these cases, when traced back, were found to be from endemic areas of the disease in the west, Eritrea.

Acute leukemia was seen in 20 (9.8%) of the cases, which is lesser than the findings of Pudasaini et al. (12.3%). Acute leukemia cases were correlated with the clinical picture as well as the presence of more than 20% of blasts in the peripheral blood smear findings. The diagnosis was later confirmed by flowcytometry.

Megaloblastic anemia meanwhile was observed in 17 (8.3%) of the cases as compared to other studies of Pudasaini et al.[5] and Atla et al.[3]—(12.3%) and (40%), respectively. The BMA findings in megaloblastic anemia were erythroid hyperplasia with megaloblatic changes and delay in maturation of myeloid series. The diagnosed confirmed later by biochemical methods.

In Eritrea, such nutritional deficiencies are a common phenomenon. Chronic myeloid leukemia was seen in 17 (8.3%) of all

TABLE 4. Bone Marrow Examination Findings

Broad category (%)	Diagnosis	No. of patients	Percentage (%)
Nutritional anemia (13.7%)	Iron deficiency anemia	3	1.5
	Megaloblastic anemia	17	8.3
	Hemolytic anemia	8	3.9
Hypoplastic anemia (4.9%)	Aplastic anemia	9	4.4
	Pure red cell aplasia	1	0.5
Hematological malignancy (28%)	Acute leukemia	20	9.8
	Chronic myeloid leukemia	17	8.3
	Chronic lymphoid leukemia	15	7.4
	Multiple myeloma	2	1.0
	Polycythemia vera	2	1.0
	Essential thrombocythemia	1	0.5
Idiopathic thrombocytopenia purpura (4.4%)	Idiopathic thrombocytopenia purpura	9	4.4
Others (42.7%)	Hypersplenism	41	20.1
	Visceral leishmanasis	31	15.2
	Infection	10	4.9
	Gaucher's disease	1	0.5
	Secondary malignancy	1	0.5
Normal bone marrow (7.8%)	Normal bone marrow	16	7.8
Total		204	100

cases and correlated with the presence of all stages of maturation in the peripheral blood smear findings and high total white blood cells in the CBC, which was confirmed by positive Philadelphia chromosome testing. Chronic lymphoid leukemia was seen in 15 (7.4%) of the cases, was correlated with the high lymphocytes cells in the CBC, and confirmed by flowcytometry; 10 (4.9%) of these cases were found to have infectious etiology other than leishmaniasis.

The rarity of the cases diagnosed in this study may be attributed to the fact that there is a long list of differential diagnoses for pyrexia of unknown origin (PUO), thus implying that BMA can hardly settle the diagnosis. The role of BMA in settling the diagnosis in PUO has been well documented by some authors,[13] as BMA diagnostic was seen in only 16.5%. Hypoplastic anemia was observed in 10 (4.9%) of the cases, which is similar to the findings of Pudasaini et al.[5] (5.3%).

In all cases of hypoplastic anemia, the marrow was hypocellular and all three lineages of the cell were suppressed. The diagnosis was based on the examination of fragments and clot section examination due to the unavailability of bone marrow biopsy. Both aspiration and trephine biopsy are recommended to be conducted simultaneously in cases of pancytopenia, especially if hypoplastic or aplastic anemia is suspected, though aspiration smears are known to be superior for morphological details. Bone marrow biopsy provides a more reliable index of cellularity, revealing bone marrow infiltration, fibrosis, and granulomas.[14]

Disorders of the platelet were observed in 4.4% of all cases. These were mostly accounted for by males in the age group of 15-30 years and diagnosed as immune thrombocytopenic purpura. Meanwhile other studies showed (6.21%), (14.5%), and (6.8%) cases of immune thrombocytopenic purpura, respectively, in their studies.[12,15] Hemolytic anemia, which showed erythroid hyperplasia in BMA, was evidenced in 8 (3.9%) of these cases, and this diagnosis confirmed later by biochemical methods and genetic disorders. This finding is comparable to that of Jha et al.[14] (19.6%).

Microcytic anemia seems to be an uncommon finding as we came across only three such cases (1.5%). The BMA finding in microcytic anemia was erythroid hyperplasias that were subsequently labeled as iron deficiency anemia after conducting an iron profile study. We encountered two cases (1.0%) of multiple myeloma which showed 22% and 12% plasma cells and correlated with the biochemical, radiological, and clinical findings compared to that of Kibria et al.[15] (9.04%).

Two cases (4.6%) of polycythemia Vera showed trilineage hyperplasia and correlated with CBC and peripheral blood findings along with the Janus kinase 2 (JAK2) mutation study. One case of Gaucher's disease was diagnosed by a bone marrow examination. As per our finding, bone marrow examination is helpful in making the primary diagnosis of storage disease.

In children, age less than 15 years (56 cases), the most common non-neoplastic disorders were found to be visceral leishmaniasis with 17 cases (30.4%), followed by hypersplenism with eight cases (14.3%). On the other hand, the most common neoplastic hematological disorder was acute leukemia 11 cases (19.6%). In adults whose age ranged from 15 to 45 years (99 cases), hypersplenism was the most common non-neoplastic disorders with 28 cases (28.3%), followed by megaloblastic anemia with 14 cases (14.1%) and visceral leishmaniasis with 13 cases (13.1%). Similarly, the most common neoplastic hematological disorder was chronic myeloid leukemia nine cases (9.1%), followed by acute leukemia eight cases (8.1%).

Among the elderly, in cases of age more than 45 years (49 cases), the most common non-neoplastic disorder was hypersplenism with nine cases (18.4%). Meanwhile, the most common neoplastic hematological disorders were chronic lymphoid leukemia with 13 cases (26.5%), followed by chronic myeloid leukemia with 10 cases (20.4%). The rate of neoplastic hematological disorders was also found to be considerable (28%), although it is lower than that found in a study done in Saudi Arabia.[11]

The most common hematological malignancy was acute leukemia 20 cases (9.8%), followed by chronic myeloid leukemia with

17 cases (8.3) and chronic lymphoid leukemia with 15 cases (7.4%). The rate of non-neoplastic hematological disorders was seen in (63.6%) of cases. On the other hand, the most common non-neoplastic hematological disorders were hypersplenism with 41 cases (20.1%), followed by visceral leishmaniasis with 31 cases (15.1%) and megaloblastic anemia with 17 cases (8.3%). Among all cases, it was found that 7.9% of BMA was absolutely normal without any pathology.

In this study, we observed that the most common BMA finding was hypersplenism diagnosed by trilineage hyperplasia on BMA and enlarged spleen. This necessitates further investigation in order to detect the underlying causes of splenomegaly. We also noticed 41 (20.1%) of the cases with visceral leishmaniasis and infectious etiology other than leishmaniasis.

There is a strong need for collaboration between physicians, hematologist, pathologists, oncologists, and technicians in order to improve the diagnostic yield of bone marrow examination. Although BMA and biopsy are an uncomfortable procedure for the patient and should only be performed when there is a clear clinical indication.[16] It is a useful technique to diagnose blood disorders for various systemic illnesses.

Limitations of our study include the small size of sample and time constraints that may not allow for generalization. Despite this limitation, this study is novel in that it is the first of its kind in Asmara, Eritrea and is expected to constitute a database for future studies.

BMA is a useful investigation tool in clinical practice. It is a safe and cost-effective procedure, particularly in a resource-scarce country like Eritrea. In this regard, the study provides valuable insights into the most common hematological malignancy and non-neoplastic hematological disorders in Eritrea.

In our study, the most common indication for this procedure was pancytopenia, whereas the most common finding was hypersplenism. This study also focused on the need to rule out the underlying causes of hypersplenism by conducting further investigations to detect the root cause of hyperactive spleen. It is important to note that there were considerable percentages of cases diagnosed with visceral leishmaniasis.

Ethics Committee Approval: Ethics committee approval was received for this study from the National Health Laboratory, Asmara, Eritrea (registration number: 34/19 and the approval date is 08/06/2019).

Informed Consent: Written informed consent was obtained from all participants who participated in this study.

Peer-review: Externally peer-reviewed.

Conflict of Interest: The author has no conflicts of interest to declare.

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