ORIGINAL RESEARCH

To conduct a morphological examination of bone marrow aspiration cytology and establish its clinical correlate

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ABSTRACT
Aim: To conduct a morphological examination of bone marrow aspiration cytology and establish its clinical correlate. **Materials and methods:** The procedure of marrow aspiration was conducted inside the pathology department, with the posterior iliac spine being selected as the preferred location for the procedure. In a limited number of individuals, the sternum was also used for aspiration. Leishman's stain was used to stain all of the slides, and in some instances, additional stains were added as needed. A limited number of uncontaminated slides and aspirate samples were examined for the purpose of immunophenotyping and cytogenetic analysis. **Results:** Among the total sample size of 276 individuals, 166 were identified as male, while 110 were identified as female. The examination conducted by the researcher revealed the presence of bicytopenia, leading to a diagnosis of iron deficiency anaemia (IDA). The predominant observation in the general examination was pallor, which was then followed by the presence of splenomegaly. The primary reasons for bone marrow aspiration (BMA), with pancytopenia being the most prevalent indication (29.3%). This is followed by unexplained fever, accounting for 13.8% of cases, and probable leukaemia, accounting for 11.2% of cases. The predominant diagnostic seen was deficiency anaemia, accounting for 31.9% of the total cases. **Conclusion:** The BMA procedure has significant value as a haematological diagnostic tool. The use of diagnostic, prognostic, and therapeutic assessment in a range of haematological and nonhematological illnesses is beneficial when applied to patients who have undergone thorough clinical evaluation and meticulous analysis of peripheral smear.
Keywords: Morphological examination, Bone marrow aspiration, Cytology, Clinical

INTRODUCTION

The bone marrow is a substantial organ inside the human body that comprises mesenchymal and hematopoietic stem cells.[1] The assessment of bone marrow function may be conducted using several methods, including clinical evaluation, biochemical analysis, and careful inspection of peripheral blood smear and bone marrow samples.[2] Bone marrow aspiration (BMA) is a crucial diagnostic technique used to assess both haematological and non-hematological disorders.[3] The use of cytochemical, immunophenotypic, and cytogenetic analyses proves to be advantageous. [4] It facilitates the prediction of outcomes and the assessment of the effectiveness of treatment as well.The user's text is already academic and does not require any rewriting. The procedure of bone marrow aspirate provides valuable data on both the quantitative and qualitative aspects of cellular morphology, whereas biopsy offers insights into the overall architectural arrangement and distribution of cells inside the bone marrow.The user's text does not contain any information to rewrite. The objective of this research was to assess the clinical characteristics of patients requiring bone marrow aspiration and to establish a correlation with the underlying pathological findings seen in bone marrow aspiration cytology.

MATERIALS AND METHODS

The marrow aspiration was done in the pathology department and the site of choice was posterior iliac spine. In few patients sternum was also used for aspiration. All slides were stained with Leishman's stain and in some cases special stain were also applied as per requirements. Few unstained slides and aspirate were evaluated for immunophenotyping and cytogenetic studies.

INCLUSION CRITERIA

All cases enrolled in various clinical departments and then reporting to pathology department for bone marrow aspiration was taken as case.

EXCLUSION CRITERIA

Bloody tap or inadequate sampling was excluded from the study.

Slides received for review was excluded as the clinical details were not available.

STATISTICAL ANALYSIS

Descriptive statistic was obtained from data collected from history, examination and laboratory investigations. Number and percentage were enumerated for all categorical variables such as clinical features, indications and bone marrow findings.

RESULT

The research included a cohort of 290 individuals, whose bone marrow aspiration cytology and case history were subjected to analysis. The data were obtained from the records of the hospital and the pathology department. In a total of 14 instances, the aspirates were seen to be either bloody or resulted in a dry tap. A total of 276 bone marrow smears were selected and included in the final analysis. Among the total sample size of 276 individuals, 166 were identified as male, while 110 were identified as female. This distribution resulted in a male to female ratio of 1.5:1. The age range of the participants in this study spans from infancy to older adulthood, including individuals from 0 to 80 years of age. The youngest patient hospitalised for failure to thrive was a female toddler aged 4.5 months. The examination conducted by the researcher revealed the presence of bicytopenia, leading to a diagnosis of iron deficiency anaemia (IDA).The age group with the highest number of patients who had bone marrow examination was 11-20 years, accounting for 19.2% of the total. This was closely followed by patients in the age range of 21-30 years, comprising 17.7% of the total. The second observation of individuals having bone marrow testing revealed that the majority of patients fell within the age range of 41-50 (17.0%), closely followed by the age range of 51-60 (16.3%). The most frequently reported problems among the patients was weakness, followed by bodily soreness and fever. The predominant observation in the general examination was pallor, which was then followed by the presence of splenomegaly.Table 1 presents the primary reasons for bone marrow aspiration (BMA), with pancytopenia being the most prevalent indication (29.3%). This is followed by unexplained fever, accounting for 13.8% of cases, and probable leukaemia, accounting for 11.2% of cases. The predominant diagnostic seen was deficiency anaemia, accounting for 31.9% of the total cases. Among these instances, megaloblastic anaemia (MA) exhibited the greatest occurrence, followed by dimorphic anaemia and iron deficiency anaemia, as shown in table 2. Among the several types of leukaemia, acute myeloid leukaemia (AML) was found to be the most prevalent. Table 3 illustrates the distribution of bone marrow aspirate results according to age groups, revealing a higher incidence of MA in individuals aged 21-30, with a closely subsequent occurrence in the age range of 31-40.

Table 1: Indication for bone marrow aspiration cytology

Pancytopenia	81	29.3%
Bicytopenia	27	9.8%
Thrombocytopenia	15	5.4%
Unexplained fever	38	13.8%
Unexplained anemia	30	10.9%
Suspected leukemia	31	11.2%
Splenomegaly	22	7.97%
Unexplained lymphocytosis	2	0.72%
Leukemia in remission	5	1.8%
Suspected plasma cell dyscrasia	22	7.97%
Haemophagocytic activity	3	1.1%

Table 2: Etiological diagnosis of bone marrow aspiration cytology

Parameter	Diagnosis	No. of cases	Percent (%)
Deficiency anemia88(31.9%)	Megaloblastic anemia	45	16.3%
	Dimorphic anemia	30	10.9%
	Iron deficiency anemia	13	4.7%

Haematolymphoid malignancy54(19.5%)	Acute leukemia AML+ALL	32 (25+7)	11.6% (9.05%+2.53%)
	Chronic myeloid leukemia- CP	15	5.4%
	Chronic Myeloproliferative Disorders	3	1.1%
	Chronic lymphocytic leukemia	2	0.7%
	Lymphoma –NHL	2	0.7%
	Myelodysplastic Syndrome(MDS)	7	2.5%
	Hypoplastic anemia	17	6.2%
	Plasma cell dyscrasia	20	7.2%
	Reactive bone marrow	34	12.3%
	Immune Thrombocytopenic purpura(ITP)	10	3.6%
Others	HemophagocyticLymphohistiocytosis	3	1.1%
	Hypersplenisim	3	1.1%
	Leishmaniasis	3	1.1%
	Metastatic carcinoma	1	0.36%
	Diseases in remission	2+1+1	1.4%
	Normal bone marrow	32	11.6%

Table 3: Age wise distribution of bone marrow aspirate findings

Diagnosis	0-10	11-20	21-30	31-40	41-50	51-60	61-70	71-80
Megaloblastic	0	9	11	10	5	6	4	0
DA	0	8	6	4	3	3	4	2
IDA	1	4	3	1	1	2	1	0
ALL	3	3	1	0	0	0	0	0
AML	0	2	3	6	4	5	4	1
CML-CP	0	1	3	5	5	1	0	0
CMPD	0	0	0	0	0	1	1	1
CLL	0	0	0	0	0	1	0	1
NHL	0	0	0	0	2	0	0	0
MDS	0	0	0	0	1	4	1	1
Hypoplastic anemia	0	8	2	1	4	2	0	0
Plasma cell dyscrasia	0	0	0	0	5	12	3	0
Reactive marrow	0	2	9	2	10	3	5	3
ITP	2	3	2	2	1	0	0	0
HLH	0	2	0	0	0	1	0	0
Hypersplenism	0	0	2	1	0	0	0	0
Leishmaniasis	0	0	1	2	0	0	0	0
Metastatic CA.	0	0	0	0	1	0	0	0
Leukemia in remission	2	0	1	0	1	0	0	0
Normal marrow	1	11	5	3	4	4	3	1
Total(%)	09(3.3)	53(19.2)	49(17.7)	37(13.4)	47(17)	45(16.3)	26(9.4)	10(3.6)

DISCUSSION

Bone marrow aspiration is a simple, safe and outpatient based procedure which helps to reach at a diagnosis in majority of patients. Trephine biopsy is carried out as a part of the same procedure, a bit painful procedure and may require admission.[6] Bone marrow study becomes indispensible diagnostic procedure when the diagnosis is not straight forward or the biochemical reports are equivocal. As ours are tertiary care center, many patients are referred to us after taking various kinds of treatment at local level and theirs hematological and biochemical results generally not fitting in any clinical scenario. So, BMA becomes an important tool for clinician to understand the underlying pathology better for further management. The most common indication for bone marrow aspiration cytology was pancytopenia and the diseases diagnosed were deficiency anemia.

Megaloblastic anemia is the most common diagnosis in our study constituting 16.8% cases. Similar finding were obtained by Goyal S et al.(17.14%) [8], Khan SP et al. (14.5%). [9] Few studies from India reported a bit higher incidence, 33.2% by Mahajan V et al.[10] and 31% by Khan TA et al. [11]. Megaloblastic anemia is more common among strict vegetarians. But in our experience we have found many patients who are non vegetarian suffering from this anemia probably due to recurrent GI infection. These patients most frequently presents with pancytopenia and the most common age range were 21-30 and 31-40. We have recorded Hb as low to 2.4 gm% and in 2 patients S.ferritin was significantly high. The second most common deficiency anemia is dimorphic anemia (DA)

constituting 10.9% followed by IDA constituting 4.7%. Incidence of pure IDA displaying predominantly micronormoblastic erythroid maturation on BMA is low in our study and also in others study, Bhut Ket al.6.5% [12]and Okinda NA et al.6.3% [13]. A bit higher incidence was recorded by Khodke et al. (14%). [14]IDA constitutes an estimated incidence of 60-80% of the world's population. [15] In deficiency anemia the bone marrow aspirates were hypercellular to normocellular.

This group includes 54patients accounting for19.5%**,** second most common findings. Out of this, 32 cases are of acute leukemia with high incidence of acute myeloid leukemia, maximum patients in the age range of 31-40 years [6] closely followed by age range 51-60(5).It is often possible to diagnose acute leukemia on peripheral smear and patients can be subtyped on the basis of morphology and cytochemical stains[6]. But for immunophenotyping and cytogenetics analysis marrow cells are material of choice. One patient was diagnosed as CML in blast crisis with BMA findings of fair number of blasts and marked basophilia. We had a large group of patients who are admitted in medicine department for unexplained heaviness or abdominal distension or pyrexia of unknown origin. Many of these patients [15] are diagnosed as CML-CP on the peripheral smear but needed baseline BMA findings for comparison during treatment and management [6]. The youngest patient diagnosed with CML-CP was 18 years old with maximum patients comprising 5 each in the age range of 31-40 and 41-50. We could diagnose 2 cases each of CLL and NHL. We received 3 patients of suspected polycythemia and were diagnosed as chronic myeloproloferative disorders (CMPD) on BMA.

This constituted 6.2% and highest incidence in the age range of 11- 20 years in our study. The marrow finding showed many fat fragments, mast cells and lymphoplasmacytic infiltrates. The BMA findings were confirmed by biopsy in 10 cases only. Epidemiologically hypoplastic anemia has a geographic occurrence opposite to that of acute leukemia i.e. more incidence of hypoplastic anemia in developing world than western countries. [16]Bhut K et al. [12]reported overall incidence similar to present study (4.5%) but they could found only 1 case each in age range of 0-10years and 11- 20 years constituting incidence of 50%. MahajanVet al. [10] reported 4.34% and a bit lower incidence by Goyal S et al. [8] 2.86%. A very high incidence of hypoplastic anemia was reported by Mainali N et al. 29.5% [17].

We had elderly patients presenting with pancytopenia with all biochemical parameters within normal limit or even high. Few patients who were diagnosed with the features favoring MDS on BMA had Vit B12 > 3000 IU and S.ferritin> 800ng/ml probably treated as deficiency anemia at PHC. In suspected cases of MDS, dysplasia in haematopoetic cells are best visualized and assessed in BMA cytology. The incidence of MDS in our study is 2.5% with maximum incidence in 51-60 years of age group. Our findings are comparable with Okinda NA etal. (2.5%) [13], MainaliNetal. (3.4%).[17]

It constitutes 7.2% of cases with maximum patients in the age range of 51-60. These patients either presented with weakness, bodyache and anemia or with features of renal dysfunction. The BMA aspirate is predominantly normocellular but in 5 cases particles were hypercellular. Two suspected cases were diagnosed as reactive plasmacytosis. Khan TA et al. [11] reported 6%, MahajanVet al. [12] 4.3% while only 2.2% by Mainali N et al. [17]

Reactive marrow is one where one or two cell lines show hyperplasia or in rare circumstances hypoplasia. In our study, cases showing myeloid hyperplasia and in few associated megakaryocytic hyperplasia were diagnosed as reactive cellular marrow. Generally these patients presented with bicytopenia or pyrexia of unknown origin. Present study show 12.3% cases of reactive marrow with maximum cases in 41-50 years of age group [10]. Bhut K et al. found 22.7% cases of reactive marrow with highest incidence in the age group of 1-40 years (33.3%).[12]

This constituted 3.6% of cases and mostly in the age group of11-20 years. ITP is considered as diagnosis of exclusion. So high index of clinical suspicion complemented with BMA cytology to rule out other hematological conditions including leukemia in children and MDS in adults is required to commence timely therapy to achieve favorable prognosis [18]. Incidence of ITP varies significantly in different studies. It was very low in the study done by MahajanV et al. on 460 patients (0.2%) [10]. High incidence was recorded by MainaliN (17.0%) [17], MunirAH (16.5%)[19]. Ours data was comparable with the study done by Okinda NA (4.2%) [13].

This is an aggressive and life threatening systemic inflammatory syndrome. Most of the cases of HLH in adults are associated with medical condition particularly infection [11]. Though hemophag-ocytosis on BMA is not essential for the diagnosis of HLH, these patients were diagnosed secondary HLH with evidence of clinical features and biochemical findings. Incidence of HLH in our study was 1.1% which was comparable with the study done by Khan SP et al.(0.8%) [9] and Khan TA et al. (1%) [11].

The infective pathology diagnosed in our study wereleishmaniasis with an incidence of 1.1%. Patients chiefly presents with fever and splenomegaly. These patients showed pancytopenia on PBS. Normal study was reported in 11.2% cases. AtlaBL[3] and Khan SP [9] reported normal study in 3.8% and 6.8% cases respectively.Gohil M et al. reported absolutely normal study without any pathology in7.96% BMA [2]. Normal bone marrow study is significantly high in the study done by MahajanV(21.7%) [12] and Okinda NA et al.(20.7%) [13]. Other findings in our study includes hypersplenism in 3 cases showing features of erythroid hyperplasia on BMA and 1cases of metastatic carcinoma. BMA showed adenocarcinoma

cells arranged in acini and sheets with foci of mucin. This patient was under evaluation for colorectal carcinoma and had CEA 2023ug/L. In 5patients BMA was done to look for residual disease, only 4 were found in remission. In 14 cases (4.8%) BMA was inadequate for evaluation and was probably due to faulty technique, obesity especially in female patients and packed marrow in cases of acute leukemia. Other studies also reported bloody/ dry tap comparable with present study. 4.5 % by Bhut K et al.[12] and 2.8% by Okinda NA et al. [13,19]

CONCLUSION

The BMA procedure has significant value as a haematological diagnostic tool. The use of diagnostic, prognostic, and therapeutic assessment in a range of haematological and nonhematological illnesses is beneficial when applied to patients who have undergone thorough clinical evaluation and meticulous analysis of peripheral smear.

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