Original Research Article

Morphological evaluation and clinical correlation of bone marrow aspiration cytology at tertiary care centre

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Abstract

Background: Bone marrow examination is an important diagnostic test for hematological and non hematological disorder in carefully selected cases after clinical, biochemical and peripheral blood smear examination. The aim of this study was to evaluate the clinical profile of the patient necessitating for bone marrow aspiration and correlate with underlying pathology.**Materials and method**: This is a retrospective study done for 1 year. A total of 290 patients were included in the study. Data were collected from hospital record and pathology department record. **Result**: 290 patients were included in the study but 276 patients were analyzed with a male to female ratio of 1.5:1. The age range of subjects varies from 0 year to 80 years with maximum patients in the age group of 11-20(19.2%). The commonest symptom was weakness (30.8%) and the commonest sign was pallor (29.7%). The most frequent indication for BMA was pancytopenia(29.3%) followed by unexplained fever (13.8%) and suspected cases of leukemia (11.2%). The most common diagnosis was deficiency anemia constituting 31.9 % of cases out of which megaloblastic anemia showed highest incidence (16.3%). Among leukemia, AML was most common (9.05%) followed by CML-CP in 5.4% cases. Reactive marrow was found in 12.3% cases followed by normal marrow study in 11.6% cases. Hypoplastic marrow was found in 6.2% cases. **Conclusion**: BMA is an important hematological investigation useful for diagnostic, prognostic and therapeutic evaluation of various hematological and nonhematological disorders in carefully selected patient.

Keywords: bone marrow aspiration, anemia, pancytopenia

Introduction

Bone marrow is one of the largest organs in body containing mesenchymal and haematopoetic stem cell. [1] Functioning of bone marrow can be assessed by clinical evaluation, biochemical assay and vigilant examination of peripheral blood smear and bone marrow examination.[2]Bone marrow aspiration (BMA) is an essential diagnostic tool in evaluation of hematological and non hematological disorder. [3, 4]It is useful for cytochemical, immunophenotypic and cytogenetics analysis. [5] It helps in prognostication and evaluation of therapeutic response also.[6]Bone marrow aspirate provides information about the numerical and individual cell morphology and biopsy about architectural pattern and distribution of cells. [7]This study was aimed to evaluate the clinical profile of the patient necessitating for bone marrow aspiration and correlate with underlying pathological lesions in the bone marrow aspiration cytology.

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Materials and methods

This was a retrospective study carried at the Department of Pathology, IGIMS, Patna. The time duration was of 1 year from Jan 2017- Dec 2017. 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.

- **Study population**

Cases were selected as per inclusion and exclusion criteria which is as follows:-

- Inclusion criteria- All cases enrolled in various clinical departments and then reporting to pathology department for bone marrowaspiration 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

A total of 290 patients were included in the study and theirs bone marrow aspiration cytology and case history was analyzed. Data were collected from hospital record and pathology department record. Out of this, in 14cases aspirates were either bloody or dry tap. 276 bone marrow smears were particulate and included in final analysis. Out of 276, 166 were male and 110 female with a male to female ratio of 1.5:1. The age range of subjects varies from 0year to 80 years. The youngest patient was 4.5 months old female child admitted for failure to thrive. Her investigation revealed bicytopenia and she was diagnosed as iron deficiency anemia (IDA).The maximum number of patients who underwent bone marrow examination was in the age group of 11-20years (19.2%) closely followed by patients in the age group of 21-30 years (17.7%). Second peek of patients undergoing bone marrow examination were in the age range of 41-50(17.0%) followed by 51-60(16.3%). Commonest complaints presented by the patients were weakness followed by bodyache and fever. The most common general examination finding was pallor followed by splenomegaly .The most frequent indication for BMA was pancytopenia(29.3%) followed by unexplained fever in 13.8% of cases and suspected leukemia in 11.2% as described in table 1. The most common diagnosis was deficiency anemia constituting 31.9 % of cases out of which megaloblastic anemia (MA) showed highest incidence followed by dimorphic anemia and iron deficiency anemia as shown in table 2. Among leukemia acute myeloid leukemia (AML) was most common.Table 3 represents the age wise distribution of bone marrow aspirate findings and shows maximum cases of MA in age group 21-30 closely followed by cases in age group 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

Broad categories	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.

Deficiency anemia

Megaloblastic anemia is the most common diagnosis in our study constituting 16.8% cases. Similar finding were obtained by Choudhary M 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 Gupta A 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.

Haematolymphoid malignancy

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.

Hypoplastic anemia

This constituted 6.2% and highest incidence in the age range of 11-20 years (8) 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 Choudhary M et al. [8] 2.86%. A very high incidence of hypoplastic anemia was reported by Mainali N et al. 29.5% [17].

MDS-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]

Plasma cell dyscrasia

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. Gupta A et al. [11] reported 6%, MahajanVet al. [12] 4.3% while only 2.2% by Mainali N et al. [17]

Reactive marrow

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 etal.found 22.7% cases of reactive marrow with highest incidence in the age group of 1-40 years (33.3%).[12]

Idiopathic thrombocytopenic purpura

This constituted 3.6% of cases and mostly in the age group of11-20 years (3). 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].

Hemophagocytic lymphohistiocytosis(HLH)

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 Gupta Aet al. (1%) [11].

Infectious conditions

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 bone marrow

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]

Others

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

BMA is an important hematological investigation. It is useful for diagnostic, prognostic and therapeutic evaluation of various hematological and nonhematological disorders in carefully selected patient after clinical evaluation and vigilant examination of peripheral smear.

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