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Full Length Research Paper

Diagnostic Outcome of bone marrow aspiration in a new centre in Nigeria

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The development of manpower for the tertiary level of health care services in developing countries is inadequate resulting in the establishment of a new centre as soon as the specialist is available. This is usually met by the high health demands from the community in the face of near lack of modern technological diagnostic advancement in the health sector. There is great need to study the morphologic outcome of bone marrow aspiration done in our centre for generation of baseline data and planning. Records of bone marrow Aspiration cytology done in Plateau State Specialist Hospital, Jos, Nigeria between January 2007 and June 2012 were studied. A total of 97 bone marrow aspiration were requested for and done in the Plateau State Specialist Hospital, Jos, within the study period. 55(56.8%) were males while 42(43.2%) were females. Eighty four (87.6%) had pathologic outcome while 13(13.4%) had normal or reactive marrow appearance. Pathologic marrow outcome were 28.6% leukaemias, 33.3% nutrient deficiency anaemias, 11.9% burkitt's lymphoma, 4.1% multiple myloma, 8.3% bone marrow failure and others 13.I%. Common haematologic disorders in our setting are nutritional anaemias and leukaemias. There is need to expand the scope of laboratory investigations beyond morphology.

Keywords: Bone marrow aspiration, features, outcome

INTRODUCTION

The haemopoietic cells are produced in the red bone marrow, this production sites is however limited to the ends of long bones and the cavity of short and flat bones in adults (Abboud, 2001). Diseases may originate or spread to the bone marrow disturbing the normal marrow architecture and haemopoietic composition. A normal marrow aspirate will be normocellular for age, have a myeloid to erythriod ratio of 3-15:1, show evidence of progressive qualitative and quantitative haemopoietic cell lines development with absence of non marrow native cells and adequate marrow iron store (Abboud, 2001). The description of detail bone marrow morphology has allowed for the assumption that clinicians are familiar with major blood disorders (Marmont and Fusco, 1951). Research works have shown the morphologic marrow appearance in various disorders. Pagana and colleges enumerated the indications for bone marrow aspiration and study to include; further investigation of observed isolated or combination abnormality in white blood cell, red blood cells or platelet, diagnosis of blood disorders, identification of known cancer spread, search for infections and tumours, sampling for medical procedures

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Table 1. Distribution of patients according to age and sex.

Age (years)	Male (%)	Female (%)	Total (%)
0-4	2(2.1%)	1(1.0%)	3(3.1%)
5-18	18(18.6%)	10(10.3%)	28(28.7%)
19-45	17(17.5%)	14(14.4%)	31(32.0%)
46-65	13(13.4%)	13(13.4%)	26(26.8%)
>65	5(5.2%)	4(4.1%)	9(9.3%)
Total	55(56.8%)	42(43.2%)	97(100.0%)

and the assessment of best treatment modalities for blood disorders (Pagana and Pagana, 2009).

An American study reported the use of bone marrow aspiration in the resolution of the causes of peripheral macrocytosis and identified megaloblastic erythropoiesis due to folate and or vitamin B12 deficiency or abnormality in their metabolism among other causes of macrocytosis such as alcohol ingestion, hypothyroidism, myelodysplastic syndrome (MDS) haemolysis and myeloproliferative diseases (Kaferle and Strzoda, 2009; Hoffbrand, 2001).

Ayub et al reported a 52.5% magaloblastic erythropoiesis in a retrospective study of their marrow aspirate. They also found marrow bone marrow failure (BMF) accountiong for 20% and leukaemia15% of the outcome of their marrow aspirates (Ayub and Rahman, 2009). A report from Jos, on the edidemiology of anaemia necessitating bone marrow aspiration (BMA) cytology implicated majorly; acute leukaemias in 24.3%, combined iron deficiency (IDA) and megaloblastic anaemias (MA) 18.4% and 10.8% aplastic anaemia (Egesie et al., 2009). Another study on the spectrum of paediatric bone marrow trephine biopsies in Bombay hospital show a 61.66% amaemia, 11.66% infections, 8.33% leukaemias and myelofibrosis in 1.66% (D' costa et al., 2007). Seiter et al reported malignant lymphoplasmacytic infiltrates of the bone marrow with associated increase in serum immunoglobulin M (IgM) and serum viscosity, and organomegally in patients with Waldenstrom Macroglobulinaemia (Seiter and Basa, 2011). A Malaysian study identified the usefulness of bone marrow analysis in chronic myelocytic leukaemia beyond diagnosis to localization of blasts, evaluation of megakaryopoiesis and grading of fibrosis (Kangla et al., 2002). A study on haematologic malignancies in Ilorin, North Central Nigeria, found a 4.9% acute lymphoblastic leukaemia (ALL), 4.9% acute myeloblastic leukaemia (AML), 5.4% chronic lymphocytic leukaemia (CLL) and 11.4% chronic myelocytic leukaemia (CML) (Babatunde et al., 2009). Tanko et al found burkitt's lymphoma (BL) and non hodgskin's lymphoma constituting 33.3% of paediatric solid tumours studied in Jos (Tanko et al., 2009).

There is scanty or no information on the outcome of bone marrow study in this centre being a new one. This study is to analyze the outcome of the bone marrow aspiration done in Plateau State Specialist Hospital and generate baseline data usable for future planning and practice.

METHODOLOGY

Records of all bone marrow aspirates done in Plateau State Specialist Hospital, Jos, North Central Nigeria, between January 2007 and June 2012 were analyzed in retrospect. The age, sex, requesting hospital, indications for marrow aspiration study and diagnosis were collated and analyzed using appropriate statistical package.

RESULTS

A total of 97 bone marrow aspirations requested for were done in the Plateau State Specialist Hospital, Jos, within the study period. 55(56.8%) were males while 42(53.2%) were females. 14(14.4%) of BMA requests were from health facilities outside the tertiary health centres. Males dominated in all age groups except the 46-65years age brackets. The highest number of bone marrow aspirations (BMA) was within the 19-45 years brackets while the least BMA was in the under five. (Table 1)

Eighty four (87.6%) had pathologic outcome while 13(13.4%) had normal or reactive marrow appearance. Among the patients with pathologic outcome, anaemia as defined by haemoglobin value below 110gms/L was the commonest indication for BMA cytology occurring in 77.8% of patients with a higher frequency in males. Fever was present in 29.2% of our subjects with a higher frequency among the male patients (53.6%). 58.3% male and 42.7% female patients had splenomegaly with an overall frequency of 12.5% while lymphadenopathy was found in 13.5% of all subjects (46.2% males and 53.8% females). While intra abdominal mass other than splenomegaly occurred in 6.3% of all patients referred for BMA at the same frequency in both sexes, the rate of occurrence of jaw mass was found in 6.3% of subjects with 60.0% among the male subjects. Mucosal and orifficial bleeding were reported by 5.2% of all patients with 60.0% occurring in females. Other indications for

Table 2. Distribution of symptoms and findings in patients with pathologic marrow aspirate.

Symptoms/sign	Male (%)	Female (%)	Total (%)
Anaemia	42(56.3%)	33(44.7%)	75(77.1%)
Fever	15(53.6%)	13(46.4%)	28(29.2%)
Splenomegaly	7(58.3%)	5(41.7%)	12(12.5%)
Lymphadenopathy	6(46.2%)	7(55.8%)	13(13.5%)
Other intra abdominal mass	3(50.0%)	3(50.0%)	6(6.3%)
Jaw mass	3(60.0%)	2(40.0%)	5(5.2%)
Mucosal bleeds	2(60.0%)	3(60.0%)	5(5.2%)
Bone pains	0(0.0%)	2(100.0%)	2(2.1%)
High PCV	2(100.o%)	0(0.0%)	2(2.1%)
Pica	0(0.0%)	1(100.0%)	1(1.0%)

Table 3. Distribution according to BMA diagnosis

Diagnosis	Age range (years)	Mean age (years)	Male(%)	Female(%)	Total(%)	P Value
ALL	5-30	10.5	5(6.0)	3(3.6)	8(9.5)	0.5
AML	5-46	17.5	3(3.6)	1(1.2)	4(4.8)	0.6
CLL	20-80	58.4	3(3.6)	4(4.8)	7(8.3)	0.5
CGL	15-57	36.8	4(4.8)	1(1.2)	5(6.0)	0.6
MA	14-80	41.6	6(7.1)	9(10.7)	15(17.9)	0.4
IDA	1-60	33.8	2(2.4)	2(2.4)	4(4.8)	0.6
Combined IDA & MA	15-60	39.0	5(6.0)	4(4.8)	9(10.7)	0.6
MDS	68-78	73.0	2(2.4)	0(0.0)	2(2.4)	0.3
BMF	19-52	36.0	4(4.8)	3(3.6)	7(8.3)	0.6
BL	4-15	9.1	6(7.1)	4(4.8)	10(11.9)	0.5
MM	60-68	62.3	1(1.2)	3(3.6)	4(4.8)	0.2
ITP	23-31	27.0	1(1.2)	2(2.4)	3(3.6)	0.4
MF	55-62	59.0	2(2.4)	1(1.2)	3(3.6)	0.5
PRV	22-78	50.0	2(2.4)	0(0.0)	2(2.4)	0.3
?ACD	-	32.0	1(1.2)	0(0.0)	1(1.2)	0.5

Key: ALL-acute lymphoblastic leukaemia, AML- acute myeloblastic leukaemias, CLL-chronic lymphocytic leukaemia, CML-chronic myelocytic leukaemia, MA-megaloblastic anaenia, IDA-iron deficiency anaemia, MDS-myelodysplastic syndrome, BMF-bone marrow failure, BL-burkitt's lymphoma, MM-multiple myloma, ITP-idiopathic thrombocytopenic purpura, MF-myelofibrosis, PRV-polycythaemia rubra vera, ACD-anaemia of chronic disease.

BMA included bone pain, paraplegia and high packed cell volume (PCV). (Table 2)

Pathologic marrow outcome were 28.6% leukaemias, 33.3% nutrient deficiency anaemias, 11.9% burkitt's lymphoma, 4.1% multiple myeloma, 8.3% bone marrow failure and others 13.I%. A male verses female distribution of BMA diagnoses showed a non significant higher prevelence of ALL(6.0%), AML(3.6%), CGL(4.8%), combine IDA and megaloblastic anaemia (6.0%), MDS(2.4%), BMF(4.8%), BL(7.2%), MF(2.4%), PRV(2.4%) and ACD(1.2%) among our male subjects while the female patients had higher rate of megaloblastic anaemia (10.8%), MM(3.6%) and ITP(2.4%). MDS, PRV and ACD were not diagnosed among our female patients. (Table 3)

While matching the BMA diagnoses and the indications for the investigations, all patients with ALL were anaemic, 75% had fever, 37.5% had splenomegaly and or lymphadenopathy and 25% had bleeding orifices. 100% of patients with AML had anaemia, 50% had fever, and 25% had organomegaly. Anaemia, lymphadenopathy and or splenomegaly were found in all patients diagnosed of CLL, while jaundice was found in only 25%. Anaemia and splenomegaly were each present in 75% of patients with CML. Anaemia was identified in all patients with megaloblastic anaemia. Other features were fever (7.6%), splenomegaly (13.4%) and paraplegia(6.7%). All patients with IDA had anaemia with splenomegaly occurring in 25%. Anaemia and splenomegaly respectively were found in 88.9% and 11.1% of patients with combined IDA and megaloblastic anaemia. All patients with BMF had anaemia, while fever was present in 28.6%, bleeding orifices and splenomegaly were each present in 14.3%. Retroviral infection was background in

Table 4. Occurrence of symptoms in patients with a particular diagnosis

Diag nosis	No	anae mia	Fever	spleno megaly	Lymph nodes	Bone pains	Abd mass	Jaw mass	bleeding	Jaudice	Paraplegia
ALL	8	100%	75%	37.5%	37.5%	50%	_	_	25%	_	_
AML	4	100%	50%	10%	15%	25%	_	_	25%	_	_
CLL	7	100%	28.6%	100%	100%	_	_	_	_	28.6%	_
CGL	9	77.8%	_	77.8%	_	_	_	_	_	_	_
MA	15	100%	7.6%	13.3%	_	_	_	_	_	20%	6.7%
IDA	4	100%	_	25%	_	_	_	_	_	_	_
CDA	9	88.9%	_	11.1%	_	_	_	_	_	_	_
BMF	7	100%	28.6%	14.3%	14.3%	_	_	_	14.3%	_	_
BL	10	50%	20%	_	_	_	70%	60%	_	_	_
MM	4	75%	_	50%	_	75%	_	_	50%	_	_

Key: ALL- Acute lymphoblastic leukaemia. AML- Acute myeloblastic leukaemia. CLL-Chronic lymphocytic leukaemia. CML-Chronic myelocytic leukaemia. MA- Megaloblastic anaemia. IDA- Iron deficiency anaemia. CDA- Combined IDA & MA. BMF-Bone marrow failure. BL- Burkitt's lymphoma. MM- Multiple myloma.

42.9% of BMF. Abdominal masses, jaw mass, anaemia, and fever presented each at the frequency of 70%, 60% 50% and 20% respectively in patients with BL. Among subjects with multiple myeloma (MM), anaemia, and bone pains were each present in 75% of patients while bleeding orifices and splenomegaly were present in 50%. All patients with MDS presented with only anaemia while anaemia was only present in 66.7% of subjects with ITP and MF. Bleeding mucosae and splenomegaly were respectively present in all patients with ITP and MF. Patients diagnosed of PRV were found with high PCV at voluntary blood donation and referred for further investigations. Anaemia secondary to probably chronic disease was identified in only one patients being managed for type 1 diabetes mellitus. (Table 4).

DISCUSSION

This study investigated the diagnostic outcome of BMA cytology done in our centre. The age range of our patients was 1-82 years similar to that reported by Egesie and others, representative of all age groups in the population (Egesie et al., 2009). 14.4% of all BMA were done on patients referred from primary and secondary levels of health care providers suggesting that the availability and accessibility of specialists could provoke evidence base medical management of patients with haematologic disorders in these category of health care centres. It further suggests the need for increase commitment of resources into the training of more specialists in haematology to meet this demand. 56.8% BMA were carried out on male patients agreeing with the 1.5:1 ratio of male to female patients with anaemia necessitating BMA reported in an earlier study (Egesie et al., 2009). The age group patient concentration was highest within the 5-18 years bracket which may be due to the common occurrence of acute leukaemias in childhood. The findings of normal and reactive marrow cytology in our study concurred with the suggestion that non haematologic disorders may present with haematologic manifestations as the 14.4% of our patients with these marrow outcome were anaemic (Basic principles in diagnosing and treating anaemias, 2004).

The common pre BMA findings in our patients were anaemia, fever, organomegalies, mucosal bleeding, bone pains, high PCV and Pica (table 2). These findings contributed to the request for bone marrow study as they are known to be related to haematologic diseases particularly when found in combination in a patient (Basic principles in diagnosing and treating anaemias, 2004). The presence of anaemia in the majority of our patients may be due to late hospital presentation occasioned by poverty and ignorance. Pica was found in a female patient who repeatedly failed to meet acceptable haemoglobin level, using the haemocue test, at voluntary blood donation. This calls for closer collaboration with the blood service as it can offer a good opportunity for the surveillance of anaemia and other disorders.

Leukaemias accounted for 28.6% bone marrow aspiration diagnosis with 9.5% ALL, 4.8% AML, 8.3% CLL and 6.0% CML. The prevelence of 28.6% leukaemias in our study is similar to that reported by Egesie in Jos and Babatunde in Ilorin, both in North Central Nigeria, but higher than in an Arab study where a 15.0% prevelence was reported agreeing with regional variations in the incidence and prevelence of leukaemias (Ayub and Rahman, 2009; Egesie et al., 2009; Tanko et al., 2009; Cancer facts and figures, 1991). The mean age of our patients with AML (table 3) is lower than that reported by the American Cancer Society (55-60 years) showing the affectation of younger persons in our setting (Cancer facts and figures, 1991). The combined prevelence of chronic leukaemias (14.3%) in our study is similar to 16.8% found in Ilorin, while 11.4% CML in their study is higher than ours (6.0%) (Babatunde et al., 2009). The occurrence of anaemia, fever, splenomegaly,

lymphadenopathy, bone pains and mucosal bleeding (table 4) are similar to symptoms earlier documented (Catovsky and Hoffbrand, 1999). This highlights the need for early appropriate consultations for comprehensive evaluation of patients with these symptoms common in haematologic disorders.

Nutritional deficiency anaemia accounted for 33.3% marrow diagnostic out come in our study. This figure is lower than 52.5% reported from an Indian study among peadiatric patients (Ayub and Rahman, 2009). It is however higher than the 18.4% deficiency diagnosis made from BMA cytology in a centre within our region (Egesie et al., 2009). Our study identified megaloblastic anaemia as the commonest cause of anaemia followed by combined IDA and megaloblastic anaemia. This does not agree with the popular knowledge of iron deficiency anaemia being the commonest cause of anaemia worldwide (Pippard and Hoffbrand, 1999). Megaloblastic anaemia being the commonest anaemia in our study differs from earlier report by Egesie et al who identified combined IDA and Megaloblastic anaemia the most common cause of anaemia but agrees with Ayub et al and Perweiz et al who found megaloblastic anaemia the most prevalent in a Gomal and Aga Khan University Hospital Pakistan studies respectively (Egesie et al., 2009; Ayub et al., 2009; Perweiz et al., 2009). The prevelence of anaemia at ante natal care booking in a secondary health care facility in North Eastern Nigeria was 51% with pure IDA accounting for 64.9% and 0.4% MA (Bukar et al., 2009). Predominance of MA in our study may be due to the adverse economic effects of protracted religious and ethnic crisis enshrining increasing poverty and ignorance among the populace. This calls for concerted efforts from government and individuals at peace building to allow for productive living which would alleviate poverty, improves standard of living and good nutrition and prevention of nutrient deficiency state. The finding of paraplegia (Dabior, 2001; Pippard and Hoffbrand, 1999), an irreversible complication of megaloblastic anaemia due vitamin B_{12} deficiency, in one of our patients with magaloblastic anaemia calls for increase awareness, index of suspicion, appropriate investigations and treatment of this disorder among health care providers at all levels.

The prevelence of lymphomas in our study (table 3) is lower than that reported by Tanko and colleagues in Jos (Dabior, 2001; Pippard and Hoffbrand, 1999). This diferrence is partly due to non referral of lymphomas other than burkitt's to our clinic for evaluation. BMA evaluation of patients with lymphomas would afford appropriate staging, choice of treatment modality and prognostication; and therefore informed counseling. Bone marrow failure in our study is similar to the 10.8% reported by Egesie in Jos (Egesie et al., 2009). Our study identified background infection with the human immunodeficiency virus (HIV) in three (42.9%) cases. This implies the likelihood of increasing prevelence of BMF with the endemic status of HIV in our setting calling for more commitment in the control of this preventable viral infection. Andrea and others while describing the pathogenesis and treatment of aplastic anaemia highlighted the role of autoimmune destruction of haemopoietic stem cells (Andrea and Ospedale, 2007). Rosenfield further enumerated other agents implicated in the pathogenesis of bone marrow failure including drugs, toxins, metabolic defects, radiation and viral infections such as hepatitis viruses, human immunodeficiency virus and pavovirus prominent among others (Rosenfield and Young 1991). The haematologic complication of HIV infection is cytopenia due to bone marrow or peripheral blood cells destruction as a result of treatment or disease (Hambleton, 1996). Other pathologic bone marrow outcome in our study are rare disorders as documented in earlier studies in Jos (Egesie et al., 2009; Tanko et al., 2009).

Combinations of features that indicated the need for BMA cytology were found occurring at various frequencies in our patients (table 4). The finding of these features in their combinations should raise the index of suspicion on the occurrence of haematologic disease and directs care towards relevant cost effective investigations which would enhance early diagnosis, treatment, prevention or limiting complications and shortening hospital stay.

CONCLUSION

We conclude from this study that haematologic disorders are frequent among disorders requiring BMA in our setting. We also conclude that nutritional deficiency anaemias are commonest haematologic disorders, followed by leukaemias and lymphomas.

RECOMMENDATIONS

We recommend closer collaboration among all specialties in segregating and consulting on patients that would require haematology reviewed for early diagnosis and treatment of haematologic disorders. The need for all health care providers in a developing country with an underdeveloped health system to be familiar with basic symptoms of major haematologic disorders is to raise a high index of suspicion and guide management. We also recommend the expansion of the scope of laboratory investigations to include specific minerals and vitamin assays, cytochemistry, immunohistochemistry and cytogenetics for better characterization and prognostication of haematologic disorders. We further recommend the development of stem cell centre for the advanced management of these diseases among others.

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