ORIGINAL RESEARCH PAPER

Pathology

FROM ANAEMIA TO LEUKEMIA: BONE MARROW ASPIRATION THE DIAGNOSTIC TOOL IN A STUDY AT TERTIARY CENTRE

KEY WORDS: BMA, Haematological, Non Haematological Disorders

Dr. Anshu Jamaiyar — Associate Professor, Department of Pathology, RIMS, Ranchi 834009.

Dr. Kumar Yogesh* — Junior Resident Academic, Department of Pathology, RIMS, Ranchi 834009. *Corresponding Author

ABSTRACT

BACKGROUND: Haematological and non haematological disorders have divergent mode of presentation that often require bone marrow aspiration for diagnosis and management. It proves to be safe, simple, cost effective and less time consuming, particularly in resource poor centre which has limited access to adjuvant diagnostic techniques. This study was conducted with the aim to evaluate the spectrum of bone marrow involvement with malignant and non-malignant haematological, and non haematological disorders to observe its efficacy in establishing it as a primary diagnostic tool.

METHODOLOGY: This was a hospital-based study, conducted in RIMS, Ranchi over a period of 25 months. A wide range of patients between age of 1 year to 80 years were included in our study. Proper history, physical examination and required ancillary investigations were recorded before the procedure. A total 858 successful BMA was done with exclusion criteria of dry tap and inconclusive results. **RESULTS:** Out of total 858 BMA, pathological findings were evident in 742 (86.48%) and bone marrow were normal in 116 (13.52%). Among pathological findings, 736 (99.19%) cases were haematological cases and 6 (0.8%) were non haematological. Out of nonhematological conditions, 2 cases were found to have each of storage disorders, granuloma and visceral leishmaniasis respectively. M:F ratio in our study was 1.67:1.

CONCLUSION: Bone marrow examination proves to be a simple, safe, early reporting technique in the diagnosis of various clinical conditions, both haematological and non haematological disorders. Its importance is further highlighted were routine investigations fails to reach a conclusive diagnosis.

INTRODUCTION:

Bone marrow examination holds pioneer position in the assessment of haematological disorders. To assess various haematological disorders, bone marrow examination is considered as a chief diagnostic procedure [1]. Examination of bone marrow is a valuable diagnostic procedure in patients with known or suspected haematological disorders and also for diagnosis of metastatic spread of non haematological malignancies and metabolic disorders [2]. In addition, it helps in staging, prognostication and evaluation of therapeutic response in various disorders [3]. It is an econimcal, quick and valuable method in making a definitive diagnosis involving the bone marrow [4,5].

Bone marrow consists of cellular and stromal components. Cellular elements consist of erythroid precursors, myeloid precursors, megakaryocytes, lymphocytes, macrophages, mast cells and plasma cells. The specialized stroma of the marrow forms a unique microenvironment for the proliferation and differentiation of haemopoietic progenitors. Bone marrow cellularity is expressed as the percentage of a section that is occupied by haemopoietic tissues.

Diseases of the bone marrow can be primary or a secondary spread to the marrow. In both, the normal cellular architecture is distorted. Anemia, being the common presentation in most of the cases whether the background is haematological or non haematological. Therefore, a detailed study of bone marrow morphology may provide the explanation for the diseases involving the bone marrow [3].

The present study was conducted to explore the common indications for bone marrow aspiration in ascertaining the diagnosis of haematological and non haematological disorders.

MATERIALS AND METHOD:

Study setting:

The present study was a hospital-based study conducted over a duration of 25 months in Department of Pathology, RIMS, Ranchi, Jharkhand.

Study design:

This was cross sectional study in which the sucessful bone marrow aspiration (BMA) record from March 2018 to April 2020 where reviewed rectrospectively.

Inclusion criteria: Only BMA cytology was reviewd which counted to total of 858 number of cases.

Exclusion criteria: inconclusive results, dry tap and bone marrow biopsies.

This study carried out in RIMS, Ranchi, Jharkhand was a cross sectional study. A total of 858 BMA cytology was done, excluding inconclusive results, dry tap and bone marrow biopsies from March 2018 to April 2020. Detailed history of each patient was taken and physical examination was carried out. This helped in achieving the adequate diagnosis, especially for anemia like dietary history, socioeconomic status, personal history stating vegetarian or non-vegetarian. Lymphadenopathy and hepatospleenomegaly were important in diagnosis of various haematological malignancies. Searching for the primary malignancies in case there are secondaries in the marrow. Drug history and adjuvant viral infections were relevant in diagnosing cytopenias. Demographic history plays an important role in the diagnosis of diseases like leishmaniasis. Blood transfusion history was a key point as patients with blood transfusion within 48 hours were denied for bone marrow aspiration.

Complete blood count, peripheral smear, total and differential leucocyte count, platelet count, blood indices and reticulocyte counts were done using automated haematology analyzer (Sysmex xt-2000i) and were cross checked manually.

Prior to the procedure informed consent from the patients/ guardian (in case of minor) was taken. Under available aseptic precautions, with vitals stable, patient was made to lie in supine position. BMA were performed using Salah needle from anterior and posterior iliac crest while in children under 2 years, it was done from upper end of the tibia below level of

tibial tubercle and in elederly, bone marrow was aspirated from sternum. The appropriate site according to age and easy accessibility was palpated and skin infilteration was done using 2% lignocaine for local anaesthesia. Salah needle was inserted in the marrow and aspiration was done. The aspirated material was spread on clean slides and was collected in a sterile EDTA (Ethylene diamine tetra acetic acid) test tube. Prepared slides were stained with Romanowsky stains and examined for cellularity, presence of megakaryoctes, immature cells, nucleated bone marrow cells and hemo parasites. Prussian blue stain was used for assessing the iron stores. PAS (Periodic acid Schiff) stain, MPO (Myeloperoxidae) stain and Sudan black stain were some of the special stains that were used to deterimine the type and classification of various leukamias.

RESULT:

A total of 858 bone marrow aspiration cytology examinations were carried during the study period. Age groups ranged from 1 year to 80 years with the mean age of 40 years. Male to Female ratio is 1.67:1. Most common site of aspiration in our study was ASIS followed by PSIS, sternum and tibia. Pathological findings were evident in 742 (86.48%) and bone marrow were normal in 116 (13.52%). Among pathological findings, 736 (99.19%) cases were haematological cases and 6 (0.8%) were non haematological. Out of non-hematological conditions, 2 cases were found to have each of storage disorders, granuloma and visceral leishmaniasis respectively. Among hematological cases, 213 were malignant conditions and 524 were non-malignant. Various malignant conditions can be formulated as AML-40, ALL – 59, CML-63, CLL-12, MDS -10, Plasma cell dyscrasias -14, Lymphoreticular malignancies5, Polycythemia vera-5, Tumor metastasis -5. Non-malignant disorders on the other hand includes 146 cases of hypoplastic marrow , erythroid hyperplasia with normoblast accounts for 179 cases, erythroid hyperplasia with micronormoblast accounts for 28 cases, erythroid hyperplasia with megaloblastic changes for 94 cases, both micronormoblast and megaloblast for 8 cases, platelet disorders for 23 cases, myeloid hyperplasia 36 cases, myeloid hypoplasia 3 cases.

Table refers to different clinical conditions requiring bone marrow examinations:

Indications	Frequency
Pancytopenia	181
Unexplained anemia	317
Abnormal peripheral blood findings	82
Suspected haematological malignancies	171
Thrombocytopenias / bleeding	52
Suspected bone metastasis	13
Unexplained fever	42

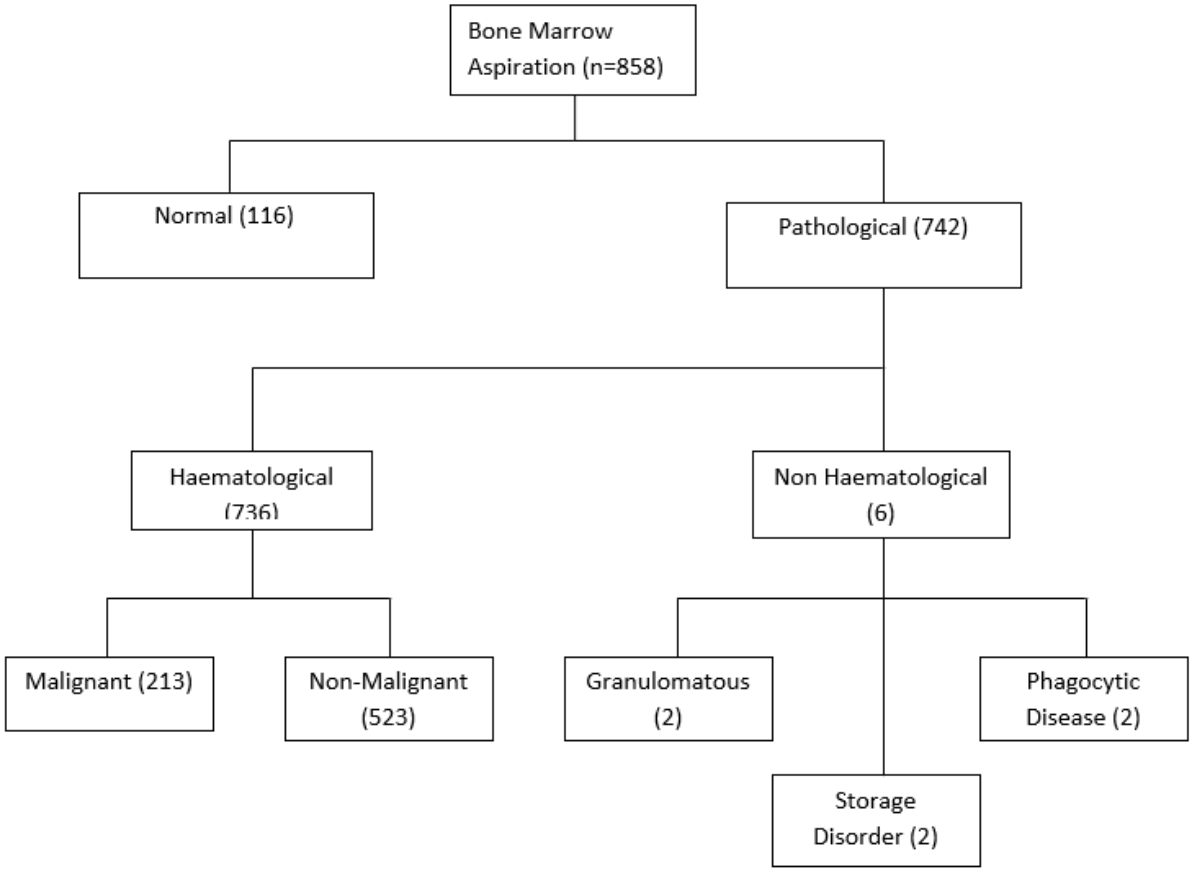
Bone marrow features	Frequency (n=858)
Pathological bone marrow	742 (86.48%)
Normal marrow	116 (13.52%)

Distribution of haematological and non haematological disorders:

Disorder:	Frequency (n=742)
Haematological disorders	736 (99.19%)
Non Haematological disorders	6 (0.81%)

Distribution of non haematological disorders:

	GENDER		SITE				
Disorder:	Male	Female	ASIS	PSIS	Sternum	Tibia	Total
Storage disorders (Gauchers disease)	0	2	1	0	0	1	2
Granuloma	2	0	2	0	0	0	2
Visceral leishmaniasis	1	1	1	0	1	0	2



Distribution of various non-malignant haematological disorders:

	GENDER		SITE				
BMA features:	**Male**	**Female**	**ASIS**	**PSIS**	**Sternum**	**Tibia**	**Total**
Hypoplastic marrow	70	76	79	50	11	6	146
Erythroid hyperplasia with normoblasts	85	94	108	42	11	18	179
Erythroid hyperplasia with micronormoblasts (iron deficiency anaemias)	19	9	19	5	2	2	28
Erythroid hyperplasia with megaloblastic changes (megaloblastic anaemias)	53	41	61	21	9	3	94
Both micronormoblasts and megaloblasts (dimorphic anaemias)	5	3	7	1	0	0	8
Platelet disorders (idiopathic thrombocytopenic pupura)	9	14	18	4	0	1	23
Hyperspleenism	1	5	2	2	1	1	6
Myeloid hyperplasia	19	17	21	10	2	3	36
Myeloid hypoplasia	1	2	2	1	0	0	3

Distribution of malignant haematological disorders

	GENDER		SITE				
BMA features:	**Male**	**Female**	**ASIS**	**PSIS**	**Sternum**	**Tibia**	**Total**
AML	21	19	26	8	6	0	40
ALL	30	29	42	9	1	7	59
CML	39	24	37	19	7	0	63
CLL	12	0	5	4	3	0	12
MDS	7	3	4	2	4	0	10
Plasma cell dyscarias (multiple myeloma)	11	3	4	9	1	0	14
Lymphoreticular malignancies	5	0	3	0	2	0	5
Polycythemia vera	2	3	3	2	0	0	5
Tumor metastasis	4	1	3	2	0	0	5

*AML: Acute Myeloid Leukemia, ALL: Acute Lymphoblastic Leukemia, CML: Chronic Myeloid Leukemia, CLL: Chronic Lymphocytic Leukemia, MDS: Myelodysblastic Syndrome.

DISCUSSION:

There is wide spectrum of haematological and non haematological disorders in both children and adults. Bone marrow aspiration cytology proves to be advantageous in reaching the final diagnosis. Age range in of the patients in our study was 1 to 80 years, mean age being 40 years. M:F ratio in our study was about 1.67:1 , which is similar to the study done by Kibira et al i.e 2:1.

Bone marrow examination helps to elucidate the underlying causes of several disorders. In our study malignant haematological disorders comprises 24.83 % and non-malignant haematological disorders were 60.96% which is contrary to the large study carried by Bong Hak Hyum over a period 25 years which states that 22% of their patients had non-malignant haematological disorders and 30% had haematological malignancies [6].

But our study correlates better with other international studies carried out by Shaheen and her coworkers [1,7]. The difference in our result as compared to those by Hyun regarding the occurance of malignant and non-malignant haematological disorders is most likely due to the presence of different anaemias in different demographic and socioeconomic and food habits.

Pancytopenia on peripheral blood examination was the most common finding. On BMA examination, hypoplastic marrow was the finding. Most common cause being idiopathic followed by various viral infections like EBV, CMV, radiation and chemical substances like alkylating agents, antimetabolites, chloramphenicol etc.

Most of the patients who came with complain of easy fatigability and on general examination pallor was present, on BMA cytology were found to show erythroid hyperplasia. Erythroid hyperplasia was accompanied with either normoblasts, micronormoblasts, megaloblasts or both micro and megaloblasts. The BMA cytology results were correlated with the proper history, dietry habit, socio economic status of the patients and ancillary blood investigations like iron profile, level of vitambin B12 and folic acid. If the BMA showed erythroid hyperplasia with micronormoblasts , along with low serum ferritin, low serum iron, raised total iron binding capacity and raised transferrin receptors in blood, the diagnosis was given as iron deficiency anemia. The support of the diagnosis was accentuated by Prussian blue stain.

On the other hand, if the BMA showed erythroid hyperplasia with megaloblasts and low level of vitamin B12 and /or folic acid with a personal history of being strict vegetarian, less dietary intake of vitamin B12 due to poverty, favoured towards the diagnosis of megaloblastic anemia. Presence of Helicobacter pylori in unsafe drinking water leading to atrophic gastritis and B12 deficiency leads to megaloblastic anaemia.

Patients with both micronormoblatic and megalobalstic changes were diagnosed as dimorphic anemia. In our study the cases of megaloblastic anemias were much more than that of iron deficiency anemia. According other cause of anemia like chronic diseases, sideroblastic anaemia, haemolytic anaemia etc were diagnosed.

Out of 58 cases with thrombocytopenia, 23 were diagnosed as idiopathic thrombocytopenic purpura. On BMA, there were increased number of megakaryoctes and on clinical examination patient presented with petichae or purpuric rashes. There are studies which suggest that bone marrow examinations are less informative in patients with isolated thrombocytopenia. [8,9]. Studies suggest that role of bone marrow examination is mainly to exclude other

haematological diseases like various leukaemias and myelodysplastic syndromes [10].

Patients with abnormal peripheral blood picture, bone marrow aspiration was done suspecting some haematological malignancies. Among the malignant haemtological disorders, highest number of cases were of CML–63 (7.34%) followed by ALL–59(6.88%), AML–40(4.66%) and CLL–12(1.40%), although the total number of cases of acute leukemia (99 cases) is more than that of chronic leukemias (75 cases). Other ancillary tests like flow cytometry, cytogenetic studies etc helped us in reaching a definite classification of a particular type of malignancies.

Other than the above mentioned malignancies, other reported malignancies in our study, in descending order of occurrence include; multiple myeloma 14(1.63%), MDS 10(1.17%), lymphoreticular malignancies, polycythemia vera, tumour metastasis each counting to 5 in number i.e 0.58% each.

In the complete course of study, cases of non haemtological disorders is very low i.e only 6 cases (0.70%).

CONCLUSION:

In situations where routine investigations fail to reach a conclusive diagnosis, BMA cytology plays a significant role in early diagnosis of the disease and positively modify the outcome of various diseases with early and accurate management. Although it is a invasive procedure but is accepted by the patients as it is simple, cheap, accurate, early reporting and valuable for the diagnosis of wide range of diseases. In case of dry tap and inconclusive results, role of bone marrow biopsies come into play.

REFERENCES:

1. Shaheen N, Khan MQA, Azim W, Ali N. Bone marrow aspiration. The diagnostic tool in haematological and nonhaematological disorders. Pak J Pathol 2010;21(1):1-4.
2. Bain BJ. Bone marrow biopsy morbidity: review of 2003. J Clin Pathol 2005; 58 (4): 406- 408
3. RockWA Jr, Stass SA,eds.Handbook of Hematologic Pathology. New York, NY:Marcel Dekker, Inc:,2000:1~26.
4. Sreedharanunni S, Sachdeva MU, Kumar N, Sharma P, Naseem S, Ahluwalia J, et al. Spectrum of diseases diagnosed on bone marrow examination of 285 infants in a single tertiary care center. Hematology. 2015;20(3):175-81
5. Riley RS, Hogan TF, Pavot DR, Forysthe R, Massey D, Smith E, et al. A pathologist's perspective on bonemarrow aspiration and biopsy: I. Performing a bonemarrow examination. Journal of clinical laboratoryanalysis. 2004;18(2):70-90.
6. Hyun BH. Bone marrow examination: Adventures in Diagnostic Hematology. Yonsei Medi J 1986;27(2):100–5.
7. Manan M, Khaliq MA, Ahmed S, Qayyum I and Idrees M. Diagnostic significance of BM examination. J Ayub Med Coll Abbottabad 2000; 12:43–45
8. Jubelirer SJ, Harpold R. The role of bone marrow examination in the diagnosis of Idiopathic thrombocytopaenic Purpura: Case series and literature review. Clin Appl Thromb Hemost 2012; 8(1):73–76
9. Westerman DA, Grigg AP. The diagnosis of Idiopathic Thrombocytopaenic Purpura in adults: Does bone marrow biopsy have a place? Med J Aust. 1999; 170(5):2162–17.
10. Mahabir VK, Ross C, Poporic S, Sur ML, Bourgeois J, Lim, et al. A blind study of bone marrow examination in patients with Primary Immune Thrombocytopaenia. Eur J. Haematol 2013; 90(2): 121–126.