Original Research Article

Indian Journal of Pathology: Research and Practice
Volume 6 Number 3, July - September 2017 (Part-I)
DOI: http://dx.doi.org/10.21088/ijprp.2278.148X.6317.21

Diagnostic Evaluation of Patterns of Bone Marrow Involvement in Myelophthisic Anemias

V. Shanthi*, B.V. Vydehi*, P.Pavani, M. Sushmalatha***, V. Tejaswini***, Tanusha Ethamakula*****

*Professor **Assistant Professor ***Tutor, Department of Pathology, Narayana Medical College, Chintareddy Palem, Nellore, Andhra Pradesh, India.

Abstract

Background: Bone marrow examination is an important diagnostic tool in the evaluation of cases of myelophthisic anemia. Myelophthisis means replacement of bone marrow elements by either the tumor tissue, granulomatous inflammations or fibrosis, which further leads to anemia. *Methods:* our study was retrospective study which reviewed bone marrow examination of 60 cases with myelophthisic anemia in Narayana Medical College and hospital, during a period of 5years (Jan 2011- Jan 2016). *Result:* Our study of 60 cases revealed, 53 cases having neoplastic involvement of bone marrow and 7 cases having non- neoplastic pathology. 53 cases having neoplastic involvement showed 49 cases with haematological and 4 cases with secondary metastatic deposits. In our study 50% cases presented with anemia, 30% with leukoerythroblastic picture, 13.33% cases presented with pancytopenia & 6.66% cases with thrombocytopenia *Conclusion:* Our study reflected that the common causes of myelophthisic anemia was neoplastic (88.33%) and tuberculosis (42.86%) commonest among the non-neoplastic involvement.

Keywords: Myelophthisic Anemia; Bone Marrow.

Introduction

Myelophthisic anemia is a kind of anemia caused due to replacement of the hematopoietic bone marrow elements by either tumor, granulomas or fibrosis. Myelophthisis occurs in conditions like myeloma, metastatic carcinoma, lymphoma, leukemia & chronic myeloproliferative disease(myelofibrosis). Metastatic carcinomas which are commonly associated with bone marrow deposits are small cell lung cancer, breast cancer or prostate cancer. Other causes include storage diseases & granulomatous disease. Cytopenia results from the release of substances such as cytokines that suppress hematopoiesis, destroys stem progenitor and stromal cells. With the disruption of normal bone marrow architecture by infiltrating cells, the marrow releases immature hematopoietic cells. Blood picture in these patients is mild to moderate anemia with normocytic erythrocytes, tear drop erythrocytes, nucleated RBCs, immature myeloid cells, megakaryocyte fragments and reticulocytopenia [1].

Bone marrow aspiration and needle biopsy have numerous advantages in determining degree of cellularity, metastatic deposits, fibrosis and conditions leading to myelophthisic anemia [2]. In our study we analysed the haematological picture and patterns of bone marrow involvement in patients with myelophthisic anemia.

Materials and Methods

The study was carried out retrospectively in the department of pathology in Narayana medical college and hospital, Nellore during period of January 2011 to January 2016. A total of 60 bone marrow biopsies and aspirations were performed on patients with anemia, who were suspected to have bone marrow infiltration. Site preferred for the procedure was posterior iliac crest by using Jamshidi needle. Peripheral blood picture and bone marrow study were analysed. 0.5ml of bone marrow aspirates were taken and were placed on the clear glass slides to prepare

Corresponding Author: V. Shanthi, Flat no. 103, Anjani SVGK Towers, Sri Hari nagar, Ramalingapuram, Nellore, Andhra Pradesh, India.
E-mail: santhijp@gmail.com

(Received on 22.04.2017, **Accepted on** 09.05.2017)

smears. Smears prepared were stained with Giemsa stain. The bone marrow biopsy specimen were decalcified and stained with Hematoxylin and Eosin. Special stains like Reticulin stain and immunochemistry was performed whenever it was required.

Result

This study included 60 cases of myelophthisic anemia diagnosed on peripheral smear and bone marrow examination during the period of 5 years January 2011 to January 2016 at Narayana medical college, Nellore.

Maximum number of cases presented with anemia (50%) and with leukoerythroblastic picture (30%), pancytopenia (13.33%), thrombocytopenia (6.66%) in decreasing order of frequency (Table 1).

Of 60 cases, 53 cases (88.33%) showed neoplastic involvement of bone marrow and 7 cases (11.67%) were non neoplastic. Among neoplastic involvement 49 cases showed haematological malignancies which included multiple myeloma (34%) (Figure 1), acute leukemias (30%), myeloproliferative disease(14%), non hodgkins lymphoma(10%), chronic lymphoid leukemia(6%), myelodysplastic syndrome(4%) and follicular lymphoma(2%) (Table 2).

4 cases of non haematological malignancies showed metastasis from prostate cancer (Figure 2), breast cancer and 2 cases showed deposits from gastrointestinal tract carcinoma .

Non neoplastic diseases involving bone marrow were granulomatous lesions (43%) (Figure 3), gelatinous transformations (14%), hemaphagocytic disorder (29%) and idiopathic hypereosinophilic condition (14%) (Table 3).

Among the hematological neoplasms, the incidence was found to be more in males except the myelodysplastic syndrome and follicular lymphoma which were found only in females in our study. Chronic lymphoid leukemia showed equal sex incidence. Among non-neoplastic diseases one case of gelatinous transformation was seen in female and remaining lesions showed increased incidence in males. In case of metatstatic deposits both male and female showed equal incidence (Table 4).

Among the hematological malignancies maximum number of plasma cell neoplasms were seen in the 5th decade, acute leukemias in 3rd decade, myeloproliferative disorder in 3rd decade, non-hodgkins lymphoma in 2nd and 4th decade, chronic lymphoid leukemia in 7th decade, myelodysplastic syndrome in 3rd and 4th decade and follicular lymphoma in 4th decade. Most of the non-neoplastic lesions were seen in age group above 30 years. One case of hemophagocytic disorder was noted in the 1st decade. Among the 4 cases of metastatic deposits 2 were seen in the 6th decade and 2 were in the 7th decade (Table 5).

Most common patterns of bone marrow involvement in neoplastic diseases were diffuse, where as among non neoplastic diseases common pattern of involvement was intertrabecular .

Table 1: Haematological findings in myelophthisic anemia patients

S. No	Presentation on peripheral smear	Number of cases (n=60)	Percentage (%)
1	Anemia	30	50
2	Leukoerythroblastic picture	18	30
3	Pancytopenia	8	13.33
4	Bicytopenia/ thrombocytopenia	4	6.66

Table 2: Hematological malignancies involving bone marrow

Hematological malignancies	Number of cases (n=49)	Percentage
Multiple myeloma	17	34.69
Acute leukemia	14	28.57
Myeloproliferative disease	7	14.28
Non hodgkins lymphoma	5	10.22
Chronic lymphoid leukemia	3	6.12
Myelodysplastic syndrome	2	4.08
Follicular lymphoma	1	2.04

Table 3: Non-neoplastic diseases involving bone marrow

Non Neoplastic Diseases	Number of Cases (n=7)	Percentage
Granulomatous lesions	3	42.86%
Hemophagocytic disorder	2	28.5%
Gelatinous transformation	1	14.28%
Idiopathic hypereosinophilic syndrome	1	14.28%

Table 4: Sex wise distribution of neoplastic and non-neoplastic lesions involving bone marrow

Lesions Involving Bone Marrow	Males (%) (N=39)	Females (%) (N=21)
Plasma cell neoplasm	13 (21.5%)	4 (6.6%)
Acute leukemias	10 (16.6%)	4 (6.6%)
Myeloproliferative disorder	4 (6.6%)	3 (4.9%)
Non hodgkins lymphoma	3 (4.9%)	1 (1.6%)
Chronic lymphoid leukemia	2 (3.3%)	2 (3.3%)
Myelodysplastic syndrome	-	2 (3.3%)
Follicular lymphoma	-	1 (1.6%)
Granulomatous lesions	2 (3.3%0	1 (1.6%)
Gelatinous	-	1 (1.6%)
Idiopathic hypereosinophilic syndrome	1 (1.6%)	-
Hemophagocytic	2 (3.3%)	-
Metastatic deposits	2 (3.3%)	2 (3.3%)

Table 5: Neoplastic and Non-neoplastic lesions involving bone marrow in different age group

Lesions involving bone marrow	1st decade	2nd decade	3rd decade	4th decade	5th decade	6th decade	7th decade	8th decade
Plasma cell neoplasm	-	-	1(1.6%)	5(8.3%)	4(6.6%)	2(3.3%)	2(3.3%)	3 (4.9%)
Acute leukemias	3(4.9%)	-	4(6.6%)	2(3.3%)	3(4.9%)	1(1.6%)	1(1.6%)	-
Myeloproliferative disorder	-	1 (1.6%)	4 (6.6%)	1 (1.6%)	-	1 (1.6%)	-	-
Non hodgkins lymphoma	-	2 (3.3%)	-	2 (3.3%)	-	-	-	-
Chronic lymphoid leukemia	-	-	-	-	1 (1.6%)	1 (1.6%)	2 (3.3%)	-
Myelodysplastic syndrome	-	-	1(1.6%)	1(1.6%)	-	-	-	-
Follicular lymphoma	-	-	-	1(1.6%)	-	-	-	-
Granulomatous lesions	-	-	1(1.6%)	1(1.6%)	-	1(1.6%)	-	-
Gelatinous	-	-	-	-	-	1(1.6%)	-	-
Idiopathic hypereosinophilic syndrome	-	-	-	-	-	1(1.6%)	-	-
Hemophagocytic	1(1.6%)	-	1(1.6%)	-	-	-	-	-
Metastatic deposits	-	-	-	-	-	2 (3.3%)	2 (3.3%)	-

Discussion

Myelophthisic anemia is caused due to bone marrow tissue replacement by fibrosis, granulomas or tumors and is characterised by presence of nucleated RBCs, tear drop cells and leukoerythroblastic blood picture on peripheral smear.

In myelophthisic anemia, fibrosis occurs due to cytokines which are released due to the injury caused by non haematological cells. The cytokines stimulate the proliferation of fibroblasts which replace the normal hematopoietic tissue and stromal cells which support the hematopoietic cells. Due to the decrease in the space available for the pluripotent stem cells in the bone marrow. They migrate to the spleen and liver for compensatory extra-medullary hematopoiesis. As these organs have suboptimal stromal support, hematopoietic elements are released into the circulation prematurely [3].

Leukoerythroblastic picture on peripheral smear indicated by the presence of precursor granulocyte cells, nucleated red blood cells and tear drop cells, suggest the possibility of metastatic tumor deposits in the bone marrow. If the bone marrow infiltration is extensive, then the patient present with pancytopenia. Pancytopenia can be present in other conditions like aplastic anemia. But in aplastic anemia, there will be absence of immature blood cells in the peripheral smear.

In our study maximum number of cases presented with anemia (50%) which correlated with study done by Kriti chauhan [4].

Many studies in the past have shown that bone marrow can have metastatic deposits from all malignancies [3]. Prostate, lung and breast malignancies are the common tumor metastasizing to the bone marrow. Degree of marrow infiltration by tumor cells is related to the amount of fibrosis. Fibrosis is more marked in carcinoma of lung, prostate, stomach and breast [5]. Other non neoplastic conditions leading to myelophthisic are inflammatory conditions like tuberculosis, fungal infections, sarcoidosis, storage disorders with macrophage proliferation, sickle cell disorders and septicemia leading to necrosis and conditions like congenital osteoporosis.

In our study , most commonest non haematological disorder causing myelophthisic anemia were non neoplastic disorder (7 cases). Only 4 cases of metastatic

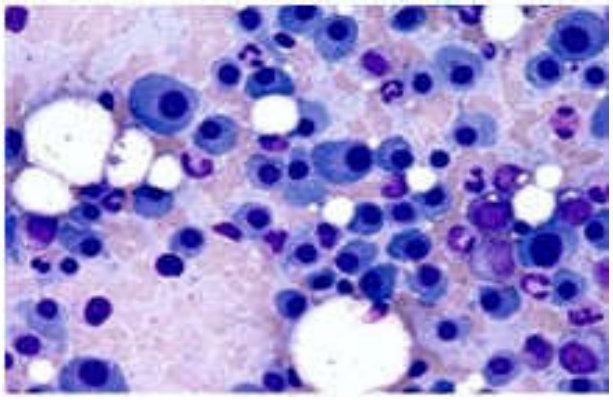

Fig. 1: Bone marrow aspiration showing plasma cells in multiple myeloma (Giemsa,X400)

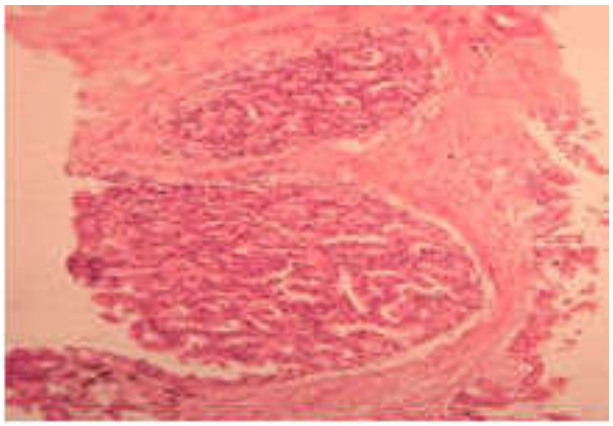

Fig. 2: Bone marrow biopsy showing prostatic adenocarcinoma deposits (H&E,X100)

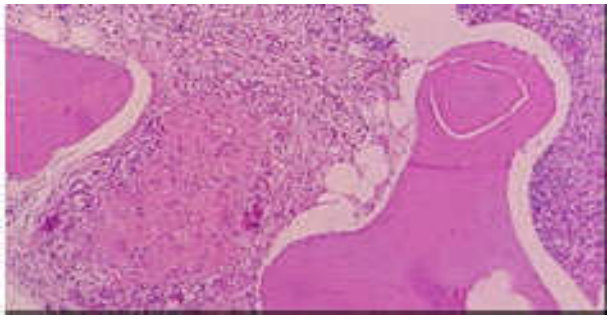

Fig. 3: Bone marrow biopsy showing bony trabeculae and granuloma with epithelioid cells (H&E,X100)

deposists were noted. Our findings did not correlate with the study done by Nitin gupta et al who showed that metastatic deposists were most common than non neoplastic conditions [6].

In the Nitin gupta et al study, metastatic carcinomatous deposists from the GIT were more common than that from the other organs which coincided with our study .

For the diagnosis of myelophthisic anemias both bone marrow aspiration and biopsy are complementary. Though the bone marrow aspiration is effective for studying the cellular morphology, bone marrow biopsy is helpful for assessing cellularity of marrow, and for identifying the lesions like granulomatous conditions or metastatic deposits.

Conclusion

Our study reflects that neoplastic disorders are the commonest cause of myelophthisic anemias and among the neoplastic disorders, haematological neoplasms are more common when compare to non haematological.

Among the non neoplastic disorders tuberculosis was the commonest condition involving bone marrow. Bone marrow procedure is essential in patients presenting with pancytopenia and leukoerythroblastic picture to evaluate the cause. Bone marrow aspirate or biopsy is valuable tool for proper diagnosis and staging the malignant disorders.

Reference

1. Metastatic tumors. Bain BJ, Clark DM, Wilkins BS, Lampert IA. In: Bone marrow Pathology. 3rd ed. England. Malden, MA:Blackwell Science, Bon Oxford 2001.p.430-61.
2. Ozkalemkas F, Aci R, Ozkocaman V et al. The bone marrow aspirate and biopsy in the diagnosis of unsuspected nonhematological malignancy: a clinical study of 19 cases. Bio Medical Central Cancer. 2005;5:144.
3. Makoni SN, Laber DA. Clinical spectrum of myelophthisis in cancer patients.Am J Hematol. 2004;76:92-3.
4. Kritichauhan, Monica Jain, Shruti Grover, Pragya shukla, Usha Rusia, Rajesh kumar Grover. Bone marrow metastasis in nonhematologic malignancies: Data from a cancer hospital. 2016;5(2):103-109.
5. Sree lakshmi I, Sunethri P, Bheeshma B, Geetha V, Jijiya Bai P, Shravan kumar O, et al. Interesting lesions of bone marrow with special reference to metastasis. J Evol Med Dent Sci. 2012;1:160-5.
6. Nitin Gupta, Ram kumar, Arvind Khajuria. Diagnostic Assessment of Bone marrow Aspiration Smears, Touch Imprints and Trephine Biopsy in Non Haematological Disorders. JK Science. 2011;13(2):70-72.