(International Print/Online Journal)

SJIF IMPACT FACTOR: 4.617
PUBMED-National Library of Medicine ID-101739732

ISSN (Print): 2209-2870
ISSN (Online): 2209-2862

International Journal of Medical Science and Current Research (IJMSCR)
Available online at: www.ijmscr.com
Volume2, Issue 2, Page No: 269-274
March-April 2019

Bone marrow aspiration and trephine biopsy in myeloproliferative neoplasms –An experience from a tertiary care centre

Shaheena Parveen[1], Manzoor Ahmad Sofi [1], Nausrat Ali [1], Fahim Manzoor [2], Nusrat Bashir[3]
[1] Senior Resident [2] Lecturer [3]Assistant Professor
Department of Pathology, GMC Srinagar J&K, India

***Corresponding Author:**

Dr.Nusrat bashir
Assistant professor,department of pathology
GMC,Srinagar,J&K,India

Type of Publication: Original Research Paper
Conflicts of Interest: Nil

ABSTRACT

Background: The aspirate and trephine biopsy specimens are complementary and when both are done, they provide a comprehensive evaluation of the bone marrow. The present study was conducted to compare the role of trephine biopsy with bone marrow aspiration for effectively diagnosing wide spectrum of myeloproliferative neoplasms(MPNs).

Materials and method: This was a retrospective hospital based study, from January 2017 to December 2018 . The study was conducted in tertiary care centre, SMHS, Srinagar, Kashmir.

Results: Total of 26 cases of myeloproliferative neoplasms were diagnosed out of which (50.0%) had chronic myeloid leukemia (CML), (26.9%) were essential thrombocythemia (ET), (15.38%) were diagnosed as polycythemia vera (PV) and (7.69 %) were primary myelofibrosis(PMF)cases. 4 cases of myeloproliferative neoplasm's were diagnosed exclusively on bonemarrow biopsy due to dilute nature of aspirate in view of marrow fibrosis

Conclusion: Diagnosis can be made on peripheral blood, bone marrow examination and molecular pathology findings. But bone marrow biopsy plays an especially important role in establishing the diagnosis when it comes to assessing cellularity, topographic relationship of different marrow elements, assessment of megakaryocytic morphology, assessment of marrow fibrosis and performing ancillary stains and immunohistochemistry.

Keywords: Myeloproliferative neoplasms(MPN), Biopsy ,Aspirate, Bone marrow

INTRODUCTION

Myeloproliferative neoplasms (MPN) are a heterogeneous group of clonal-origin hematopoietic stem cells alterations, characterized by excessive production of myeloid-lineage cells, which is reflected in increased cellularity in peripheral blood and bone marrow [1,2]. The 2016 revised "Blue Book", the official document of the World Health Organization (WHO) classification system for tumors of the hematopoietic and lymphoid tissues, has now been published [3]. Under the category of myeloproliferative neoplasms (MPNs), the revised document includes seven subcategories: chronic myeloid leukemia, chronic neutrophilic leukemia, polycythemia vera (PV), primary myelofibrosis (PMF), essential thrombocythemia (ET), chronic eosinophilic leukemia not otherwise specified and MPN, unclassifiable (MPN-U); of note, mastocytosis is no longer classified under the MPN category. The combination of clinical, morphological, and molecular genetic features is thought by the WHO as the most suitable attempt to define disease entities such as MPNs (tables 1,2)[3,4,5]. In India as mentioned in various cancer registries, chronic myeloid leukemia (CML) amongst myeloproliferative neoplasm (MPN) is one of the most common adult leukemias in Indian population. It constitutes 30% to 60% of all adult leukemias [6,7]. Clinical presentation, peripheral blood film (PBF) examination, bone marrow examination

(BME) along with molecular studies is essential for the diagnosis [8].

Material and method

This was a retrospective hospital based study, from January 2017 to December 2018 where in reviewed cases taking into account there clinical presentation, peripheral blood smear, BMA(Bone marrow aspirate), and BMB(Bone marrow biopsy) and mutation studies. The study was conducted in tertiary care centre, SMHS, Srinagar, Jammu and Kashmir. A total of 26 cases of MPN were collected during this time period. The peripheral smear and BMA smears were stained by Leishman stain. For iron stores perls stain was used and graded as per Gale etal system. BMBs were stained by routine hematoxylin and eosin (H&E). Reticulin staining was performed by Gomori's method and graded using WHO guidelines [4]. Total leucocyte count, bone marrow aspiration and imprint smear's findings were correlated with bone marrow biopsy sections .Mutational analysis included JAK2V617,EXON 12 and CALR mutation.

Results

A total of 26 cases diagnosed as MPN(Myeloproliferative neoplasm) on complete blood count(Table- 2), peripheral blood examination, BMA and BMB(Table-1) with cytogenetic and molecular studies. This constituted 13 cases (50.0%) of chronic myeloid leukemia(CML)(Fig-3), 7 cases (26.9%) of ET(Essential thrombocythemia)(Fig-2), 4 cases (15.38%) of PV(Polycythemia vera), and 2 cases (7.69 %) of PMF(Primary myelofibrosis)(Fig-1). There was a wide range of age distribution with most of the patients between 40 to 80 years and males being affected predominantly (males=15 and females=11) in all disease categories.

Most common clinical presentation was abdominal pain in CML, portal vein thrombosis in PV, thrombotic complications in ET and easy fatiguibility in PMF. Basic laboratory investigations included CBC, the peripheral blood smear, an erythropoietin (EPO) level, and biochemistry tests (lactate dehydrogenase [LDH], uric acid, vitamin B12, and iron status and ultrasonography). Table 3 show haematological parameters in these patients. Patients also had nonspecific abnormalities like increased serum LDH (listed by the WHO as one of the minor criteria for PMF), uric acid, and vitamin B12.

In chronic myeloid leukemia (CML) , 10 cases were in chronic phase,2 cases in accelerated phase and one case in blast phase. One case of PV was in prepolycythemic phase with normal PBF where as 3 cases had erythrocytosis with neutrophillic leucocytosis. All cases of ET had thrombocytosis with median platelet count of 8 lakh cells per microlitr with giant platelets on PBF.

On bone marrow examination, CML-Chronic phase showed hypercellular marrow with granulocytic hyperplasia and megakaryocytic hyperplasia and basophilia in 10 cases. one case of CML showed increased blasts of more than 40% with biopsy showing clusters of blasts. Bone marrow was done in all the 7 cases of ET, out of which 5 showed hypercellular marrow with megakaryocytic hyperplasia and hyperlobated megakaryocytes and 2 cases had diluted aspirate picked up of bonemarrow biopsy.All cases of PV showed Hypercellular marrow with panmyelosis and and peomorphic megakaryocytes.. In PMF, aspirate was dilute in both cases and biopsy showed diffuse fibrosis with atypical megakaryocytes and clustering with grade 2 reticulin fibrosis in one of the case. In the other case, marrow was cellular with marked megakaryocytic hyperplasia, atypia and grade 1 fibrosis.

BCR-ABL was positive in all cases of CML. JAK2V617 was present in 60% of PV and remaining 40% showed exon-2 mutation. In ET, mutation study was not followed up. Both cases of PMF were JAK2V617 positive.

Discussion

Diagnosis of myeloproliferative neoplasm requires combination complete blood count (CBC), comprising differential and platelet count, marrow aspiration, and marrow biopsy with recent development in diagnosis including sensitive tests such as standard cytogenetics and molecular genetics [9]. BMA and BMB both are very important procedures for the diagnosis and are also useful for follow up of the patients undergoing chemotherapy [10,11]. Transformation of hematopoietic stem cell forms the main essence of myeloproliferative neoplasms. [12,13].

The different entities included under MPN have specific morphologic features which assist in

Volume 2, Issue 2; March-April 2019; Page No. 269-274

distinguishing them from each other. Despite these differences these disorders share many common attributes too. Hence, it is important to recognize features which can help in distinguishing them from one another. It is a well-known fact that bone marrow aspiration and bone marrow biopsy complement each other. In our study, we did a comparative evaluation of all BMA and BMB of MPN patients, to see the complementary role of both the procedures, to study the advantages and disadvantages of both the procedures done simultaneously.

Bone marrow aspiration is comparatively easy to perform with less discomfort to the patient, better appreciation of cellular morphology, being more suitable for cytochemical stains and other ancillary studies like flow cytometry, cytogenetics, culture etc ; however, the disadvantages included are, that cellularity cannot be assessed properly, some times we can get dry taps because of marrow fibrosis or if marrow is packed with blasts as in case of CML-Blast phase. Megakaryocytic morphology and fibrosis and cell topography is best assessed on bone marrow biopsy. Ancillary Techniques like immunohistochemistry can be used on biosy sections [14]. Assessment of marrow fibrosis has been shown to have clinical and prognostic implication in different neoplasms. In chronic myelogenous leukaemia, this parameter has been demonstrated to have predictive value on therapy and outcome[15].

CML is one of the most common leukaemia's in adults and was the first hematological neoplasm where cytogenetic alterations and the development of leukemia could be associated [16]. In this study, there were 13 cases of chronic myeloid leukemia [CML] [n = 13], which were concordant on aspiration and biopsy similar to Ghodasara and Gonsai. The aspirates are better able to classify the phases of CML as compared to biopsy [17]. Evaluation of megakaryopoiesis, grading of fibrosis and localization of blasts are possible on a trephine biopsy.

In histological slices of ET, predominantly the megakaryocytic lineage was affected without marked left-shift in granulopoiesis and with adipose tissue preservation. Megakaryocytes were large or gigantic, with abundant cytoplasm, which in some cases displayed emperipolesis. It is quite characteristic of ET that megakaryocytes exhibit multilobulated nuclei that can resemble "deer antlers/staghorn" which was he case with us . Conversely to the megakaryocyte dense clusters observed in PV and PMF, megakaryocytes in ET are arranged in small paratrabecular clusters or clusters close to the sinusoids or appear as isolated megakaryocytes. This features differ from pre-fibrotic phase early PMF, where megakaryocytes are dysplastic with marked atypia, show dense grouping and exhibit hyperchromatic and hyperlobulated nuclei (cloud-shaped or bulbous), with marked alteration of the nucleus:cytoplasm ratio. In ET, there is grade 0 or 1 fibrosis and, therefore, if ET diagnosis is being considered and BM displays marked fibrosis (grade 3), the diagnosis most probably does not correspond to ET[18].

Both the cases of MF in our study were diagnosed on BMB. BMB is superior to BMA in diagnosis of PMF because diffuse osteomyelosclerosis, intrasinusoidal hematopoiesis and vascular proliferation and fibrosis are picked up on BMB. Hence, BMB is more helpful in confirmation and grading [6].

Conclusion

MPNs consist of a diverse group of clonal disorders in which especially megakayocytes exhibit distinctive features. Hence, clinical and hematological findings along with characteristic bone marrow morphology, megakaryocytic features can help arrive at an accurate diagnosis of MPNs .

References:

1. Madelung AB, Bondo H, Stamp I, et al. World Health Organization-defined classification of myeloproliferative neoplasms: morphological reproducibility and clinical correlations--the Danish experience. Am J Hematol. 2013;88:1012-6.
2. Stein BL, Gotlib J, Arcasoy M, et al. Historical views, conventional approaches, and evolving management strategies for myeloproliferative neoplasms. J Natl Compr Canc Netw. 2015;13:424-34.
3. Swerdlow, S. H. (eds). WHO classification of Tumours of Haematopoietic and Lymphoid Tissues. 4th edn, (International Agency for Research on Cancer, Lyon, France, 2017).

Volume 2, Issue 2; March-April 2019; Page No. 269-274

4. Arber, D. A. The 2016 revision to the World Health Organization classification of myeloid neoplasms and acute leukemia. Blood 127, 2391–2405 (2016).

5. Vardiman, J. W. The 2008 revision of the WHO classification of myeloid neoplasms and acute leukemia: rationale and important changes. Blood 114, 937–951 (2009).

6. Aziz Z, Iqbal J, Akram M, et al. Treatment of chronic myeloid leukemia in the imatinib era: Perspective from a developing country. Cancer 2007;109:1138-45.

7. Bhutani M, Vora A, Kumar L, et al. Lympho-hemopoietic malignancies in India. Med Oncol 2002;19:141-50.

8. Sokal JE, Baccarani M, Tura S, et al. Prognostic discrimination among younger patients with chronic granulocytic leukemia: relevance to bone marrow transplantation. Blood 1985;66:1352–7.

9. Lee SJ. Chronic myelogenous leukemia. Br J Haematol. 2000;111:993–1009.

10. Riley RS, Hogan TF, Pavot DR, et al. A pathologist's perspective on bone marrow aspiration and biopsy; Performing a bone marrow examination. *J Clin Lab Anal.* 2004;18(2):70–9.

11. Islam A. Bone marrow aspiration prior to bone marrow core biopsy using the same bone marrow biopsy needle. A good or bad practice. *J Clin Pathol.* 2007;60:212–15

12. Spivak JL, Silver RT. The revised World Health Organization diagnostic criteria for Polycythemia vera, Essential thrombocythemia, and Primary myelofibrosis: An alternative proposal. Blood 2008;112(2):231-9

13. Jameel A, Jamil SN. Clinico-pathological profile of chronic myeloid leukemia. JPMI 2006;20(3):235-238

14. Manoj K Patro, T Santosh, Atany K Bal, et al.corelation of bone marrow aspiration and trephine biopsy in various haematological disorders: a study of 3 years.annals of pathology and laboratory medicine.2018;5(3):194-203.

15. Kvasnicka HM, Thiele J, Schmitt-Graeff A, et al. *Bone marrow features improve prognostic efficiency in multivariate risk classification of chronic-phase Ph (1+) chronic myelogenous leukaemia: a multicenter trial*. *J Clin Oncol* 2001;19:2994–3009.

16. Steensma DP. The chronic myeloproliferative disorders: An historical perspective. Curr Hematol Rep. 2003;2:221-30.

17. Ghodasara J, Gonsai RN. Comparative evaluation of simultaneous bone marrow aspiration and bone marrow trephine biopsy – A tertiary care hospital based cross-sectional study. Int J Sci Res. 2014;10:2058–61.

18. Sun T. BCR-ABL1 negative myeloproliferative neoplasia. En: Flow cytometry, immunohistochemistry and molecular genetics for hematologic neoplasms. 2a ed. Lippincot Williams & Wilkins; 2012. pp. 69-77

Volume 2, Issue 2; March-April 2019; Page No. 269-274

Tables:

Table 1 : Subtypes of myeloproliferative neoplasm's on bone marrow examination.

	No.(n=26)	Percentage	Males	Females
CML	13	50.00%	8	5
ET	7	26.9%	4	3
PV	4	15.38%	2	2
MF	2	7.69%%	1	1
Total	**26**	**100**	**15**	**11**

Table 2: Hematological characteristics of patients with myeloproliferative neoplasm's

Diagnosis	Haemoglobin Mean(g/dl)	Total WBC count ($x10^9$ /L)	Total platelet count ($x10^9$/L)
CML	**9.0**	**157.50**	**3.50**
ET	**12.9**	**20.67**	**8.54**
PV	**18.9**	**14.81**	**4.26**
MF	**6.5**	**32.94**	**5.19**

Images:

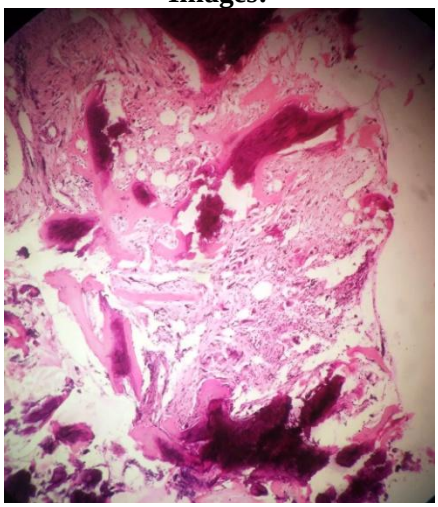

Fig- 1 Bone marrow biopsy (H&E): Marked megakaryocytic hyperplasia, atypia and fibrosis in PMF.

Volume 2, Issue 2; March-April 2019; Page No. 269-274

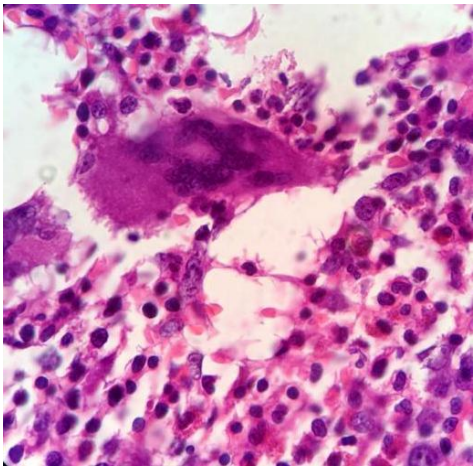

Fig- 2: Biopsy section showing typical hyperlobated megakaryocyte in ET.

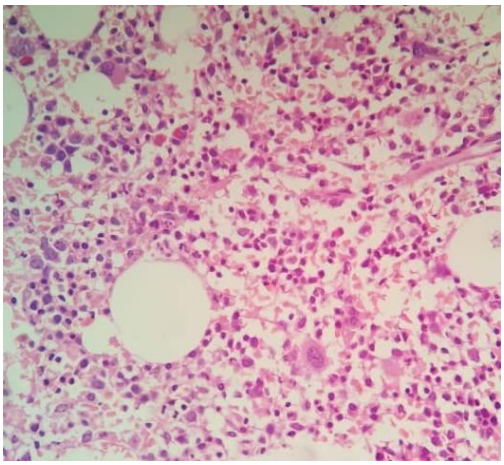

Fig- 3: Biopsy section showing granulocytic hyperplasia with typical hypolobated dwarf megakaryocyte in CML.

Volume 2, Issue 2; March-April 2019; Page No. 269-274