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Pathology

MEGAKARYOCYTIC ALTERATIONS IN THROMBOCYTOPENIA: A BONE MARROW ASPIRATION STUDY

Dr Khushboo Kumari — Junior Resident (Academic) Deptt Of Pathology Rims Ranchi.

Dr Manoj Kumar Paswan — Associate Professor, Deptt Of Pathology Rims, Ranchi.

Dr Vinay Bhushan* — MBBS, MD (pediatrics), Ex- Senior Resident Ucms& Gtbh (new Delhi), Specialist Pediatrician At Sbmch Hazaribagh Jharkhand (India) *Corresponding Author

ABSTRACT **Background:** The study was conducted to understand megakaryocytic alterations and their contribution in the diagnosis of cases of thrombocytopenia. **Aims** :(i) Incidence of thrombocytopenia in different hematological disorder with comparison to male and female ratio. (ii)To evaluate morphological megakaryocytic alterations in bone marrow aspiration in case of non-MDS related thrombocytopenia. **Material Methods:** This was a prospective study conducted on all consecutive cases of bone marrow aspirate over duration of six month in RIMS, Ranchi. Megakaryocytic morphology was studied with a 100 X objective. Data were analyzed with SPSS version 11.5. **Results:** Among 52 cases commonest cause of thrombocytopenia for which bone marrow examination was sought was AML(22 cases).The second most common cause was ITP (16 cases).There were 8 cases of megaloblastic anemia, 3 cases of Aplastic Anemia,2 cases of blast of CML .Thrombocytopenia was commoner in female(29 cases) than in males(23 cases).Dysplastic forms were seen in 16 cases, bare megakaryocytic nuclei in 18 cases and micromegakaryocytes in 9 cases of ITP.The dysplastic form were seen in megaloblastic anemia ,aplastic anemia and AML 4 cases,3 cases and 3 cases respectively.Emperipolesis was seen in 12 cases. **Conclusion:** Many similarities were observed in megakaryocytic morphology among different hematological disease. However we come to know that which hematological disordered show which type of morphological changes in megakaryocytes.

KEYWORDS : Bone Marrow aspiration, Non-Myelodysplastic syndrome, Thrombocytopenia.

INTRODUCTION

Megakaryocytes produces platelets, larger the size of megakaryocytes more number of platelets we get than smaller size megakaryocytes. Thrombocytopenia is defined as platelet count less than 150,000/cumm[1]. Thrombocytopenia is seen in different hematological disorders. Despite the number and diversity of disorders that may be associated etiologically, thrombocytopenia results from only four processes : Artifactual thrombocytopenia, deficient platelet production, accelerated platelet destruction, and abnormal distribution or pooling of the platelets within the body[2].Dysplastic changes are well known in megakaryocytes in thrombocytopenia associated with myelodysplastic syndrome(MDS).However, they are also observed in megakaryocytes in non-myelodysplastic hematological conditions like immune thrombocytopenic purpura (ITP),infection associated thrombocytopenia(IAT), hypersplenism, aplastic anemia(AA),acute myeloid leukemia lymphoma syndrome (LLS),bone marrow metastasis, blast crisis of chronic myeloid leukemia; but scant data exist on the prevalence of dysplastic changes in megakaryocytes in non-myelodysplastic hematological condition[3].

Normal maturation and platelet formation results forms megakaryocytic deoxyribonucleic acid (DNA) replication that occurs without cell division resulting in a large lobulated,polypoid nucleus. A wide variety of growth factor like thrombopoietin act synergistically with other hematopoietic cytokines and transcriptional factors stimulating the maturation and growth of megakaryocytes. A defect in any of the stages of megakaryocytopoiesis can lead to dysmegakaryocytopoiesis and thrombocytopenia.[3]

MATERIALS AND METHODS

This was a prospective study of 52 cases conducted on all consecutive cases of bone marrow aspirates over duration of six month in department of pathology hematology section RIMS, Ranchi. The inclusion criteria of study was all the cases of bone marrow come with complain of thrombocytopenia and exclusion criteria was patient with thrombocytopenia but lack bone marrow requition (i, e.come for CBC and PBS).Informed consent was obtained from the subjects and confidentiality maintained throughout the study. Ethical approval was taken from the ethical Review board.

A proper clinical history, physical findings, complete blood counts, peripheral smears and other relevant laboratory investigation required were noted. Peripheral smear were prepared and stained according to the guidelines in practical hematology using Giemsa stain.[7] Bone marrow aspiration site was posterior superior iliac spine, anterior superior iliac spine ,smear was made with the aspirated sample and after air-dried ,stained with Giemsa and examined under light microscope(Olympus CH 20i model)

The number of the megakaryocytes was considered as normal(one megakaryocytes per one to three low-power fields,)increased (more than two megakaryocytes per low-power field) or decreased (one megakaryocytes per five to ten low - power fields).[4]The morphological changes of megakaryocytes that were studied included nuclear segmentation, presence of immature forms, dysplastic forms, micromegakaryocyte, emperiopolesis ,platelet budding,cytoplasmic vaculolization,bare megakaryocytic nuclei and hypogranular forms. The presence of abnormal megakaryocytes which included the micromegakaryocytes, dysplastic forms, megakaryocytes with separated lobes and hypogranular form were considered as dysmegakaryocytopoiesis. Normal megakaryocytes were considered to have four to sixteen nuclear lobes. Immature megakaryocytes were defined as young forms of megakaryocytes with scant bluish cytoplasm and lacking lobulation of the nucleus which occupied most of the cell.[5] Dysplastic megakaryocytes are those megakaryocytes with single or multiple separated nuclei.Micromegakaryocytes are whose sizes are smaller than large lymphocyte/monocyte with single or bilobed nucleus. Morphological changes of megakaryocytes assessed in MDS and non MDS condition. Collected data were checked for completeness and entered into Microsoft excel 10 and analyzed with SPSS version 11.5.

RESULTS

The following observations were made in this study:

(i) Thrombocytopenia was commoner in female (29 cases, 55.76%) than in males (23 cases, 44.23%).
(ii) Our study shows commonest cause of thrombocytopenia for which bone marrow examination was sought was AML(22 cases,42.3%).The second most common cause was ITP(16 cases,30.7%).There were 8 cases of megaloblastic anemia ,3 cases of aplastic anemia ,2 cases of blast crisis of CML.
(iii) Our Study shows changes in morphology of megakaryocytes in various hematological disorders. Dysplastic forms were seen in 16 cases, bare megakaryocytic nuclei in 18 cases and micromegakaryocytes in 9 cases of ITP.

(iv) The dysplastic form were seen in megaloblastic anemia, aplastic anemia and AML 4 cases, 3 cases and 3 cases respectively. However platelet budding seen only in ITP and Aplastic anemia.Emperipolesis was seen in 12 cases with lymphocytes in five cases and nucleated red blood cells in four cases.

DISCUSSION

Thrombocytopenia, either persistent, isolated or in associated with pancytopenia refractory to treatment is one of the commonly encountered hematological problems for which a bone marrow study is sought. The routinely prepared Giemsa stained bone marrow aspirate smears can help to observe the number and morphologic features of the megakaryocytes associated with different cases of thrombocytopenia. This can improve the diagnostic accuracy for a wide range of hematological disorders thereby enabling proper therapeutic interventions.[3]

In the study conducted by Muhury M et al,maximum number of case (38/144 cases,26.4%)was seen in less than ten year of age group followed by 18.7% cases(27/144 cases) in 21-30 years of age .Least number of cases was seen in more than 61 years of age (9/144 cases,6.3%).Thrombocytopenia was commoner in males (24 cases,63.2%)than in female (14 cases,36.8%)in the first decade.[3]

The commonest cause of thrombocytopenia for which bone marrow examination was sought was AML (27/144 cases, 18.75 %).The second most common cause was ITP (19/144 cases, 13.19 %) which was followed by ALL and dimorphic anemia (18/144 cases each, 12.5%)[3]

In the study done by Hu T et al, they observed overproliferation of bone marrow MKs in the most ITP patients. The abnormality of MKs might be one of the reasons for thrombocytopenia in some patients with ITP.[6]

Dysplastic forms ,cytoplasmic vacuolization ,platelet budding and emperipolesis was seen in 1 case each and micromegakaryocytes in 1 case of MTP in the present study.Emperipolesis,seen in 1 of the 17 case of MTP with lymphocyte in this study, was also observed in the study done by Roznan and Vives-Corrons.Their results show that megakaryocytes emperipolesis is a frequent event in different clinical conditions provided that a large number of megakaryocytes is examined, and with more than 200 megakaryocytes on the smear it can be demonstrated without exception.Consequently,they do not support the idea that the detection of megakaryocytic emperipolesis on bone marrow aspirate has any diagnostic significance.[8]

The cytoplasmic vacuolization seen in 1 case which ultra structurally represents mitochondrial swelling was also observed by Levine[9]and Houwerzij et al[4], and this reflects an increased megakaryocytes turnover and indicates degenerative changes such as those of apoptosis and Para-apoptosis.

In different condition of thrombocytopenia morphological study of megakaryocytes in bone marrow slides help us to rule out myelodysplastic or non myelodysplastic conditions which cause thrombocytopenia. It is very valuable tool in underdeveloped and developing countries due to poor facility for well sophisticated megakaryocytes studies like cultural studies, specific marker studies, electron microscope and ultrastructural studies.

As per our study we show diagnostic accuracy for different causes of thrombocytopenia will be improved by correlating different forms of morphological alteration of megakaryocytes observed in bone marrow aspiration Smear.

CONCLUSION

There are many similarities in morphological changes of megakaryocytes among different hematological diseases; never the less ,the diagnostic approach will vary when detailed knowledge about morphological changes of megakaryocytes is available.However,as seen in this study, presence of immature megakaryocytes, dysplastic form and micro megakaryocytes nuclei were found to be significant in Idiopathic Thrombocytopenic purpura.Understanding of the morphological changes of megakaryocytes in bone marrow aspirates can improves the diagnostic accuracy for a wide range of hematological disorders.

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Disclosure of conflict of interest:
None

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