Original Research Article

Megakaryocytic Alterations in Thrombocytopenia: A Bone Marrow Aspiration Study

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Abstract

Background: Thrombocytopenia is defined as platelet count less than 150,000 /mm^3 (150x109 /litre) and is commonly seen in various haematological disorders and nonhematological conditions and may be associated with dysplastic megakaryocytes which is a feature of myelodysplastic syndrome. **Objective:** To study the morphological variations of megakaryocytes on bone marrow aspiration smears in Non MDS related thrombocytopenia in MGM Medical College and MY Hospital Indore. **Materials and Methods:** Retrospective study of 76cases of non MDS thrombocytopenic patients. Patients presenting with platelet count <150,000/mm3 from June 2019 to July 2020 at MGM medical college, Indore were included in the study**. Results:** The most common cause of thrombocytopenia was megaloblastic anaemia followed by acute leukaemia, chronic leukaemia idiopathic thrombocytopenic purpura. Both dysplastic and nondysplastic features were observed in the above mentioned conditions. The most common dysplastic feature was nuclear segmentation followed by micromegakaryocytes and hypogranular forms. The common nondysplastic features observed were immature forms (most common) bare nuclei, and hypolobation. **Conclusion:** Dysplastic megakaryocytes are common in non-MDS-related thrombocytopenia and their mere presence should not lead to the diagnosis of MDS. Hence, proper diagnosis should be made on megakaryocyte morphology. Patient's clinical findings and other haematological parameters. This understanding can improve the diagnostic accuracy for wide range of haematological disorder.

Keywords: Megakaryocyte, Bone marrow aspiration, dysplastic features, nonmyelodysplastic syndrome, thrombocytopenia
Study Design: Observational Study

Introduction

Thrombocytopenia characterized by platelets count <150,000/mm^3 is a common indication for which bone marrowaspiration is often performed. There are causes include bothhaematological and nonhaematologicalconditions.The most common haematological conditions for thrombocytopenia are megaloblastic anaemia, aplastic anaemia, leukaemia, multiple myeloma, bone marrow metastasis, etc., Thrombocytopenia can be isolated or maybe associated with bicytopenia or pancytopenia [1].

Dysmegakaryocytopoiesisis characterized by various megakaryocytic alterations in bone marrow aspirates and including both dysplastic and non-dysplastic features. Aim of this study was todetermine the morphological features of megakaryocytes in a patient with non-MDS thrombocytopenia.

Materials and Methods

Aims & objective – To study the morphological variations of megakaryocytes on bone marrow aspiration smears in Non MDS related thrombocytopenia in MGM Medical College and M Y Hospital Indore.

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This was a retrospective study. Total of 76cases were studied. Patients presenting with platelet count <150,000/mm3 from June 2019 to July 2020 at MGM medical college, Indore were included in the study. Relevant clinical information was collected from records.Patient's platelet count was obtained initially by automated analyzer and it was later confirmed manually by preparing a peripheral smear.

Cases with confirmed pseudothrombocytopenia on peripheral smear and cases with inadequate bone marrow aspirate were excluded from the study [6]. The BMA smears were examined as per the standard guidelines and the findings were recorded and analysed. The number of megakaryocytes was expressed as number per 10 low power field (LPF) and was further subdivided into absent, decreased (1/5–10 LPF), normal (1/1–3 LPF), and increased (>2/LPF) [1-3].Morphological features of megakaryocytes were studied under 100X, for dysplastic and Non dysplastic changes on bone marrow examination [6]. Dysplastic features included multinucleated forms, micro megakaryocytes, and hypogranular forms. Normal megakaryocytes are usually have 4-16 nuclear lobes.

Micromegakaryocytes are those megakaryocytes with a size same as that of large lymphocytes or monocytes and had single or bilobed nuclei. Hypogranular forms are those megakaryocytes which had a clear cytoplasm with no or sparse granules. Nondysplastic features included immature forms, emperipolesis, platelet budding, cytoplasmic vacuolization, and bare megakaryocyte nuclei [1].The morphological characteristics and number of the megakaryocytes in thrombocytopenia cases was documented and then assessed.

Results

Among the 76 cases thrombocytopenia was slightly more common in males compared to females with M: F ratio 2:1. Thrombocytopenia was seen in all age groups but most of the cases were between age of

41-50 yrs (44.7%). (Table 1) common clinical presentation was superficial bleeding (28.6%) followed by anaemia (19.3%) and weakness (11.7%). According to table no.2 most common cause of the thrombocytopenia is megaloblastic anaemia (47%) followed by acute leukaemia (23..6%) and least common cause is myelodysplastic syndrome(2.6%) As shown in table no.3. Increase in the number of megakaryocyte in BMA was observed in 20 cases (26.3%) which included cases of ITP, megaloblastic anaemia . 21 cases (27.6%) showed reduced in the number of megakaryocytesincluding acute leukaemia, megaloblastic anaemia, chronic leukaemia, aplastic anaemia and, MDS. Megakaryocytes were completely absent in 12(15.7%) cases and in 23cases (30.2%) count was normal.Table no. 4 and 5 shows dysplastic changes and nondysplastic changes observed in thrombocytopenic patients. Common dysplastic features seen were multiple segmented nuclei **(fig 2)** micromegakaryocytes and hypogranular forms. Among the three findings multiple segmented megakaryocytes were much more common and seen in 33 cases (43.4%) including 19 cases of megaloblastic anaemia and 09 cases of acute leukaemiaMicromegakaryocytes were encountered in 22 cases (28.9%) including 8 cases of megaloblastic anaemiaand , 6 cases of acute leukaemia. Hypogranular forms were seen in 21 cases (27.6%) in 07 cases of ITP and9 cases of megaloblastic anaemia.

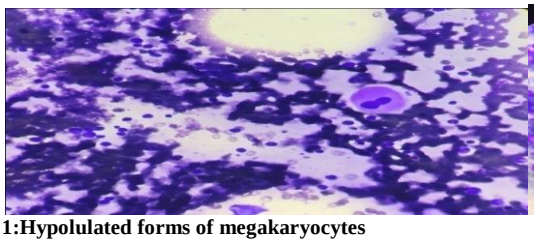

Fig 1:Hypolulated forms of megakaryocytes

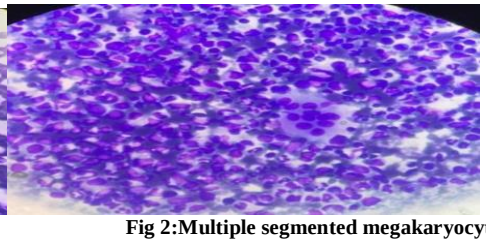

Fig 2:Multiple segmented megakaryocytes

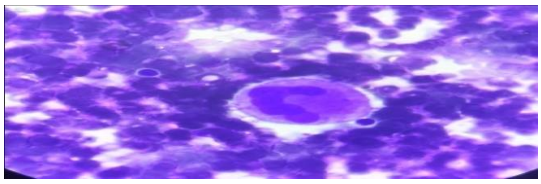

Fig 3: Normal megakaryocyte

Commonly encountered non dysplastic features were immature forms of megakaryocytes, bare nuclei, nuclear budding and hypolobulated froms(fig 1).Immature forms of megakaryocytes were common finding among the nondysplastic changes which was seen in 34 cases (44.7%) including megaloblastic anaemia, acute leukaemia, ITP and chronic leukaemia. Bare nuclei was another common finding which was seen in 19 cases (25%) including in 14 cases of megaloblastic anaemia, 5 cases of acute leukaemia .Emperipolesis was not a common finding it was observed only in 2 cases(2.63%) [9].

Discussion

Thrombocytopenia whether being persistent, isolated or in association with pancytopenia refractory to treatment is one of the commonly encountered hematological disorder for which a bone marrow aspiration study is sought. Bone marrow aspirate smears can demonstrate the dyspoietic features of the megakaryocytes associated with the non-MDS conditions. This improves the diagnosis of wide range of hematological disorders thereby allowing proper therapeutic interventions [4].Normal maturation and platelet formation results from megakaryocytic deoxyribonucleic acid (DNA) replication which occurs without cell division resulting in large lobulated, polypoid nucleus. A variety of growth factors thrombopoietin act synergistically with other hematopoietic cytokines and transcriptional factors stimulating the maturation and growth of megakaryocyte [5]

Any defect in the stages of megakaryocytopoiesis can lead to dysmegakaryocytopoiesis and thrombocytopenia.In our study a total of 76cases of true thrombocytopenia were included. The most common cause of thrombocytopenia was megaloblastic anaemia (47%) which was followed by acute leukaemia 23.6(%) and ITP(13.15%).A similar study also show shift to, immature, young hypolobulatedmegakaryocytes which was the morphological featurenoted in ITP cases done by Muhury M et al.

Table 1 :Age wise distribution of cases

S.No.	Age Group(yrs)	No. of cases (%)
1	0-10	02(2.63%)
2	11-20	07(9.21%)
3	21-30	09(11.84%)
4	31-40	11(14.47%)
5	41-50	34(44.73%)
6	51-60	13(17.1%)
Total		76(100%)

Table 2: Causes of thrombocytopenia

S.No	Bone marrow impression	No. of cases (%)
1	Megaloblastic anaemia	36(48.64%)
2	Acute Leukaemia	18(23.61%)
3	Idiopathic thrombocytopenic purpura	10(13.15%)
4	Aplastic anaemia	06(7.8%)
5	Chronic Leukaemia	04(5.26%)
6	Myelodysplastic syndrome	02(2.6%)
Total		76(100%)

Table 3: Distribution of megakaryocytes

S.No.	Bone marrow impression	No. of cases (%)	Absent (%)	Reduced (%)	Normal (%)	Increased (%)
1	Megaloblastic anaemia	36	-	04(11.1%)	22(61%)	10(27.7%)
2	Acute Leukaemia	18	08(44.4%)	10(55.5%)	-	-
3	Idiopathic thrombocytopenic purpura	10	-	-	-	10(100%)
4	Aplastic anaemia	06	04(66.6%)	02(33.3%)	-	-
5	Chronic Leukaemia	04	-	03(75%)	01(25%)	
6	Myelodysplastic syndrome	02	-	02(100%)	-	-
Total		76	12	21	23	20

Table 4: Dysplastic features in megakaryocytes in various cases

S.No.	Bone marrow impression	No. of cases (%)	Multiple segmented (%)	Micromegakaryocytes (%)	Hypogranularfroms (%)
1	**Megaloblastic anaemia**	**36**	**19(52.7%)**	**08(22.2%)**	**09(25%)**
2	**Acute Leukaemia**	**18**	**09(50%)**	**06(33.3%)**	**03(16.6%)**
3	**Idiopathic thrombo-cytopenic purpura**	**10**	**-**	**03(30%)**	**07(70%)**
4	**Aplastic anaemia**	**06**	**04(66.6%)**	**02(33.3%)**	**-**
5	**Chronic Leukaemia**	**04**	**01(25%)**	**02(50%)**	**01(25%)**
6	**Myelodysplastic syndrome**	**02**		**01(50%)**	**01(50%)**
Total		**76**	**33**	**22**	**21**

Table 5: Nondysplastic features in megakaryocytes in various cases

S.No.	Bone marrow impression	No. of cases	Immature forms	Bare nuclei	Budding	Emeripolesis	Hypolobulation
1	**Megaloblastic anaemia**	**36**	**08(22.2%)**	**05(13.8%)**	**01(2.7%)**	**01(2.7%)**	**03(8.3%)**
2	**Acute Leukaemia**	**18**	**08(44.4%)**	**05(27.7%)**	**01(5.5%)**	**01(5.5%)**	**03(16.6%)**
3	**Idiopathic thrombocytopenic purpura**	**10**	**03(30%)**	-	**02(20%)**	-	**05(50%)**
4	**Aplastic anaemia**	**06**	**04(66.6%)**	-	-	-	**02(33.3%)**
5	**Chronic Leukaemia**	**04**	**03(75%)**	-	-	-	**01(25%)**
6	**Myelodysplastic syndrome**	**02**	**01(50%)**				**01(50%)**
Total		**76**	**34**	**19**	**05**	**02**	**16**

Conclusion

Dysplastic megakaryocytes are common in non-MDS-related thrombocytopenia and their mere presence should not lead to the diagnosis of MDS. Hence, proper diagnosis should be made on megakaryocyte morphology. Patient's clinical findings, and other haematological parameters. This understanding can improve the diagnostic accuracy for wide range of haematological disorder.All cases of thrombocytopenia morphological finding of megakaryocytes in bone marrow aspiration smears should be correlated with Patient's clinical findings, and other haematological parameters.

References

1. Choudhary PK, Singh SK, Basnet RB. Study of megakaryocytesin bone marrow aspiration smears in patients with thrombocytopenia. J Pathol Nepal 2013;3:476-81.
2. Muhury M, Mathai AM, Rai S, Naik R, Pai MR, Sinha R. Megakaryocytic alterations in thrombocytopenia: A bone marrow aspiration study. Indian J Pathol Microbiol 2009; 52:490-4.
3. Lewis SM, Bain BJ, Bates I. Bone marrow biopsy. In: Practical Hematology. 10th ed. Philadelphia: Churchill Livingstone; 2006.p. 116-20.
4. Muhury M.Megakaryocytic alterations in thrombocytopenia: A bone marrow aspiration study. Indian J Pathol Microbiol 2009; 52:490-4
5. Battinelli. Delivering new insight into the biology of megakary-opoiesis and thrombopoiesis. Curr Opin Hematol 2007;14:419-26.
6. Jubelirer SJ, Harpold R. The role of the bone marrow examination in the diagnosis of immune thrombocytopenic purpura: case series and literature review. ClinApplThromb Hemost 2002;8:73-6.
7. Frenkel MA,Tupitsyn NN. Megakaryocytic dysplasia in acute nonlymphoblastic leukemias.TerArkh 1995;67:12-6.
8. Wang C, JYR, Liu L. Ultrastructural study of the megakaryocytes in megaloblasticanemia. Chinese journal of Zhonghua NeiKeZaZhi 1990;29;158-60.
9. Tavassoli M. Modulation of megakaryocyte emperipolesis by phlebotomy: megakaryocytes as a component of marrowblood barrier. Blood Cells1986;12:205-16.
10. Sashida G, Takaku TI, Shoji N et al. Clinico-hematologic features of myelodysplastic syndrome presenting as isolated thrombocytopenia: an entity with a relatively favorable prognosis. Leuk Lymphoma. 2003;44:653-8.
11. Hwang Y, Seong CM, Chung WS. Myelodysplastic syndrome mimicking idiopathic thrombocytopenic purpura.Korean J Lab Med 2010;30:105-
12. Wong KF, Chan JK. Are 'dysplastic' and hypogranular megakaryocytes specifc markers for myelodysplastic syndrome? Br J Haematol1991;77:5

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