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Original Article

Megakaryocytic Changes in Cases of Thrombocytopenia

Sneha Singh[1], Smita Subhaschandra Kadadavar[2], S S Hiremath[3]

Author Affiliation: [1]Tutor, [2]Assistant Professor, [3]Professor & HOD, S Nijalingappa Medical College & HSK Hospital, Bagalkot, Karnataka 587102, India.

Corresponding Author:
Sneha Singh, Tutor, S Nijalingappa Medical College & HSK Hospital, Bagalkot, Karnataka 587102, India.
Email: singhsneha5050@gmail.com

Abstract

Purpose: Dysplastic changes in megakaryocytes are important features of myelodysplastic syndrome (MDS). This study was done to understand various megakaryocytic alterations including the dysplastic forms in hematological disorders presenting with thrombocytopenia in non-MDS.

Methods: A prospective study of bone marrow aspiration in 120 patients with thrombocytopenia was conducted for a period of 1year from July 2019 to June 2020 in Department of Pathology, S.Nijalingappa Medical College and HSK hospital, Bagalkot, Karnataka to assess the number and morphology of megakaryocytes in non-MDS related thrombocytopenia.

Results: Dysplastic features were observed in 100%, 86.36%, 70.17% & 33.33% cases of acute leukemia, dimorphic anemia, megaloblastic anemia and aplastic anemia respectively.

Conclusion: The presence of dysplastic megakaryocytes should not lead to the diagnosis of MDS as it is also common in non MDS related thrombocytopenia. Hence, patients clinical & hematological parameters should always be correlated.

Keywords: Megakaryocytes; Thrombocytopenia; Non-MDS; Bone marrow.

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Introduction

Platelet counts of less than 150×10^9/L are indicative of thrombocytopenia. Megaloblastic anemia, aplastic anemia, leukemia, and other hematological disorders that cause thrombocytopenia are all popular hematological presentations for which bone marrow tests are frequently performed.[1] It's related to either bicytopenia or pancytopenia.[2]

Dysplastic changes in megakaryocytes are well-known in thrombocytopenia associated with MDS, but they can also be seen in non-myelodysplastic hematological conditions.[3]

Megakaryocytic modification in bone marrow aspirate, including dysplastic and non-dysplastic characteristics, characterizes dysmegakaryopoiesis. Multiple segmented nuclei, micromegakaryocytes (size of large lymphocyte/monocyte with a single or bilobed nucleus), and hypogranular types are all dysplastic characteristics of megakaryocytes (megakaryocytes with pale grey or water clear cytoplasm and sparse or no granules). Immature types, emperipolesis, budding, cytoplasmic vacuolizations, and bare nuclei are non-dysplastic characteristics. Immature megakaryocytes are

young types with a lack of lobulations and sparse bluish cytoplasm. If there is blebbing of cytoplasm on the surface of a megakaryocyte, it is known to be budding. The existence of another cell within the cytoplasm of a megakaryocyte is known as emperipolesis.[3]

This study aimed to see how megakaryocyte morphology changed in a patient with non-MDS thrombocytopenia.

Materials and Methods

From July 2019 to June 2020, the Department of Pathology, S. Nijalingappa Medical College & HSK Hospital, Bagalkot, Karnataka, conducted a prospective analysis of 100 cases of bone marrow aspirate of patients with platelet counts of 150 x 10^9/L. Each patient signed a written informed consent form. A proforma was used to collect relevant clinical data. By preparing a peripheral smear and staining it with Leishman's stain, the automated platelet count was further verified. In each of these cases, blood films were taken to search for symptoms of pseudo-thrombocytopenia, such as platelet agglutination, satellitosis, and phagocytosis by other cells.[1]

The research removed cases of pseudo-thrombocytopenia and insufficient material on bone marrow aspiration. Smears were stained with Giemsa stain and analyzed after bone marrow aspiration was performed under strict aseptic conditions. The results were registered after the bone marrow aspiration smears were tested according to standard guidelines. Megakaryocyte number and morphology were investigated.

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).[3,4,5,6]

Dysplastic changes were only deemed significant when they affected 10% or more of the megakaryocytes observed.[1]

Results

Out of 110 cases of thrombocytopenia, 82 cases (74.5%) were observed in males and 28 cases (25.45%) were in females. Thrombocytopenia was the most common in the age group of 30-39 years (28%) as shown in Table 1. The least number of cases were seen in the age group of 70-89 years.

Table 1: Distribution of age in cases of thrombocytopenia.

Age Group in Years	No. of Cases	% of Cases
0-9	03	2.72
10-19	17	15.45
20-29	14	13.63
30-39	38	34.54
40-49	15	13.63
50-59	10	9.09
60-69	12	10.90
70-79	00	00
80-89	01	0.90
Total Number of Cases	110	100

Thrombocytopenia causes are shown in Table 2. The most common cause for thrombocytopenia was Megaloblastic anemia.

Table 2: Common Causes of Thrombocytopenia.

Clinical Diagnosis	No. of Cases	% of Cases
Megaloblastic anemia	57	51.81
Dimorphic anemia	22	20
Iron deficiency anemia	14	12.72
ITP	10	9.09
Aplastic anemia	06	5.45
Acute leukemia (AML-M3)	01	0.90

There was an increase in the number of megakaryocytes in BMA smears in cases of ITP, iron deficiency anemia, megaloblastic anemia, dimorphic anemia with the sensitivity of 70%, 57.14%, 19.29%, and 9.09% respectively as shown

Table 3: No. of megakaryocytes per low power field.

Bone Marrow Impression	(n)	Normal	Increased	Decreased	Absent
Megaloblastic anemia	57	40 (70.17%)	11 (19.29%)	06 (10.52%)	-
Dimorphic anemia	22	18 (81.81%)	02 (9.09%)	02 (9.09%)	-
Iron deficiency anemia	14	04 (28.57%)	08 (57.14%)	02 (14.28%)	-
ITP	10	03 (30%)	07 (70%)	-	-
Aplastic anemia	06	-	-	04 (66.66%)	02 (33.33%)
Acute leukemia (AML-M3)	01	-	-	01 (100%)	-

in Table 3. Decreased number of megakaryocytes was seen in acute leukemia. Megakaryocytes were absent in two cases of aplastic anemia.

Table 4 Depicts dysplastic megakaryocytes in different hematological disorders. Dysplastic megakaryocytes were most common in aplastic anemia, followed by dimorphic anemia, megaloblastic anemia, ITP, and iron deficiency anemia.

Table 4: Prevalence of dysplastic & non-dysplastic changes in various hematological disorders.

Bone Marrow Impression	N	Dysplasia	Non-Dysplasia	Total
Megaloblastic anemia	57	40 (70.17%)	17 (29.82%)	47
Dimorphic anemia	22	19 (86.36%)	03 (13.63%)	22
Iron deficiency anemia	14	04 (28.57%)	10 (71.42%)	14
ITP	10	03 (30%)	07 (70%)	10
Aplastic anemia	06	02 (33.33%)	04 (66.66%)	06
Acute leukemia (AML-M3)	01	01 (100%)	-	01

Multiple segmented nuclei and micromegakaryocytes were the most common dysplastic features found, as shown in Table 5. 30 cases of megaloblastic anemia and 3 cases of ITP were found to have multiple-segmented nuclei, followed by 2 cases of dimorphic anemia and 2 cases of iron deficiency anemia.

In 18 cases of megaloblastic anemia, 12 cases of dimorphic anemia, 1 case of ITP, 4 cases of aplastic anemia, and 1 case of acute leukemia, micromegakaryocytes were found. In four cases of ITP, hypogranular types were found.

Immature types were the most common non-dysplastic characteristics, followed by hypolobulation, bare nuclei, and platelet budding.

In 23 cases of megaloblastic anemia, 6 cases of dimorphic anemia, 7 cases of ITP, 4 cases of iron deficiency anemia, and 1 case of aplastic anemia, immature megakaryocytes were found. In 14 cases of megaloblastic anemia, 3 cases of dimorphic anemia, 2 cases of iron deficiency anemia, 5 cases of ITP, and 1 case of aplastic anemia, hypolobulation was observed. In 16 cases of megaloblastic anemia, 3 cases of dimorphic anemia, and 2 cases of iron deficiency anemia, bare nuclei were found.

Table 5: Morphological changes in megakaryocytes in various conditions.

Bone marrow impression	Immature forms	Bare nuclei	Cytoplasmic vacuolization	Platelet budding	Micromega karyocyte	Hypo -granular	Hypo -lobulation	Multiple Segmented nuclei
Megaloblastic anemia	23	16	00	00	18	04	14	30
Dimorphic anemia	06	03	01	02	12	15	03	02
Iron deficiency anemia	04	02	00	00	00	10	02	02
ITP	07	00	01	01	01	04	05	03
Aplastic anemia	01	00	00	01	04	02	01	00
Acute leukemia (AML-M3)	00	00	00	00	01	00	00	00
Total	41	21	02	04	36	35	25	37

Discussion

Similar to Choudhary et al., 82 cases (74.5%) of thrombocytopenia were observed in males and 28 cases (25.45%) in females.[1] Thrombocytopenia was most prevalent in the 30-39 year age group (34.54 percent) and least common in the 70-89 year age group (0.90 percent), close to the findings of Shashikala et al.[2] Megaloblastic anemia was the most common cause of thrombocytopenia, followed by dimorphic anemia and iron deficiency anemia, close to the findings of Choudhary et al., who found that megaloblastic anemia was the most common cause of thrombocytopenia, followed by acute leukemia and ITP.[1] In contrast to the study of Muhury M et al. the most common cause was AML followed by ITP, ALL, and dimorphic anemia.[3]

Out of 57 cases of megaloblastic anemia, 11 cases (19.29%) had an increased number of megakaryocytes, 40 cases (70.17%) had normal and 06 cases (10.52%) had decreased number of megakaryocytes (Figure 1). Dysplastic mega karyocytes were found in 40 cases (70.17%) which

is similar to that found by Muhury M et al. (75%).[3] In a similar study done by Shalatha NP et al. dysplastic megakaryocytes was found in 100% of the cases of megaloblastic anemia and suggested further investigations as they can be mistakenfor MDS.[7]

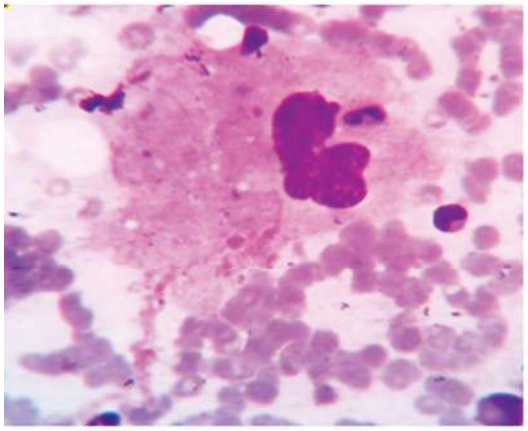

Fig. 1: normal megakaryocyte with platelet formation (100x).

The most common dysplastic changes in megaloblastic anemia were multiple-segmented nuclei (30 cases, 52.63%) (Figure 2) and micromega karyocytes (18 cases, 31.57%) similar to Chaudhary et al., Shashikala et al. &Muhury M et al.[1,2,3] In contrast to that study done by Parul G et al. observed hypogranular forms to be the most common dysplastic feature.[8] Wickramasinghe et al. also found multiple separate nuclei as the most common dysplastic feature and believed that this is caused due to diminished and ineffective DNA synthesis leading to nuclear maturation defect.[9]

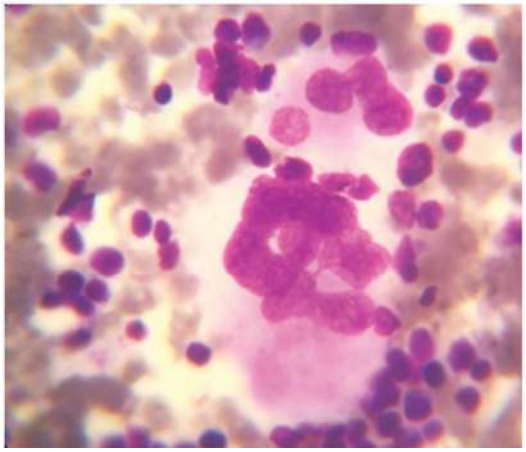

Fig. 2: Hyperlobulated megakaryocyte with background showing erythroid precursors and RBC's (100x).

Among non-dysplastic features; the most common in megaloblastic anemia were immature forms which are found in 23 cases (40.35%), bare nuclei in 16 cases (28.07%), and hypolobated forms (Figure 3)in 14 cases (24.56%) similar to Shashikala et al.[2]

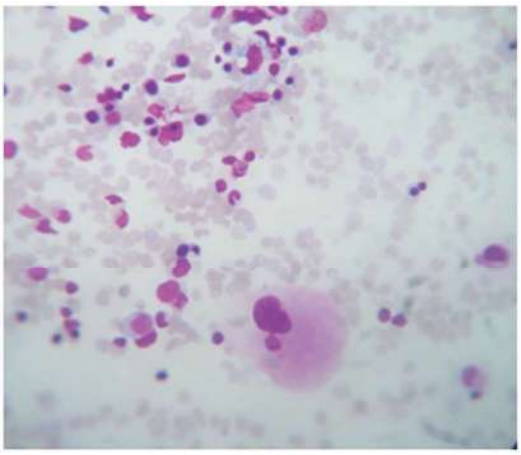

Fig. 3: Hypolobulated megakaryocyte with background showing erythroid, myeloid precursors and RBC's (100x).

Out of 22 cases of dimorphic anemia; dysplastic changes were observed in 19 cases (86.36%), the most common being hypogranular forms which are found in 15 cases (68.18%), and micromegakaryocytes which is found in 12 cases (54.54%) similar to that observed by Parul G et al. and Tejinder singh et al.[8,10]

Out of 14 cases of Iron deficiency anemia; 8 cases (57.14%) show an increased number of megakaryocytes similar to Parul G et al.[8] Dysplastic features were seen in 04 cases (28.57%) and 10 cases (71.42%) show non-dysplastic features similar to Choudhary et al.[1] In contrast to Parul G et al. where 83.30% cases were observed to have dysplastic feature.[8] The most common dysplastic feature is hypogranular forms seen in 10 cases (71.42%) similar to Parul G et al. where 66.6% of cases show hypogranular forms.[8]

Out of 10 cases of ITP; 7 cases (70%) has increased the number of megakaryocytes similar to Choudhary et al.[1], Muhury M et al.[3], and Parul G et al.[8] Dysplastic megakaryocytes were observed in 03 cases (30%) similar to Choudhary et al. (21.2%) and Parul G et al. (35.5%).[1,8] In contrast to Muhury M et al. where 89.5% of cases show dysplastic megakaryocytes.[3]

The most common morphological alteration found were immature forms seen in 07 cases (70%) followed by hypolobulation seen in 05 cases (50%) similar to Shashikala et al.[2] but a contrast to Parul G et al.[8] were hypolobulation was the most common finding followed by hypogranular forms. This finding was in contrast to micromegakaryocytes observed by Shi xd et al.[11]

Out of 6 cases of aplastic anemia; dysplastic megakaryocytes were found in 02 cases (33.33%) similar to Shashikala et al.[2] and contrast to

Parul G et al.[8] were 100% cases show dysplastic megakaryocytes. The most common morphological change is micromgakaryocytes (04 cases, 66.66%) followed by hypogranular form (02 cases, 33.33%) similar to Parul G et al.[8] and Chaudhary et al.[1] This is in contrast to the findings of Tricot et al.[12] who found normal morphology in all cases.

In 1 case of acute leukemia (AML-M3), the most common dysplastic feature observed was micromegakaryocytes. The observations are similar to Chaudhary et al.[1] and Muhury M et al.[3] Acute leukemia shows a decreased number of megakaryocytes similar to Shashikala et al.[2] which shows 65% cases with decreased megakaryocytes.

Conclusion

Megaloblastic anemia was the most common cause of thrombocytopenia in this study, followed by dimorphic anemia, iron deficiency anemia, ITP, aplastic anemia, and acute leukemia. Aplastic anemia, dimorphic aemia, ITP, megaloblastic anemia, aplastic anemia, and iron deficiency anemia were the most common findings in acute leukemia. As a result, we conclude that the existence of dysplastic features alone does not rule out MDS, but other possibilities should be considered. This analysis did not contain any MDS cases. Comparative study including MDS cases may be done to know the significance of dysplastic megakaryocytes.

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Compliance with Ethical Standards

Conflicts of interest: Authors have no conflicts of interest to declare.

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