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Morphology Of Megakaryocytes and Dysmegakaryopoisis in Bone Marrow Aspiration Smears in Various Hematological Disorders

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Abstract

Background-Megakaryocytes (MK)arises from pluripotent haematopoietic stem cells (HSCs), that under the influence of thrombopoietin (TOP) produce1000 -3000 platelets. Morphology of megakaryocyte plays an important role in thrombopoiesis. A defect in any stage of megakaryocytopoiesis can lead to dysmegakaryopoiesis and thrombocytopenia.

Objective-This study was conducted to understand various morphological changes in megakaryocytes in the bone marrow aspiration smears and their role in the diagnosis of various hematological disorders.

Materials And Methods- This is a prospective study done in the Department of Pathology, Mahatma Gandhi Medical College, Indore from February 2019 to February 2021.

Results-50 cases with altered megakaryocyte morphology and number were studied.

Conclusion: Dysplastic megakaryocytes are not only common in myelodysplastic syndrome (MDS) but also common in various non-MDS disorders. For proper diagnosis, megakaryocyte morphology, patient's clinical findings, and other hematological parameters, all should be considered so that it can improve the diagnostic accuracy for wide range of hematological disorders, which can be helpful in proper therapeutic interventions in various hematological disorders with altered megakaryocyte morphology and number.

Keywords:Megakaryocytes,Dysmegakaryopoiesis,bone marrow aspiration

INTRODUCTION

Megakaryocytes (MK)arise from pluripotent hematopoietic stem cells (HSC).These HSCs develop into 2 types of precursors, burst-forming cells and colony-forming cells, both of which express the CD34 antigen (2). Development of both of these cell types continues along a restricted lineage resulting in the formation of megakaryocyte precursors that develop into megakaryocytes (1). Thrombopoietin (TPO) is the primary regulator of thrombopoiesis and is the only cytokine required for megakaryocytes to maintain constant platelet mass (3). TPO acts in combination with other factors like IL-3, IL-6, and IL-1 (4). Mature MKs give rise to circulating platelets by the acquiring the cytoplasmic structural and functional characteristics which are necessary for platelet action [5,6]. The production of platelets by megakaryocytes requires series of events that result in the release of thousands of platelets from a single megakaryocyte. Abnormalities in this process of platelet formation can lead to clinically significant disorders.

Dysplastic changes are seen commonly in cases with thrombocytopenia associated with myelodysplastic syndrome (MDS). However, dysplastic changes of

megakaryocytes may also be observed in non-MDS hematological condition like immune thromobocytopenicpurpura (ITP), megaloblastic anemia,aplastic anemia,iron deficiency anemia (IDA), chronic myeloid leukemia, (CML) Juvenile myelomonocytic leukemia(JMML),multiple myeloma,acute leukemias.

AIM:

This study was conducted to understand various morphological changes in megakaryocytes in the bone marrow aspiration smears and their role in the diagnosis of various hematological disorders.

MATERIALS AND METHODS

This is a prospective study done in the Department of Pathology, Mahatma Gandhi Medical College, Indore. We included bone marrow aspirates with altered morphology and number of megakaryocytes which we received in our department from February 2019 to February 2021.Evaluation of bone marrow aspirate smears was done for various morphological changes in megakaryocytes and what was their role in diagnosis of various hematological disorders was studied.

The received bone marrow aspirate smears were stained with Fields stain and were examined according to the standard guidelines and the findings were noted. The morphology and number of the megakaryocytes was studied. The number of megakaryocytes is expessed as the standard protocol as number /10 low-power field (LPF) and was further divided into absent, decreased (1/5–10 LPF), normal (1/1–3 LPF) and increased (>2/LPF). The morphological changes of megakaryocytes included both dysplastic and nondysplastic features. Dysplastic features included multiple separated nuclei (Pawn ball MKs), micro megakaryocytes, and hypogranular forms. Nondysplastic features included immature forms, emperipolesis, cytoplasmic vacuolization and bare megakaryocyte nuclei. At least thirty megakaryocytes were evaluated on BMA smears, and dysplastic changes were reported only when 10% or more of megakaryocytes showed changes.

RESULTS-

50 cases with altered megakaryocyte morphology and number were studied.

The cases include Myelodysplastic syndrome,Immune thrombocytopenic purpura,megaloblastic anemia,aplastic anemia,iron deficiency anemia,chronic myeloid leukemia,Juvenile myelomonocytic leukemia,multiple myeloma,acute leukemias.

Table 1-Number of cases showing increased/Decreased or normal number of megakaryocytes.

Disease	**Number of cases with megakaryocytes per low power field(lpf)**			
	Normal (1 Mk /1-3 LPF)	**Increased (>2Mk /LPF)**	**Decreased (1 Mk/5-10 LPF)**	**Total Cases**
ITP	00	07	**0**	**07**
Megaloblastic anemia	03	**06**	**0**	**09**
Iron deficiency anemia	**02**	**03**	**0**	**05**
CML –Chronic phase	**01**	**02**	**00**	**03**
Aplastic anemia	**00**	**00**	**05**	**05**
Acute myeloid leukemia	**01**	**00**	**04**	**05**
Acute Lymphoid leukemia	**02**	**00**	**04**	**06**

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Myelodysplastic syndrome	**05**	**01**	**02**	**08**
JMML	**01**	**00**	**00**	**01**
Multiple myeloma	**01**	**00**	**00**	**01**

Dysplastic changes were observed most commonly in cases of myelodysplastic syndrome which include multiple segmented nuclei,hypogranular forms,hypolobated forms micro megakaryocytes and cytoplasmic vacuolation.

Micro megakaryocytes were seen as a predominant feature in ITP

Table 2-Cases with dysmegakarypoisis:

Disease	Muliple segmented nuclei	Hypogranular forms	Hypolobated forms	Micromegakaryocytes	Cytoplasmic vaculation
ITP	02	03	03	05	01
MDS	05	04	06	03	02
Megaloblastic anemia	03	04	02	01	00
Acute leukemia	00	01	04	01	00
Iron deficiency anemia	00	01	01	01	00
CML	01	02	02	03	00
JMML	01	01	00	00	00
Multiple myeloma	02	02	01	00	00
Aplastic anemia	00	01	01	00	00

Table 3-Cases with non-dysplastic features:

Disease	Immature forms	Emperipolesis	Cytoplasmic budding	Bare nuclei.
ITP	04	02	01	01
MDS	05	01	04	03

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Megaloblastic anemia	02	01	01	00
Acute leukemia	03	00	00	01
Iron deficiency anemia	01	01	00	00
CML	02	01	01	00
JMML	01	00	00	00
Multiple myeloma	02	00	01	00
Aplastic anemia	01	00	00	00

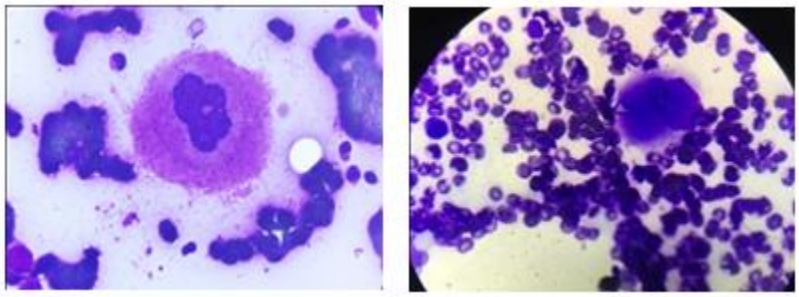

Fig-(1A) Fig-(1B)

Figure 1: Bone marrow aspirate smear showing(1A) Mature megakaryocyte with budding of cytoplasm and tiny platelets are formed(1B) Immature megakaryocyte with scanty basophilic cytoplasm and small size with regular border.

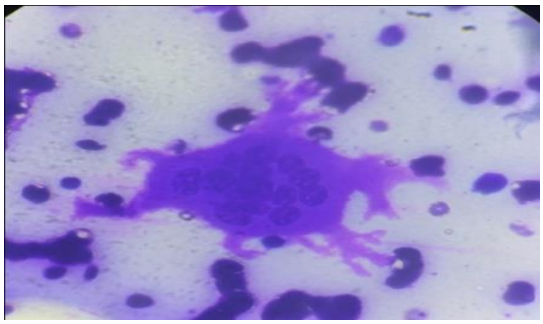

Figure 2: Bone marrow aspirate smear showing multinucleated megakaryocyte with separated nuclei(Pawn ball appearance).

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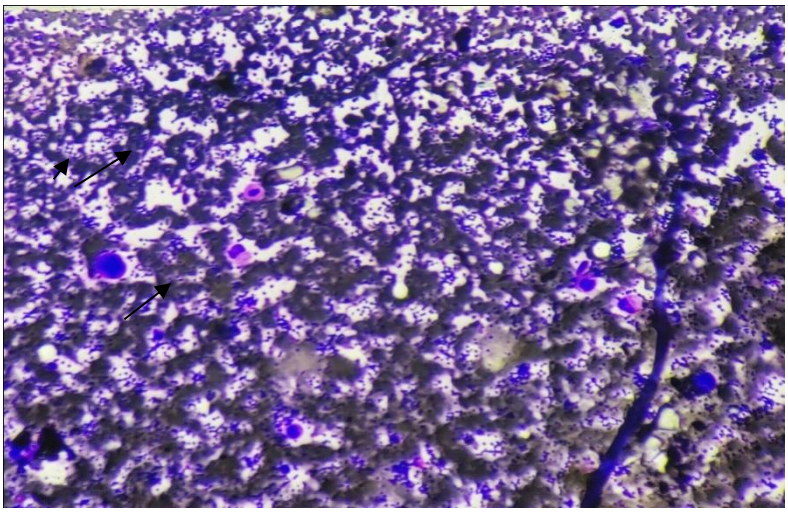

Fig-(3A)

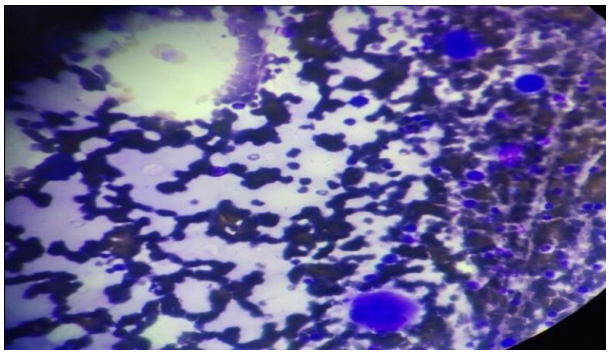

Fig-(3B)

Figure 3: Bone marrow aspirate smear showing micromegakaryocytes: (3A) low power view showing megakaryocytic hyperplasia with small immature megakaryocye with smooth borders and single lobed nucleus, (3B) high power field.

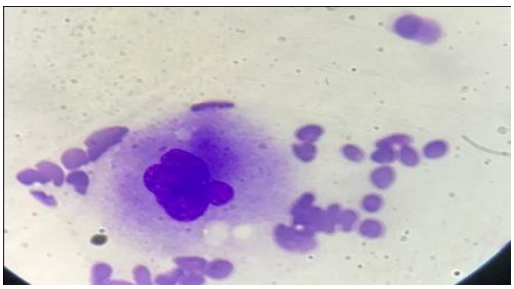

Figure 4: Bone marrow aspirate smear showing megakaryocytes with less number of nuclear lobes (hypolabated form) .

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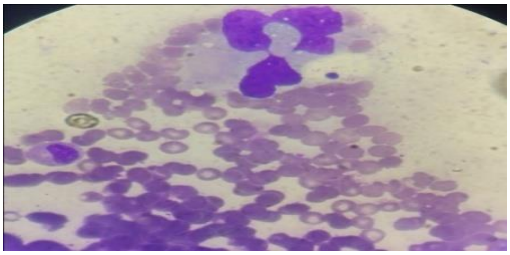

Figure 5: Bone marrow aspirate smear showing megakaryocytes with cytoplasmic vacuolization.

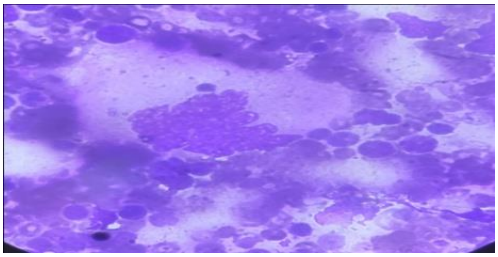

Figure 6: Bone marrow aspirate smear showing mature megakaryocyte shows emperiopolesis of a hemopoietic cell.

DISCUSSION-

The cells in megakaryocytic series are least in number (less than 1%of nucleated cells) but largest of all hematopoietic cells. The number of megakaryocytes is 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)

Megakaryocyte number was increased in almost all cases of Immune thrombocytopenic purpura.Similar findings were found in study done by

Muhury M et al which showed increased number in ITP [12]

Megakaryocyte number was decreased in 05 cases of aplastic anemia and 08 cases in acute leukemias out of total 11 cases.Similar findings were found in study done by Tricot et al and Dameshek W et al which showed decreased number in acute leukemias and aplastic anemias.

Megakaryocytic proliferation and differentiation is abnormal in patients with myelodysplastic syndromes (MDS) [13]. A normal megakaryocyte has four to sixteen nuclear lobes (Fig1A) and an immature megakaryocyte (Fig1B) is defined as a young form of megakaryocyte with scant blue cytoplasm and lack of lobulation of the nucleus which occupies almost all of the cell.

In present study Immature megakayrocyteswere seen in 04 cases of ITP, 05 cases of MDS,03 cases of acute leukemias,02 cases of megaloblastic anemia, CML and multiple myeloma,01 case of IDA, JMML and aplastic anemia each. Similar findings were observed in study done by Houwerzijl et al[7].

Dysplastic megakaryocytes are MKs with single/ multiple separate nuclei (Pawn ball appearance) (Fig2). Dysmegakaryopoisis is a main feature of myelodysplastic syndrome.

In present study,out of total 08 cases of MDS,05 cases showed multiple segmented nuclei,which was the most common dysplastic feature found in MDS.Similar finding was observed in the study done by Tejinder Singh Bhasin et al ..[8]

Micromegakaryocytes(Fig3A and 3B) were defined as megakaryocytes whose size was that of a large lymphocyte/monocyte and which had a single/bilobed nucleus.Micromegakaryocyte is an important feature noted in ITP.In present study,out of 07 cases of ITP,05 cases showed micromegakaryocytes.

The study done by Houwerzijl et al[7] also showed the presence of micromegakaryocyte as an important

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feature of ITP.The study done by Deka et al.. showed the megakaryocytes were less round in ITP[9]

Hypolabated forms (Fig4)aremegakaryocyte with less number of nuclear lobes. In the present study, out of 08 cases of MDS,06 cases show Hypolobted forms.

Hypogranular forms were defined as megakaryocytes with pale grey or water clear cytoplasm and sparse or no granules.

In the present study, out of 08 cases of MDS,04 cases show Hypogranular forms.

The cytoplasmic vacuolization (Fig5) reflects an increased megakaryocyte turnover.in present study it was seen in 02 cases of MDS out of 08 cases. Similar findings was also observed by Levine and Houwerzij et al[7]

The non dysplatic features include immature forms and these were seen in 04 cases of ITP and 05 cases of MDS.

In present study emperipolesis (Fig6) was found in 02 cases of ITP. The study done by Rai et al reported Emperipolesis in 13 out of 19 cases of ITP [10] . These findings correlated with the study of Rozman C. and Vives Corrons JL [11] which also showed increase in megakaryocytic emperipolesis in idiopathic thrombocytopenic purpura (ITP). However,emperipolesis on bone marrow aspirate do not have any diagnostic significance

CONCLUSION: There are many similarities in various morphological changes of megakaryocytes in different hematological diseases,Dysplastic megakaryocytes are not only common in MDS but also common in various non-MDS disorders.So, the presence of dysplastic megakaryocytes should not lead to the diagnosis of MDS.For proper diagnosis, megakaryocyte morphology, patient's clinical findings, and other hematological parameters, all should be considered so that it can improve the diagnostic accuracy for wide range of hematological disorders,which can be helpful in proper therapeutic interventions in various hematological disorders with altered megakaryocyte morphology and number.

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