ORIGINAL RESEARCH PAPER

Pathology

CHANGES IN MEGAKARYOCYTES IN VARIOUS HEMATOLOGICAL CONDITIONS : A STUDY OF BONE MARROW ASPIRATION IN A TERTIARY CARE CENTRE

KEY WORDS:

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ABSTRACT

INTRODUCTION Dysmegakaryopoiesis is characterized by various Megakaryocytic alterations in bone marrow and includes both dysplastic and non dysplastic features. Dysplastic changes are mostly seen in myelodysplastic syndrome however megakaryocyte alteration have also been noted in some bone marrow aspiration in non myelodysplastic conditions. **AIMS OBJECTIVE** To evaluate changes in megakaryocytes in various hematological conditions in bone marrow aspiration examination. **MATERIAL AND METHODS** Study was done at Central Pathology lab in the Department of Pathology GAJRA RAJA MEDICAL COLLEGE GWALIOR over a period of 1.5 year FROM NOV 2019 TO MAY 2021. Total 84 bone marrow were received out of 14 were dilute so excluded from study and results were prepared from 70 cases. Age range was 9 months to 75 years **RESULTS AND OBSERVATIONS** In this study out of 70 patients, 43 were male and 27 were female. Patients were categorised into neoplastic and non neoplastic category. Out of 70 cases 46 were non neoplastic forming majority while 24 were neoplastic. Out of non neoplastic, megaloblastic anemia was most common while acute leukemia was most frequent in neoplastic category. Bone marrow was evaluated for cellularity. 47 were hypercellular marrow forming majority with 15 cases showing normal cellularity and 08 as hypocellular. Acute leukemia and megaloblastic anemia were two conditions which had hypercellular marrow. The number of the megakaryocytes was considered normal when one megakaryocyte per 3 low power fields was encountered, increased if more than two megakaryocytes per low power field were seen and decreased when one megakaryocyte per five to ten low power fields was documented and absent when no megakaryocytes were seen per ten low power field. Our study showed 27 cases of megakaryocytic hypocellularity, 22 cases normal number of megakaryocytes and 18 as increased number of megakaryocytes. Normally megakaryocytes 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. Dysplastic megakaryocytes are those with single, multiple/separated nuclei. Micro megakaryocytes were defined as megakaryocytes whose size was that of large lymphocyte or monocyte and which had a single / bi-lobed nucleus. Our study – showed normal megakaryocyte morphology in 32/70 (45%) cases and 35/70 (50%) were with altered morphology. **CONCLUSION** Dysplastic Morphologic changes in megakaryocyte were not only seen in MDS but also in various non MDS conditions which should be considered during diagnosis. Understanding and detailed knowledge of changes in megakaryocytes, including both cellularity and morphology, can improve the diagnostic accuracy for a wide range of hematological disorders

INTRODUCTION

Any abnormality in development of megakaryocytes results in Dysmegakaryopoiesis which results in clinically significant diseases like Thrombocytopenia that is platelet count <150000/microlitre.[1] Thrombocytopenia is commonly seen in various hematological disorders including Myelodysplastic syndrome (MDS) as well as various non Myelodysplastic syndrome (MDS) hematological conditions.[2]

Dysmegakaryopoiesis is characterized by various Megakaryocytic alterations in bone marrow and includes both dysplastic and non dysplastic features. Dysplastic changes are mostly seen in myelodysplastic syndrome however megakaryocyte alteration have also been noted in some bone marrow aspiration in non myelodysplastic conditions.[3]

The bone marrow examination is carried out for Leukemia, Myelodysplastic syndrome or Aplastic anemia. It can show alteration of Megakaryocyte in bone marrow and platelets in peripheral smear.[4] One of the commonest cause of megakaryocytic abnormality is Immune Thrombocytopenic Purpura (ITP) and bone marrow analysis in these patients show shift to young, immature, less polyploid megakaryocytes and micromegakaryocytes in some cases.[56]

Present study aims at finding of changes in megakaryocytes in various diseases.

MATERIAL AND METHODS

Study was done at Central Pathology lab in the Department of Pathology GAJRA RAJA MEDICAL COLLEGE GWALIOR over a period of 1.5 year FROM NOV 2019 TO MAY 2021.

The bone marrow aspiration procedure was done by the clinicians and the smears are examined by the pathologists at central pathology lab.

In all the cases detailed history is taken and clinical findings were noted.

Inclusion Criteria:- Cases with

1. Unexplained anaemia
2. Lymphadenopathy
3. Pancytopenia
4. Leucopenia and leucocytosis
5. Unexplained thrombocytopenia and thrombocytosis
6. Leukemia
7. Myeloproliferative disorders
8. Lymphoproliferative disorders.

Exclusion Criteria :–

1. Cases with bleeding disorders like haemophilia, and patient with platelet count less than 10,000/cum.

2. Diluted or dry tap marrow.

RESULTS AND OBSERVATIONS

Total 84 bone marrow were received out of 14 were dilute so excluded from study and result were prepared from 70 cases. Age range was 9 months -75 years.

Table 1 - Age and Sex wise Distribution of Cases

Age Group	No of Cases	Males	Females	CHI SQUARE	P VALUE
0-10	20	12	08	3.215	0.689
11-20	22	12	10		
21-30	06	04	02		
31-40	06	05	01		
41-50	05	02	03		
>50	11	08	03		
TOTAL	70	43	27		

Table 2 : Specific diagnosis

Category	Diagnosis	No of cases
Non-neoplastic (46)	Megaloblastic anemia	19
	Micronormoblatic (IDA)	4
	Dimorphic/Mixed nutritional	12
	Normoblastic Marrow	2
	Aplastic/hypoplastic	5
	Immune thrombocytopenic Purpura (ITP)	4
Neoplastic (24)	Subleukemic leukemia	2
	Acute Leukemia	11
	Chronic leukemia	4
	Plasma cell disorders	2
	Myelodysplastic syndrome	4
	Myelofibrosis	1

Out of 70 cases 46 were non neoplastic forming majority while 24 were neoplastic. Out of non neoplastic, megaloblastic anemia was most common while acute leukemia was most frequent in neoplastic category.

Bone marrow was evaluated for cellularity. 47 were hypercellular marrow forming majority with 15 cases showing normal cellularity and 08 as hypocellular. Acute leukemia and megaloblastic anemia were two conditions which had hypercellular marrow.

Table 3 : Bone marrow cellularity in each case

Diagnosis	No of cases	Bone marrow cellularity			
		Normal	Hyper Cellular	Hypo Cellular	Absent
Megaloblastic anemia	19	4	14	1	
Micronormoblastic (IDA)	4		4		
Dimorphic/Mixed nutritional	12	5	6	1	
Normoblastic Marrow	2	2			
Aplastic/Hypoplastic	5			5	
Immune thrombocytopenic Purpura (ITP)	4	1	3		
Subleukemic Leukemia	2	1	1		
Acute leukemia	11		11		
Chronic leukemia	4		4		
Plasma cell disorder	2	1	1		
Myelodysplastic Syndrome	4	1	3		
Myelofibrosis	1			1	

The number of the megakaryocytes was considered normal when one megakaryocyte per 3 low power fields was encountered, increased if more than two megakaryocytes per low power field were seen and decreased when one megakaryocyte per five to ten low power fields was documented and absent when no megakaryocytes were seen per ten low power field. Our study showed 27 cases of megakaryocytic hypocellularity, 22 cases normal number of megakaryocytes and 18 as increased number of megakaryocytes.

Table 4 : Megakaryocyte number

Diagnosis	No of cases	Megakaryocyte cellularity			
		Normal	Increased	Decreased	Absent
Megaloblastic anemia	19	7	6	6	
Micronormoblastic (IDA)	4	2	2		
Dimorphic/Mixed nutritional	12	7	2	3	
Normoblastic Marrow	2	2			
Aplastic/Hypoplastic	5			4	1
Immune thrombocytopenic Purpura (ITP)	4		4		
Subleukemic Leukemia	2			2	
Acute leukemia	11	1		8	2
Chronic leukemia	4	1	2	1	
Plasma cell disorder	2	1		1	
Myelodysplastic Syndrome	4	1	2	1	
Myelofibrosis	1			1	

Dysplastic megakaryocytes are those with single, multiple/ separated nuclei. Micro megakaryocytes were defined as megakaryocytes whose size was that of large lymphocyte or monocyte and which had a single / bi-lobed nucleus.

Our study – showed normal megakaryocyte morphology in 32/70 (45%) cases and 35/70 (50%) were with altered morphology.

Table 5 : Morphological changes

Diagnosis	Immamture megak	Bare megak Nucleus	Seperated nuclear segment	Small/Micro Mega k	Hypolobated megak	Emperi Polesis	Other vacuol Ation, Hypo GranulAtion)	No Alteration
Normoblastic Marrow	00	00	00	00	00	00	00	02
Megaloblastic Anemia	02	01	02	00	04	02	04	10

IDA	01	02	00	00	01	00	00	01
Dimorphioc Anemia	02	02	05	01	01	02	02	04
Hypoplastic/ Aplastic	00	00	00	00	00	00	01	04
ITP	03	00	02	00	01	02	01	00
Subleukemic Leukemia	00	00	00	00	00	00	00	02
Acute Leukemia	02	02	02	01	02	02	01	09
Chronic Leukemia	03	01	00	03	00	01	00	00
MDS	02	00	01	02	02	01	03	00
MM	00	00	01	00	00	00	01	01
Myelofibrosis	00	00	01	01	00	00	01	00

DISCUSSION

Total 84 Bone marrow aspiration sample were received out of which 14 were dilute so results were prepared from 70 cases. Study had 62 percent male and 38 percent female.

Diagnostic Categories:

In our study, we largely categorized the study group into two categories neoplastic and non neoplastic based on the bone marrow analysis.46 Cases were non neoplastic (65%) forming majority whereas 24 cases were neoplastic (35%). Studies by Bhasin et.al., Sapre et.al., Choudharyet.al.7, Pokharel8 also had majority of non neoplastic cases quantitating to 55%, 82%, 71.22% and 65.79% respectively.

Bone Marrow Cellularity:

Bone marrow cellularity study showed 47/70 i.e., 67% of total cases to be hypercellular. Hypocellular bone marrow was seen 8/70 12% cases. While 15/70 21% cases were normocellular. Sengupta M. et.al9. also carried out similar analysis where maximum number of their cases (48.2%) were hypercellular, whereas normocellular and hypocellular formed 24.8% and 27.1% respectively. Another study by Sapre et.al10 showed majority of their cases were normocellular (44%) followed by hypercellular (32%) and hypocellular (24%).

Megakaryocyte Number

Megakaryocyte cellularity was largely classified into increased, normal, decrease and absent based on number of megakaryocytes per low power field. The number of the megakaryocytes was considered normal when one megakaryocyte per 3 low power fields was encountered, increased if more than two megakaryocytes per low power field were seen and decreased when one megakaryocyte per five to ten low power fields was documented and absent when no megakaryocytes were seen per ten low power field.

Megakaryocyte Morphology

Normally megakaryocytes 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. Dysplastic megakaryocytes as those with single, multiple/separated nuclei. Micro megakaryocytes were defined as megakaryocytes whose size was that of large lymphocyte or monocyte and which had a single / bi-lobed nucleus.

Our Study –

showed normal megakaryocyte morphology in 32/70 (45%) cases and 35/70 (50%) were with altered morphology.

CONCLUSION

Dysplastic Morphologic changes in megakaryocyte were not only seen in MDS but also in various non MDS conditions which should also be considered during diagnostic evaluation.

Understanding and detailed knowledge of changes in megakaryocytes, including both cellularity and morphology, can improve the diagnostic accuracy for a wide range of hematological disorders thereby enabling proper therapeutic interventions. This can help in developing countries like INDIA due to non availability of advanced megakaryocyte studies like specific marker studies, electron microscope and ultra-structural studies.

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