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Original Research

Bone marrow examination in megaloblastic and iron deficiency anemias with emphesis on megakaryocytes

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ABSTRACT:

Introduction: Megakaryocytes is a cell that produces platelets.Any abnormality in the development results in dysmegakaryopoiesis which result in clinically significant symptoms like thrombocytopenia. Megaloblastic anemia is one of most important cause of thrombocytopenia and iron deficiency anemia leads to reactive thrombocytosis. This study is undertaken to evaluate bone marrow cellularity and megakaryocytic changes in cases of iron deficiency and megaloblastic anemia. **Material and methods:** Bone marrow was evaluated in cases of iron deficiency and megaloblastic anemia. Slides were evaluated for bone marrow cellularity and graded as normal, hypercellular and hypocellular marrow. Megakaryocyte changes like count or number were observed under low power subjective assessment as done – that megakaryocytes are decreased, normal or increased and morphological assessment was done under high power. **Results:** Total no of cases was 23, out of which 19 were Megaloblastic anemia and remaining 4 were iron deficiency anemia. Out of 19 megaloblastic cases – bone marrow cellularity was normal in 4 cases, while 14 hypercellularity and only 1 as hypocellularity. While all 4 cases of iron deficiency anemia had hypercellular bone marrow.Out of 19 megaloblastic anemia cases 7 were having normal megakaryocytic count, 6 as increased while remaining 6 had decreased megakaryocytes.Hypolobation was most common morphological abnormality noted along with hypogrnaulation and separated nuclei in megaloblastic anemia. Bare megakaryocytes were most commonly noted in 2 (50%) cases of IDA. **Conclusion:** Bone marrow is hypercellular in most of cases of iron deficiency anemia while it can be hypercellular or normal bone marrow in megaloblastic anemia. Number of megakaryocytes can be normal, decreased or increased with dysplastic feature on morphology are observed in megaloblastic anemia.

Key words: Cellularity, Morphology, Aspiration, Dysplastic, thrombocytopenia

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INTRODUCTION

Wright put forth the hypothesis that blood platelets are derived from cytoplasm of megakaryocytes and the basic elements of thrombopoiesis were established.[1]

Any abnormality in the development results in dysmegakaryopoiesis which result in clinically significant symptoms like thrombocytopenia. Thrombocytopenia is commonly seen in various haematological disorders including myelodysplastic syndrome (MDS) as well as various non myelodysplastic hematological conditions.[2] Dysplastic changes are mostly seen in myelodysplastic syndrome however megakaryocyte alteration has also been noted in some bone marrow aspiration in non myelodysplastic conditions.[3]

The bone marrow examination is carried out for Leukemia, aplastic anemia Myelodysplastic syndrome and many other conditions[4]. It can show alteration of Megakaryocyte in bone marrow and hence, platelets in peripheral smear.

Studies on the evaluation of megakaryocytic alteration and their contribution to thrombocytopenia can provide information regarding pathogenesis of various hematopoietic disorders however our main focus is in iron deficiency and megaloblastic anemia. It is necessary to asses megakaryocyte number (quantity) as well as its morphology (Quality). In films of an aspirate quantity can only be a subjective assessment – that megakaryocytes are decreased, normal or increased. Normal (1 megakaryocyte/1-3 low -power fields), increased (>2 megakaryocytes

/low- power field), or decreased or absent (1/no megakaryocyte/5-10 low power fields).[5]
Morphological changes can be related to size (normal, micro megakaryocytes), cytoplasmic (hypo granular, hyper granular, vacuolization, emperipolesis, loss of cytoplasmic blebs), nuclear (nuclear
separation, hypolobated, hypersegmented, bare nuclei). Abnormal megakaryocytes include micro megakaryocytes, dysplastic forms, megakaryocyte with separated lobes. Hypogranular forms were considered as dysmegakaryopoeisis.[6]

AIM AND OBJECTIVE OF STUDY ARE

To evaluate bone marrow cellularity in cases of iron deficiency and megaloblastic anemia.
To evaluate megakaryocytic changes in cases of iron deficiency and megaloblastic anemia.

MATERIAL AND METHODS

This study was done in the Department of Pathology, Gajra Raja Medical College, Gwalior and Jayarogya Group of Hospital (J.A.H), Gwalior (M.P) over a period from 1st November 2019- 31st May2021.
The bone marrow aspiration procedures were done by the clinicians andAfter aspiration, 0.5ml marrow 1 or 2 drops of aspirate is immediately placed on the glass slide. Direct films are immediately prepared by transferring unanticoagulated aspirate to the fresh slide and covering the aspirate with another slide, gently pressing the two slides together to express most of the blood on gauze sponge and then pulling the slides apart longitudinally.Then the films are air dried. 3-4 slides were taken for routine staining and the rest slides are wrapped and kept for future staining purpose.
Leishman stain was used for staining of slides. Smears were examined by the pathologists at central pathology lab
In all the cases detailed history is taken and clinical findings are noted.
Number and morphology od megakaryocytes were evaluated in all cases of iron deficiency and megaloblastic anemia. Data was prepared and results were prepared.

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

Total no of cases was 23, out of which 19 were Megaloblastic anemia and remaining 4 were iron deficiency anemia.
Bone marrow cellularity was assessed in every case and were categorised as Normal cellularity, hypocellular and hypercellularity.
Out of 19 megaloblastic cases – bone marrow cellularity was normal in 4 cases, while 14 hypercellularity and only 1 as hypocellularity.
While all 4 cases of iron deficiency anemia had hypercellular bone marrow.

Table 1: Bone Marrow Cellularity

Diagnosis	Normal bone marrow cellularity	Hypercellular bone marrow	Hypocellular bone marrow	Total
Megaloblastic anemia	04	14	01	19
Iron deficiency anemia	00	4	00	4

Bone marrow was assessed for megakaryocytes count and was graded as normal megakaryocytic count, increased and decreased.
Out of 19 megaloblastic anemia cases 7 were having normal megakaryocytic count, 6 as increased while remaining 6 had decreased megakaryocytes.
Iron deficiency anemia cases shows variability between increased and normal count. 2(50%) cases had normal count while remaining 2(50%) had increased in megakaryocyte count.

Table 2: Megakaryocyte number

Diagnosis	No of cases	Megakaryocyte cellularity			
		Normal	Increased	Decreased	Absent
Megaloblastic anemia	19	7	6	6	
Micronormoblastic (IDA)	4	2	2		

After megakaryocyte count, morphology was also assessed for any changes.
10 cases of megaloblastic anemia did not show any abnormality. Hypolobation was most common morphological abnormality noted along with hypolobation and vacuolation.
Out of 4 cases of iron deficiency anemia, 3 had shown morphological abnormality. Bare megakaryocytes were most commonly noted in 2 (50%) cases.

Table 3: Morphological changes in megakaryocytes

Diagnosis	Immamturemegak	Bare megak Nucleus	Seperated nuclear segment	Small/Micro Mega k	Hypolobatedmegak	EmperiPolesis	Other vacuol Ation, Hypo GranulAtion)	No Alteration
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

Fig 1: Megakaryocytes showing emperipolesis

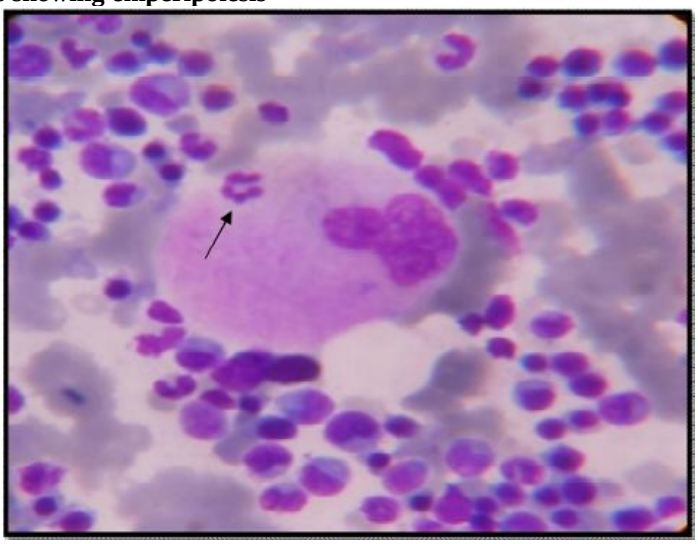
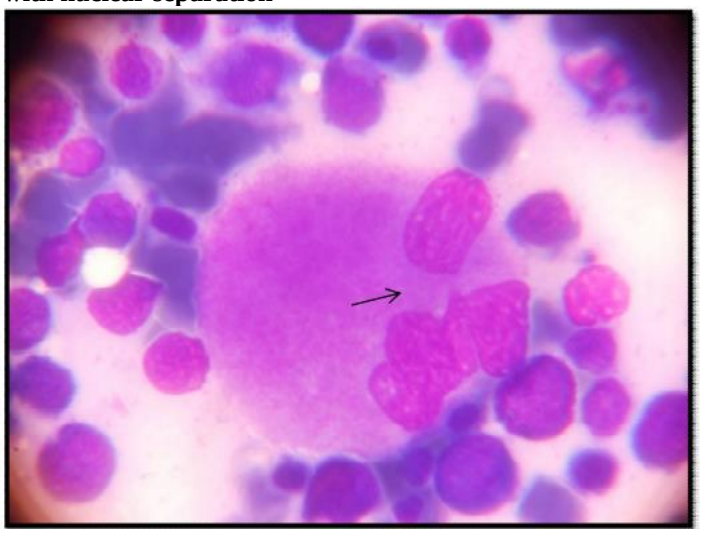


Fig 2: Megakaryocyte with nuclear separation



DISCUSSION

Total 23 Bone marrow aspiration of iron deficiency anemia and megaloblastic were evaluated in which MEGALOBLASTIC ANEMIA was much more common than iron deficiency anemia.

MEGALOBLASTIC ANEMIA

On peripheral smear pancytopenia and macrocytic picture is seen in megaloblastic anemia. Confirmation is done by bone marrow examination.

Bone marrow examination showed hypercellular marrow. Few other studies also showed similar

results.Number of megakaryocytes wasvariables in megaloblastic anemia as 7 cases had normal megakaryocytic count and 6 each as increased and decreased megakaryocyte count. Rajalakshmi Birur Rajashekar et al found megakaryocyte count in meagaloblastic anemia was normal, increased and decreased in 25%, 41.7% and 33.3 % respectively[7]. Similar variability is seen in other studies by Mansuri B, and Thekdi KP et al[8].Nine out of Nineteen (47%) shows altered morphology. Gupta et.al, Chaudhary et.al, Muhury et.al[9], showed similar findings. Wikramsingh[10] also observed dysplastic megakaryocytes with separation of nuclear of nuclear lobes and nuclear fragments and attributed this to diminished DNA synthesis.

Table 4: Changes in megakaryocytes in MA

Studies	Megakaryocyte Morphological changes in Megaloblastic anemia(%)
*Present study	47%
Gupta et.al	41.7%
Chaudhary et.al	42.3%
Muhuryet.al	75%

IRON DEFICIENCY ANEMIA

There were 4 cases of iron deficiency anemia. All 4 had hypercellular bone marrow. Similar results in study in experimenting animals– Regeneration of Marrow Tissue in Chronic Iron Deficiency[11].

We found 2(50%) cases of iron deficiency anemia had increased megakaryocyte number while remaining 2 had normal megakaryocyte number. Megakaryocyte does not decrease in iron deficiency anemia. Study titled as – Iron deficiency alters megakaryopoiesis and platelet phenotype independent of thrombopoietin[12] has showed that iron deficiency increases megakaryocytic differentiation and alters phenotype without change in TPO.

Morphologically 3 out of 4 cases showed altered morphology. 2 out of 4 cases had bare megakaryocytes being most common finding. Immature megakaryocytes and hypolobated megakaryocytes were other findings.Evstatiev *et al*. have studied the effect of iron deficiency on megakaryopoiesis in experimental animals and found that iron deficiency inhibits proliferation but increases ploidy in megakaryocytic cell lines. This may affect the normal maturation process[11].

Among the nondysplastic features in IDA, immature forms, bare nuclei, and hypolobated forms were also noted by Shashikala Vinayakamurthy and Rojaramani Potluri et alin study - A study of megakaryocyte morphology in bone marrow aspiration smears of cases of thrombocytopenia.[12]

However, our sample size in iron deficiency cases is less, so further studies can be done for more accuracy.

CONCLUSION

Bone marrow is hypercellular in most of cases of iron deficiency anemia while it can be hypercellular or normal bone marrow in megaloblastic anemia.

Megakaryocyte count will be either increased or normal in iron deficiency anemia while bare megakaryocytes can be seen.

Number of megakaryocytes can be normal, decreased or increased with dysplastic feature on morphology are observed in megaloblastic anemia.

CONFLICT OF INTEREST

No conflicts

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