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Clinical, haematological and bone marrow aspiration evaluation in Megaloblastic anemia - study of 80 cases in a tertiary care hospital Telangana

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Abstract

Background: Megaloblastic anemias (MA) characterized by distinctive hematopoietic cytological and functional abnormalities in peripheral blood and bone marrow cells and is frequently mediated by underlying biochemical deficiencies in cobalamin and /or folate. Over last two to three decades, incidence of MA seems to be increasing. This anemia concerned with significant cause of ill health and because of excellent response to treatment, these anemias are of great clinical importance.

Aim: To study the clinical presentations, diagnosis and evaluation of hematological parameters and bone marrow aspiration cytology in megaloblastic anemia.

Materials and Methods: It was retrospective and prospective study conducted in tertiary care hospital, during period of two and half years (January 2015 to June 2017). Clinical, hematological and bone marrow aspiration cytology evaluation of megaloblastic anemia performed.

Results: 80 cases were diagnosed as megaloblastic anemia by bone marrow aspiration cytology. Age of the patient ranged from 15 to 80 years with mean age of 36 years. There was male preponderance almost in all age groups. Generalised weakness, shortness of breath and fever are common clinical presentation and pallor and hyperpigmentation are common physical findings. The commonest blood film picture was macrocytic and dimorphic picture. Bone marrow aspirate appears cellular in 82% cases & show megaloblastic erythroid hyperplasia with increased iron stores are among common findings.

Conclusions: This study showed that megaloblastic anemia commonly presented with pancytopenia or bicytopenia at tertiary level care. Clinical findings like fever, hyperpigmentation along with basic hematological parameters like peripheral blood smear findings RBCs histogram & MCV gives early clue to primary physician for diagnosis of megaloblastic anemias. MA is commonest cause of pancytopenia and bone marrow aspiration cytology alone enough to confirmed the diagnosis so as to avoid unnecessary bone marrow aspiration biopsy.

Keywords: Megaloblastic anemia; MCV; PS findings; BM morphology.

Introduction

The megaloblastic anemias are disorders caused by impaired DNA synthesis and are characterised by distinctive abnormality in the haematopoietic precursors in the bone marrow in which the maturation of nucleus is delayed to that of the cytoplasm, resulting larger nucleated red cell precursors which termed as Megaloblast by Ehrlich in 1880[1].

Megaloblasts are both morphologically and functionally abnormal with result that the mature red cells formed from them and released into the peripheral blood are also abnormal in shape (poikilocytosis) and size (Macrocytosis). The red cell indices reveal an elevated MCV (Mean corpuscular volume), MCH (Mean corpuscular haemoglobin) & normal or reduced MCHC (Mean corpuscular haemoglobin concentration) [2].

Bone marrow aspiration performed in cases of lack of typical peripheral smear features and atypical clinical presentation. The ready availability of accurate assays for Vitamin B12 and folic acid has lessened the importance of bone marrow examinations [3].

The present study intended to evaluate the varying clinicohaematological manifestations and distribution among various age groups in patients diagnosed as megaloblastic anemia, attending Yashoda Hospital, Hyderabad Teleangana.

Materials and Methods

This descriptive study was carried out for two and half years (January 2015 to June 2017) in department of laboratory medicine on both IP/OP patients diagnosed as megaloblastic anemia. Patients age ranged from 15 to 80 and both sexes included. Patient with hemoglobin less than 11 gm/dl were included. Among exclusion criteria, patient with hypothyroidism, alcoholic liver diseases, myeloproliferative neoplasm, patient on chemotherapy and radiotherapy.

Clinical profile include detailed history, clinical examination & haematological profile included hemogram with RBCs indices, peripheral blood smear morphology and bone marrow aspiration/ biopsy imprint morphology/biopsy.

Blood samples of patient were obtained by routine phlebotomy procedure. 3.0 ml EDTA (K2E 5.4 mg Ethylene diamine tetra acetic acid) Vacutainer (13x75mm) anticoagulated blood was collected by needle holder and processed through Automated Hematology analyser (Beckman-Coulter LH-750).

A total of 80 patients were taken up for the study. All the 80 cases were subjected to bone marrow aspiration examination after obtaining written consent from patient or guardian. Bone marrow aspiration done by Salahs needle no.(16) from Posterior superior iliac spine or sternum and 0.3ml sample collected for morphology and 1.5 ml in EDTA and 1.5 ml in Heparin vacutainer. Leishman stain and Giemsa stains prepared on aspirated sample cytosmears and Perls stain to assess the iron store. Disposable Jamshidi needle (11 GX 100mm) was used for bone marrow biopsy.

Serum Vitamin B12 and serum folic acid estimation done in patient one who not received nutritional supplement before admission.

Results

Out of total 870 marrow, 80 cases diagnosed as megaloblastic anemia on bone marrow aspirate. 50 cases were male and 30 cases are females. The mean age was 36 years. Male to female ratio was 1.4:1. Most common affected age group was 15 to 30 years, followed by 31-40 years and least was more than 60 years age group (**Chart 1**). Male patients are predominance in almost all age groups.

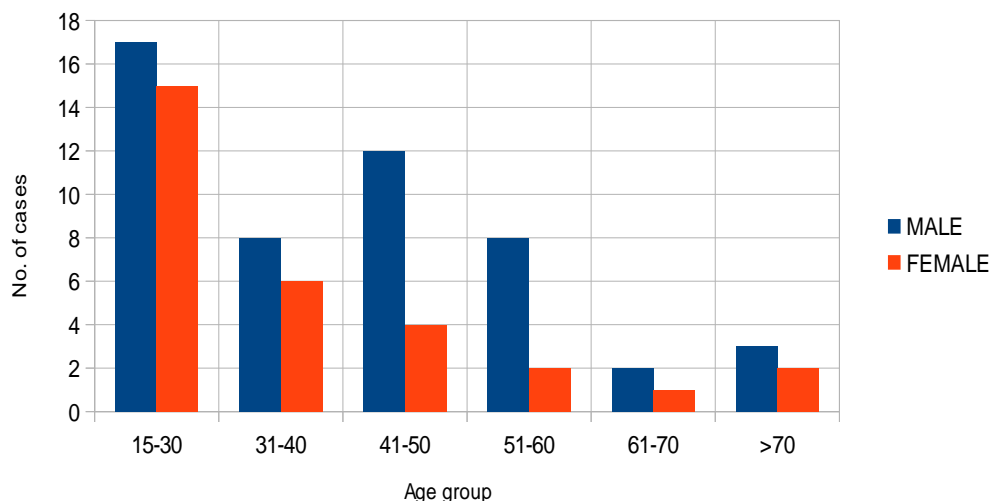


Chart :1; Age and sex distribution in 80 cases of Megaloblastic anemia.

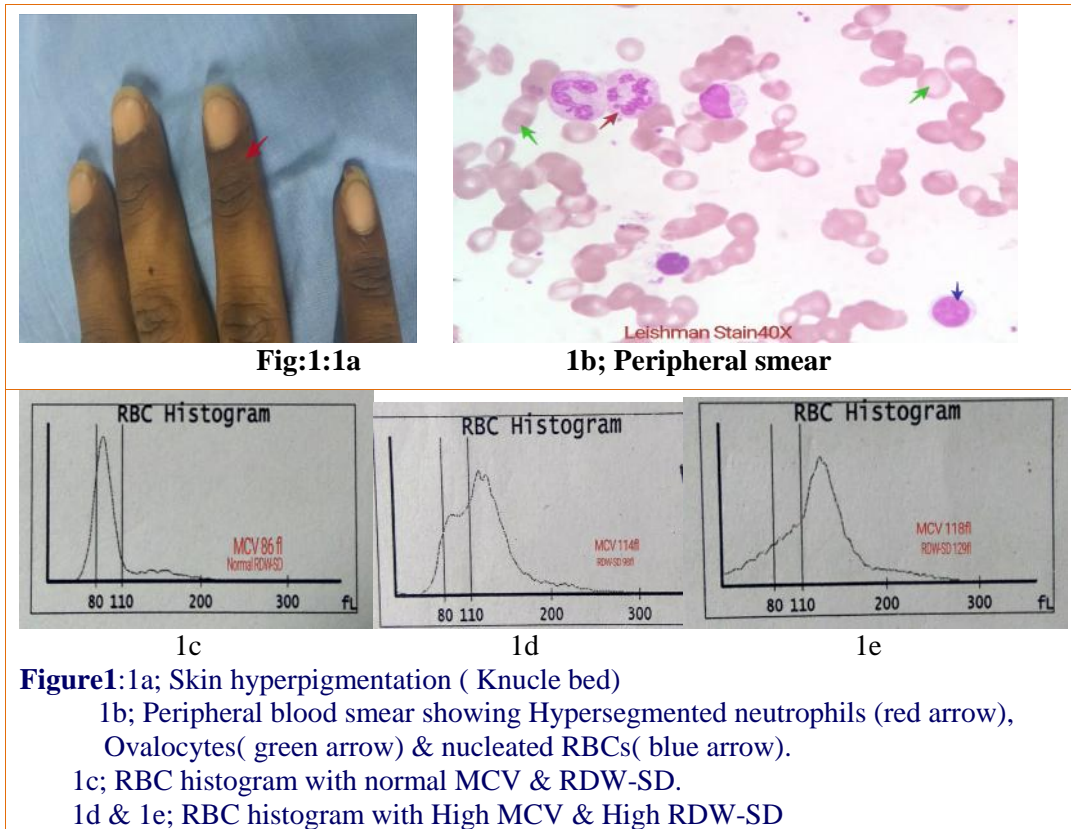
Chief complaints and physical signs in patients of megaloblastic anemias are listed in Table.1.

Table 1; Chief complaints and Physical Findings in 80 cases

S.No	Chief complaints and Physical Findings	No.Case	%
1	Generalised Weakness	65	81%
2	Fever	31	38.75%
3	Shortness of breath	30	37.5%
4	Anorexia	28	35%
5	Neurological (Giddiness, Headache, numbness)	14	17.5%
6	Bleeding manifestation	06	7.5%
7	Pallor	77	96.25%
8	Skin Hyperpigmentation	30	37.5%
9	Jaundice	26	32.5%
10	Splenomegaly	24	30%
11	Hepatomegaly	18	22.5%

The main chief complaints was generalised weakness, fever, and Shortness of breath. Other main symptoms were Shortness of breath, neurological symptoms like giddiness and numbness. On General examination

pallor was commonest finding followed by skin hyperpigmentation (knuckle pad) (Figure: 1; 1a) and jaundice. Splenomegaly was more common than hepatomegaly.



Hematological parameters as per Automated hematology analyser show Anemia alone in 14 cases only, Anemia+ Leucopenia(03cases), Anemia +

Thrombocytopenia (21cases) and pancytopenia (42cases) see figure 1.

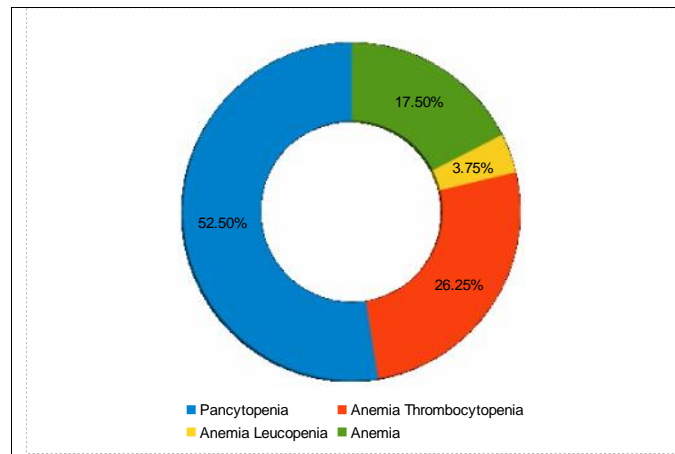


Figure 2: Distribution of cytopenia in 80 cases of megaloblastic anemia.

Hematological parameters sub grouped in to mild, moderate and severe form are shown in (Table :2). Moderate form of cytopenia is common among all three formed element i.e Most common hemoglobin

range group 5.61to 8.0 gm% (37.7%) ,White blood cells 1100 to 2500/cumm (47.73%) and Platelets 31000 to 80000/cumm (49.21%).

Table 2; Hematological parameters sub-classification

Parameters	Range	Cases	%
Hemoglobin			
Severe	<5 gm%	27	33.75%
Moderate	5.1 to 8.0 gm%	37	46.25%
Mild	8.1 to 11 gm%	16	20%
White blood cells (WBCs)			
Severe	0 to 1000/cumm	01	2.27%
Moderate	1100 to 2500/cumm	21	47.73%
Mild	2600to 4000/cumm	22	50%
Platelets			
Severe	Less than30000/cumm	07	11.11%
Moderate	31000 to 80000/cumm	31	49.21%
Mild	81000 to 140000/cumm	25	39.68%

RBC indices MCV above normal in 80% cases with mean value 101fl.

Reticulocyte count more than 2% seen in 38 %cases with maximum value was 8%.

Peripheral smear RBC morphology show macrocytes and macrovalytes (commonly), nucleated RBCs and basophilic stippling. Hypersegmented neutrophils seen in 90% cases ranged from 2% to 10%.

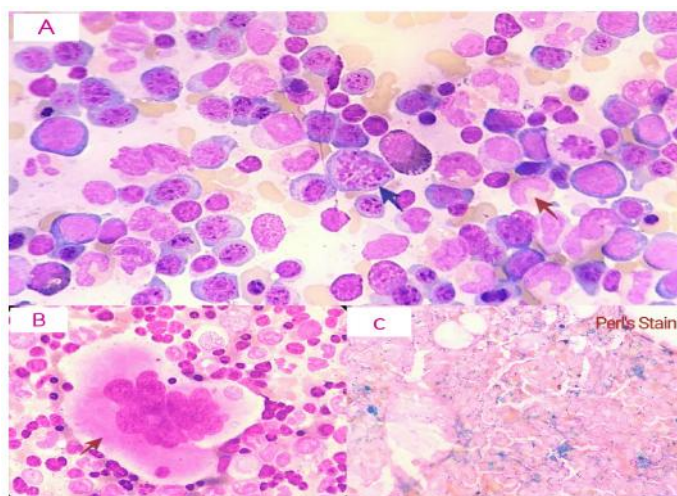


Figure:3; 3A; Bone marrow aspirate with megaloblast with sieve like chromatin (blue arrow) & giant stab forms (red arrow).

3B; Bone marrow aspirate with hyperpolyploid form megakaryocytes

3C; Perls stain with increased iron store.

Bone marrow aspirate are cellular and particulate in 82% cases while diluted in rest, where bone marrow biopsy performed and imprint and histology findings noted. Megaloblast with sieve like chromatin is most common findings (Figure: 3A). Myeloid series show giant metamyelocytes,stab forms and prominence of

eosinophils in 25% cases,Megakaryocytes are enlarged and hyperpolyploid (Figure 3B). Perls stain for iron store increased in 60% cases (Figure:3C). Serum Vitamin B12 and folic acid estimation done in 55 cases, forty cases show deficiency of Serum VitaminB12 and folic acid deficiency in six cases.

Discussion

Megaloblastic anemia is distinctive type of anemia sharing common features of defect in DNA synthesis that affects rapidly dividing cells in bone marrow leading to macrocytosis and variable cytopenias. The prevalence of megaloblastic anemia due to nutritional deficiency, expected to be more common in vegetarian than non-vegetarian. Refsum et al [4] reported that 75% of selected urban population from India showed metabolic evidence of hyperhomocysteinemia and increase in serum methylmalonic acid, consistent with cobalamin deficiency which attributed to vegetarian diet.

Age of presentation was common among second and third decade with predominance in males. Other study megaloblastic anemia reported to occur older age groups with same male predominance [5,6]. Present study revealed most common complaint was generalised weakness, fever, shortness of breath and anorexia and common clinical finding was pallor, hyperpigmentation and jaundice.

Hyperpigmentation seen 37.5% cases, commonly over dorsum of hands and feet. Sen, *et al.* study show 79% skin changes [7]. Hyperpigmentation results from decreased glutathione which induces tyrosinase activity, which in turn mobilizes melanocytes to keratinocytes, causing increased melanin synthesis [8].

It is generally believed that as severity of anaemia increases, thrombocytopenia develops followed by leucopenia and pancytopenia. Pancytopenia seen 52.5% cases, similar findings (40-70%) have been reported by other author [9,10]. The mean hemoglobin in present study was 6.06g/dl which was close to Unikrishnan V et al where the mean Hb was 5.6g/dl. Macrocytosis reflected by Mean corpuscular Haemoglobin (MCV) is an early diagnostic indicator of Vitamin B12 deficiency, regardless of hemoglobin concentration. In our study >95 fl consider to label macrocytosis, however mean MCV was 101fl in megaloblastic anemia cases. Other studies consider MCV >95 fl & 100fl to label RBCs as macrocytes [11, 12, 13].

Peripheral smear with predominantly macrocytic anemia with hypersegmented neutrophils seen in 74% cases which was similar to study done by Khanduri et al [14].

Macrovalocytes, basophilic stippling with high MCV are strong marker of underlying megaloblastic anemia.

Bone marrow aspirate mostly cellular showed megaloblasts with varying degree of dyserythropoiesis with few giant forms of metamyelocytes and stab forms in myeloid series. Similar findings also found by Mussarat et al [15]. Assessment of the bone marrow iron stores by Perls Prussian blue reaction show increased iron deposit in 60% cases, Mussarat et al [15] found 57.30% increased iron deposit in patients of megaloblastic anemia.

All our cases showed good response to treatment with Vitamin B12 and folic acid supplements following the report based on bone marrow aspiration cytology. In spite of severe thrombocytopenia there was no fatal bleeding episode like intracranial haemorrhages.

Conclusion

To conclude that prevalence of megaloblastic anemia increasing and spectrum of presentation of megaloblastic anemia is wide, from asymptomatic to life threatening bicytopenia, pancytopenia or neurological deficit. This study reinforces the fact that generalised weakness, hyperpigmentation, fever and mild splenomegaly are helpful clinical sign and symptoms and with haematological parameters like MCV, peripheral smear picture are early reliable way of evaluating megaloblastic anemia. Clinicians especially primary health care physician should aware of this and suspect early to avoid many late consequences at primary level that helps to avoid unnecessary investigations, thus proving a cost effective management especially in our country. The present study also conclude that megaloblastic anemia is commonest cause of pancytopenia & painful biopsy reserved only for diluted and dry aspirate.

References

1. Ehrlich P, Uber regeneration and degeneration der rothen Blutschreiben bei Anaemien, Berliner klinische Wochenschrift.1880; 117, 405.
2. Braunwald E et al. Harrison's principles of Internal Medicine. 19th ed. New York, McGraw-Hill, 2015.
3. Bain BJ. (2006) Morphology of blood cells. In: Blood Cells.4th ed. Blackwell Publishing: 70
4. Refsum H, Yajnik CS, Gadkari M, et al (2001) Hyperhomocysteinemia and elevated methyl malonic acid indicate a high prevalence of cobalamin deficiency in Asian Indian. Am J Clin Nutr 74:233-241.

- 5.Charke K et al.Vitamin B12 and Folic acid deficiency in late life age 2004; 33:34-41.
- 6.Baik,H W Russell RM.Vitamin b12 deficiency in elderly-*Annu RevNutr*1999;19:357-77
- 7.Sen, *et al.*: B12 Deficiency with dermatologic manifestations- *ijd*;2017, IP: 111.93.13.4]
- 8]Lee SH, Lee WS, Whang KC, Lee SJ, Chung JB.Hyperpigmentation in megaloblastic anemia. *Int J Dermatol.* 1988; 27(8):571-5.
- 9.Hirachands et al - Clinico hematological profile in Megaloblastic anemia -*Journal of Institute of Medicine*, 2014; 36:1
- 10.Hamid GA et al- Pattern of Pancytopenia in Yemen.*Turk J Hematol* 2008; 25:71-74.
- 11.Unnikrishnan V, Dutta TK, Badhe BA, Bobby Z, Panigrahi AK. Clinico – aetiologic profile of macrocytic anemias with special reference to megaloblastic anemia. *Indian J. Hematol. Blood Transfus.* 2008; 24(4):155-65.
12. Mahmoud MY, Lugon M, Anderson CC. Unexplained Macrocytosis in Elderly Patients. *Age and ageing.* 1996; 25(4):310-2.
13. Savage DG, Ogundipe A, Allen RH, Stabler SP, Lindenbaum J. Etiology and diagnostic evaluation of macrocytosis. *Am J Med Sci.* 2000; 319(6):343-52.
14. Khanduri U,Sharma A, Joshi A Occult cobalamin and folate deficiency in Indians. *Natl Med J India.* 2005; 18:182–3.
- 15.Mussarrat N, Fazal-e-R, Mohammad TK (2009) Clinical and hematological features of megaloblastic anemia alone or in combination with iron deficiency anemia- an analysis of 349 patients. *J Med Sci (Peshawar print)*17(2):81-84.

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