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Original Research Article

Megaloblastic Anaemia: A Clinical Spectrum and Haematological Profile

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Abstract

Aims and Objectives: 1. To know different parameters leading to megaloblastic anaemia and its diagnostic approach. 2. To know the incedence with reference to age and sex. *Materials and Methods:* This was a institute based retrospective study. The study period was for 1 year. In total 25 cases were scrutinised. *Results:* In total 25 children with megaloblastic anemia in period of one year were studied. The patients from age group from 6 months to 12 years were included in the study. All patients had diagnosed megaloblastic anaemia. *Conclusion:* Megaloblastic anemia is one of the common causes of undiagnosed anemia in the above mentioned age group, mostly due to faulty weaninf and food habits. It has a treatment easily available, simple and easily affordable. But if not treated, it causes morbidity due to anaemia as well as due to neurological manifestations.

Keywords: Megaloblastic Anemia; CNS Involvement; Pancytopenia.

Introduction

Megaloblastic anemias are a group of disorders featured by release of defective erythrocytes in circulation due failure of normal process of erythrocyte development in bone marrow. The cause is usually deficiency of either B12 or folic acid. Also megaloblastic anemia may occur due to inherited or acquired abnormalities affecting the metabolism of the vitamins.

The defective DNA synthesis may not be related to the deficiencies like B12 or folic acid. Macrocytosis may be found in adults who have a routine complete blood count. In up to 60% of cases, macrocytosis is not associated with anemia. But an isolated macrocytosis should always be investigated. Early deficiency of B12 or folic acid presents as macrocytosis without anaemia. This is beacause of macrocytosis preceding the development of anemia. The average Indian vegetarian diet is almost always deficient in B12 and folic acid [1].

The faulty weaning practices in infants after 6 months of age leads to nutritional anaemis. Early weaning starting at 4 months go age can lead to malnutrition, developmental delay and affects normal neurological and cognitive development in infants.

Material and Methods

An institute based retrospective analysis of case records of all patients admitted and diagnosed as megaloblastic anemia was done. The patients with

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a diagnosed aplastic anaemia were not included in the study. The study period is for 1-year and all the patients admitted from the age group of 6 months to 12 years were included in the study. The data were collected, and multivariate analysis was done to determine the correlation between symptoms, signs, and hematological investigations.

Results

25 children with megaloblastic anemia in the above said period were studied. There was a bimodal distribution with 66.6% of patients being between 6 months and 3 years and 33% being in the age group of 10-12 years. Megaloblastic anemia was found to be more in female patients. Female to male ratio being 1.6:1. The most common clinical features presenting in almost all cases were pallor, fatigue, and CNS involvement. The frequency of symptoms and signs are as listed in [Table 1] and [Table 2] respectively. Severe anaemia is found with hemoglobin <7g% in15 patients(60%). Macrocytosis was found in 84.2% of peripheral smears (Figure 1) and bone marrow confirmed megaloblastic anemia in 93.6%. Vitamin B_{12} assay that was done in eight patients showed low levels (<100 pg/mL), where B12 levels less than 200pg/ml is considered as deficiency. Normal rnge of B12 is 200-900pg/ml varying according age and gender. Anaemia was resolved in total 10 patients who followed up i.e. 40% showed resolution. The mean time taken for resolution of anemia was 52. 1 days considering a good compliance with treatment. The neurological signs were also resolved in 7 patients after the treatment.

Table 1:

Sr. No	Symptoms	Percentages
1.	Pallor	100
2.	Fatigue	80
3.	Neurological	4.5
4.	Jaundice	3.9
5.	Bleeding manifestation	1.8
6.	Recurrent fever	2.3
7.	Weight loss	1.5

Table 2:

Sr. No.	Signs	Percentages
1.	Wasting/failure to thrive	85
2.	Pallor	100
3.	Skin hyperpigmentation	98
4.	Hepatomegaly	11.4
5.	Neurological signs	4.5
6.	Splenomegaly	2.7

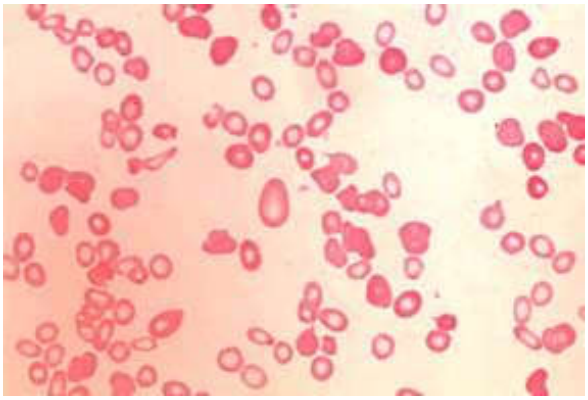

Fig. 1: Smear showing macrocytes with some normocytes

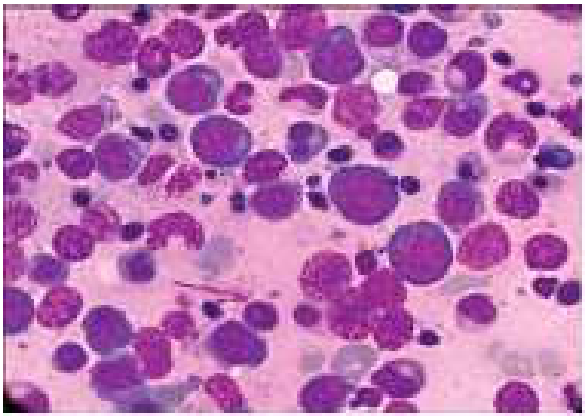

Fig. 2:

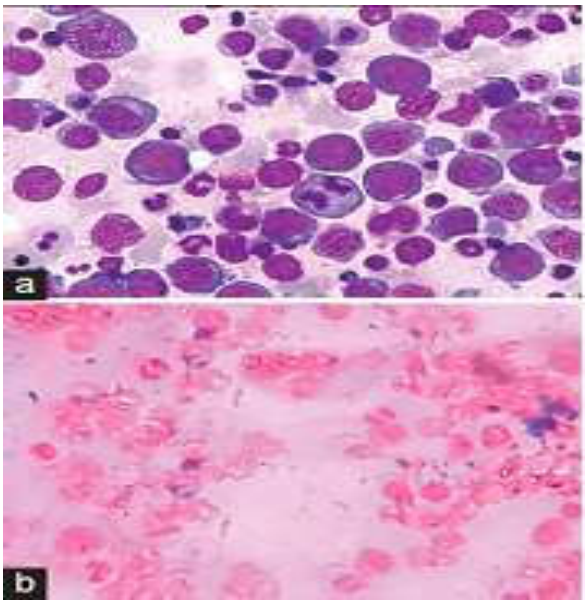

Fig. 3a and 3 b:

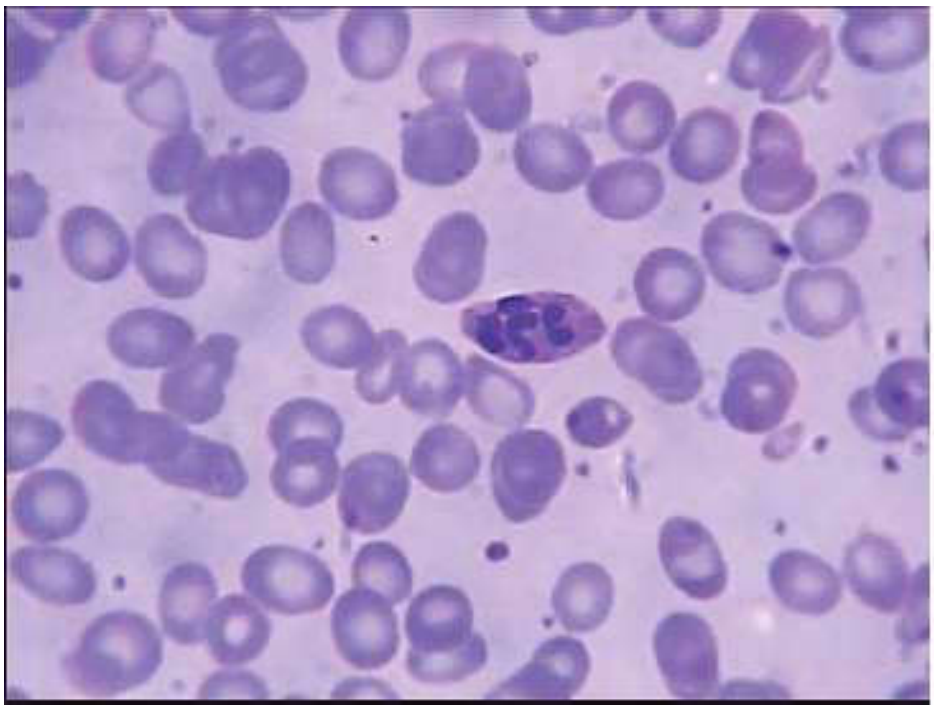

Fig. 4: Giant metamyelocytes.

Discussion

Megaloblastic anemia is a myeloid metaplasia with abnormal immature blood cells in the spleen and liver, associated with myelofibrosis. But the actual bone marroe studies shows a disorder limited to erythroid cell line, erythroid hyperplasia being a main feature.Rarely, the megaloblastic features in bone marrow studies can be misinterprited with leukaemias due to the immature appearance of megaloblastic nuclei and occasionally intense myeloid proliferation in the marrow. The morphologic hallmark is nuclear-cytoplasmic dissociation, which is mostly appreciated in precursor cells in the bone marrow aspirate.

There are different causes for the deficiency of both Vitamin B_{12} and folate including the

- Parasitic infections like Diphyllobothrium latum,
- Alcohol intake
- Vegetarian diet,
- Drugs like oral contraceptives and anticonvulsants.
- In cases with reduced or absence of hydrochloric acis secretion and loss of pepsin secretion,

Vitamin B_{12} is not directly secreted in intestines from proteins in food. While patients with gastrectomy and pernicious anemia, intrinsic factor is not present for transporting in the ileum. The only dietary sources of Vitamin B_{12} are non vegeterian foods such as kidney, liver, heart, muscle meats, fish, eggs, cheese and milk. Folic acid is present in vegeterian foods but B_{12} is eficient in all vegeterian food. Vegetarians are more prone for megaloblastic anemia as compared to that of nonvegetarians.

Vitamin B_{12} is synthesized in the human large bowel by microorganisms. Still humans are deficient and completely depend on dietary sources because it is not absorbed at the site of synthesis.

The peripheral smears in megaloblastic anaemia patients shows:

- Nutrophil granulocytes may show multisegmentes nuclei. The explanation for the multisegmented nuclei is the decreased production and a compensatory prolonged lifespan for circulating neutrophils, which increase numbers of nuclear segments with age. Neutrophils with characteristic hypersegmented nuclei appear in the blood early in the course, but they do not arise directly from the giant metamyelocytes Figure 4.
- Aniocytosis (increased variation in RBC size) and poikilocytosis (abnormally shaped RBCs).

- Macrocytes (larger than normal RBCs) are present.
- Ovalocytes (oval-shaped RBCs) are present.
- Howell- Jolly bodies (chromosomal remnant) also present.

Megaloblastic nuclei are larger than normoblastic nuclei. The chromatin appears abnormally dispersed. The retarded condensation is cause for dispered chromatin. Figure (2). Giant band forms and metamyelocytes Figure 3a and 3b with unusually large and often mishappen nuclei along with mitotic activity are typically seen. Perl's stain, which is used for detection of iron, was also done. And it was positive for iron Figure 3b.

Bone marrow aspiration smear showing megaloblasts with uncondensed chromatin and royal blue cytoplasm. Macrocytosis associated with a megaloblastic marrow is usually accompanied by anemia due to fault in normal process of erythropoiesis. The bone marrow is hypercellular, showing evidence of abnormal proliferation and maturation of multiple myeloid cell lines. It affects the erythroid series in early changes.

(a) bone marrow aspiration smears showing megaloblasts, mitotic figures metamyelocytes. (b) Smears showing positive for Perl's stain

The common feature of all megaloblastic anemias is a defect in DNA synthesis that affects rapidly dividing cells in the bone marrow and other tissues. Many patients with out any clinical manifestations are detected through the finding of a raised mean corpuscular volume on a routine blood count. The routine blood counts shows a pancytopenia with derranged blood indices.

Coming to the symptoms of megaloblastic anaemia, annorexia certainly a prominent feature associated with weight loss and generalised weakness. Other symptoms include glossitis, angular cheilosis, low grade fever in the more severely anemic patients, raised direct billirubin i.e. unconjugated jaundice and melanin skin hyperpigmentation is is a reversible skin change, diarrhea or constipation. Patients also present with headache and giddiness with black out episodes.

Severe thrombocytopenia, occasionly, can lead to bruising. The patients with anaemia associated with low leucocyte count are more prone for infections. Most commonly affecting the respiratory or urinary tracts.

The progression of megaloblastic anaemia further manifests with leucopenia and thrombocytopenia. These can be severe in advanced cases but are not common when anemia is mild. Some studies conclude that 40% of normal Indian subjects with normal hemograms were cobalamin deficient [2]. This is due to the unbalanced diet in Indian society not including sufficient sources of B12 in daily diet. Also due to faulty cooking methods.

The onset of megaloblastic anemia is usually insidious with typical anemic symptoms of lethargy, weakness, and varied degree of pallor. Dyspeptic symptoms like diarhea, constipation, indigestion or nausea with vomitting are common. Glossitis with a beefy red tongue or more commonly a smooth pale tongue is characteristic feature for megaloblastic anaemia. Loss of weight and loss of appetite are common complaints. The infants and children with megaloblastic anaemia present with loss of appetite, failure to thrive, irritability, severe pallor, icterus and easy fatigaubility. The infants who are breast fed with mothr strictly taking vegetarian diet are more prone for developing megaloblastic anaemia as various studies suggests.

There is decreased secretion of intrinsic factor and hydrochloric acid undering cause being atrophy of the gastric parietal cells. Bouts of diarrhea may be the result of epithelial changes in the gastrointestinal tract. In antenatal period supplementing the folic acid aloneis also harmful. The folic acid always to be given along with cobalamine. Supplementing folate alone when there is occult cobalamin deficiency, it may precipitate neurological complications [3].

The megaloblastic anaemia is common in children who are breast fed for longer time. The infants in whom weaning has not been initiated at proper time and not with proper diet are more prone for cobalamine and folate deficiency. Neurologic disturbances occur only in cobalamin deficiency, not in folic acid deficiency. The neurological signs like muscle weakness, dementia, peripheral neuropathy are the most serious and dangerous clinical signs because neurological damage may be permanent if the deficiency is not treated promptly. Megaloblastic anaemia, as the studies shows, is a severe form of anaemia as the neurological damage is usually permanent if left untreated.

Table 3:

Sr. No	Investigations	Mean
1.	Hemoglobin	5.8+/-2.5
2.	MCV	96+/-10.5
3.	MCH	34.04+/-4.5
4.	Corrected reticulocyte counts	1.5+/-2.3
5.	Leucocyte counts	5,600+/-2800
6.	Neutrophil counts	1190+/-900
7.	Platelet counts	90,000+/- 40,000

Conclusion

To conclude megaloblastic anemia is one of the common causes of undiagnosed anemia. The treatment is simple and easily affordable. If not treated, it can cause morbidity both because of anemia and attendant neurological involvement. The ost common manifestations in megaloblastic anemia include triad of pallor, hyperpigmented skin, and neurological involvement. Neutropenia is a common related finding in megaloblastic anemia. It can also be accompanying with leucopenia in a small number of patients. A correct diagnosis and prompt therapy is important in managing the megaloblastic anaemia. It gives a complete and a momentous recovery.

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