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Megaloblastic anaemia in infancy in a tertiary care hospital: Case series

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Abstract

Megaloblastic anaemia causes macrocytic anaemia from ineffective red blood cell production, and intra medullary hemolysis. Megaloblastic anaemia presents with multisystematic involvement and can be of diagnostic dilemma. It is cause predominantly due to deficiency of cobalamin (vitamin B12) and folate (vitamin B9) deficiency or both. It is seen in infants with faulty weaning practices and low vitamin B12 stores in mothers and in neonates born to vegan mothers. Megaloblastic anaemia is one of the reversible causes of neurological manifestation if diagnosed and treated early in infancy. We report a case series of 10 patients who had unusual clinical manifestations and were subsequently diagnosed as megaloblastic anemia. Infants were started on injectable vitamin B12 and we observed a significant clinical improvement in all the patients.

Keywords: Megaloblastic Anemia, Infancy, Vitamin B12 , Folic Acid , Neuroregression

Introduction

Megaloblastic anaemia is a macrocytic hypochromic anaemia. It is caused due to deficiency of cobalamin (vitamin B12), folate (vitamin B9) both. Vitamin B12 and folate are water soluble vitamins which play a major role in effective erythropoiesis. Megaloblastic anaemia in infancy is rare. It is related to maternal deficiency of vitamin B12 or folate, prolonged exclusive breastfeeding, which is commonly observed in developing countries. Micronutrient deficiencies, inborn errors of metabolism, malabsorption syndrome, and autoimmune disorders, or some other rare causes of megaloblastic anaemia in infancy. (1) The infants born to vegetarian mothers with low vitamin B12 stores are more prone to develop megaloblastic anaemia in infancy.(2) Megaloblastic anaemia presents with varied clinical features and multi systemic involvement like pallor, diarrhea, failure, to thrive, hepatomegaly, glossitis, cheilosis, hyper pigmentation of skin and

knuckles, irritability, lethargy, easy, fatigue, ability, tremors, hypotonia, developmental, delay, and regression of milestones.(8) It is characterized by low hemoglobin levels, elevated mean corpuscular volume (MCV >100 fl) , low retic count, low serum vitamin B12 levels (< 200 pg/ml) or low folic acid levels (< 3 ng/ml). The recommended daily allowance is 0.4 µg/day till 6 months of age in 0.5 µg/per day from 6 to 12 months of age. Megaloblastic anaemia is one of the reversible causes of neurological manifestations if diagnosed and treated early. We report a case series of infants with varied manifestations of megaloblastic anaemia in a tertiary care hospital.

Materials and methods

Study design and setting: Single center observational study in tertiary care hospital

Study methodology: This study was undertaken in our tertiary care hospital over a period of 18 months from January 2021 to June 2022.

Inclusion Criteria :

1) Children less than 1 year of age presenting with clinical features of Megaloblastic anemia.

2) Serum B12 level less than 200 pg/ml

Or

3) Complete blood count with MCV > 97 femtolitre.

Exclusion Criteria: Children more than 1 year age.

Case Presentations

Case 1 - 9 month old male, hospitalized with gastroenteritis and acute febrile illness. He was exclusively breastfed till 7 months of age. Anthropometry revealed weight for height <3rd centile falling into severe acute malnutrition. On clinical examination we had severe Parlor with hepatomegaly. Investigations revealed macrocytes and low vitamin B12 levels. Bone marrow aspiration showed megaloblastic changes.

Case 2 - 10 months old male admitted with fever and regression of milestones. He had history of delayed weaning and predominantly consuming cows milk. On examination he was lethargic, pallor and knucke pigmentation was present. His developmental age was 5 months and was moderately acute malnourished. Lab investigations revealed bicytopenia and low vitamin B12 levels.

Case 3 - 8-month-old female infant born of 3rd°, consanguineous marriage, full term home delivery, exclusively breastfed till date presented with fever for one month and developmental delay. Anthropometric measurements were below third centile. She had hepatomegaly, lethargy and pallor. Investigations were suggestive of macrocytic anaemia and low B12 levels.

Case 4 - 11 month old male patient presented to hospital with tremors and regression of milestones. He was a full term, normally delivered born of non-consanguineous marriage. She was exclusively breastfed till date and anthropometrically was severely acute malnourished. On examination he had hypotonia, hyperpigmentation of skin, sparse hair and pallor. Investigations revealed pancytopenia and low vitamin B12 level.

Case 5 - 9 months old male child presented with failure to thrive and severe pallor. Dietary history revealed consumption of only cow's milk and he was calling below third percentile anthropometrically. On examination he had hepatomegaly, knuckle pigmentation and haemic murmur. Investigations were suggestive of pancytopenia and bone marrow showed megaloblastic changes.

Case 6 - 4 months old male child presented with excessive irritability. He was exclusively breastfed , with

normal development. He was moderately acute malnourished and on examination had severe pallor, irritability, hepatomegaly and sparse hair. Peripheral blood smear showed macrocytes, Howell jolly bodies, basophilic stippling. Bone marrow was suggestive of megaloblastic anaemia.

Case 7 - 6-month-old female infant was admitted with complaints of not gaining weight adequately. She was the full term normally delivered a child and was exclusively breastfeed till date. There was a regression of milestones with developmental age of three months. On examination hypotonia, lethargy and pallor were present. Investigations were suggestive of dimorphic anemia and low vitamin B12 levels.

Case 8 - 9 months old female infant, born full term product of 3rd degree consanguineous marriage and was exclusively breastfed till 8 months of age, presented with complaints of fever with respiratory distress and failure to thrive. Her weight for height was <3rd centile, suggestive of severe acute malnutrition and on examination she had right-sided crepitation, hepatosplenomegaly and pallor. Investigations showed dimorphic anaemia with low vitamin B12 levels. Bone marrow was suggestive of megaloblastic changes.

Case 9 - 11 months old male infant born full term by caesarean delivery with birth weight of 3 kgs presented with complaints of acute gastroenteritis. He was exclusively breastfed with improper weaning practices. He had regression of developmental milestones with current developmental age of five months. Anthropometry was suggestive of moderate acute malnutrition and on examination child had hypotonia, blackish knuckle pigmentation, lethargy and hepatomegaly. Investigation showed macro-ovalocytes and low vitamin B12 levels.

Case 10 - 10 months old male infant born full term by cesarean section with birth weight of 2.5 kgs. He was started on cow milk since two months of age, currently presented with seizures and developmental delay. On examination he was severely acute malnourished with pallor and hepatomegaly. Investigations were suggestive of bicytopenia and low vitamin B12 levels.

Fig 1: Knuckle pigmentation of fingers.

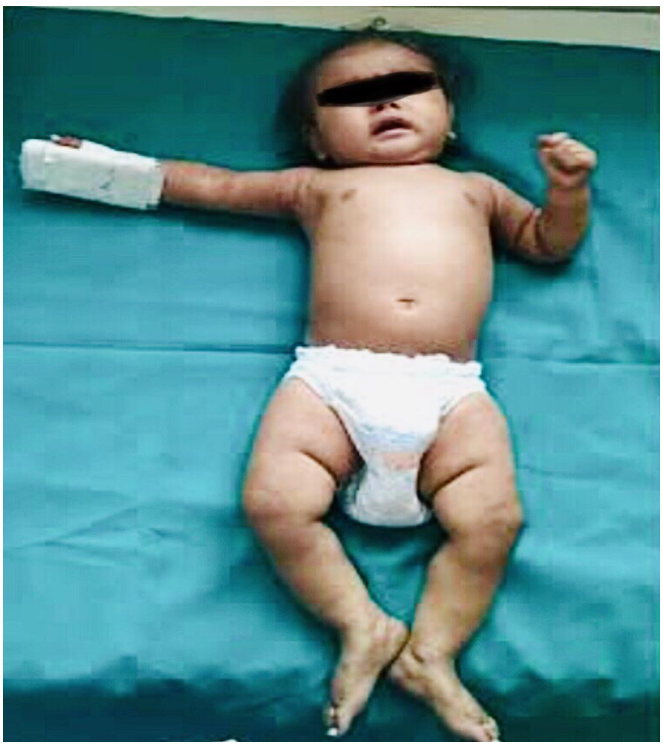

Fig 2: Infantile tremor syndrome

Table 1: Laboratory findings of case reports

Case	HB (g%)	TLC (cumm)	MCV (fl)	MCH (pg)	MCHC (g/dL)	Platelet count (cumm)	Reticulocyte count (%)	PBS	Serum Vit B12 (pg/ml)	Bone Marrow
1	9	12200	103.9	22.9	32.7	1.1 L	0.8	Anisocytosis Schistocytes	148	Myeloid hyperplasia with toxic granules
2	8.2	7840	102.7	24.2	33.5	78,000	0.5	Anisocytosis Macrocytes	138	-
3	8.7	7200	106.1	23.4	34	1.65 L	0.6	Anispoikilocytosis Tear drop cells	136	-
4	7.4	3150	104.2	21.2	31.1	40,000	0.4	Dimorphic anaemia	140	-
5	2.7	5470	105	22.3	32.1	35,000	0.8	Anisocytosis Macro-ovalocytes Tear drop cells	130	Megaloblastic anemia
6	7.4	6000	106.8	21.3	35.8	45,000	0.7	Anisopoikilocytosis Macrocytes, Howell jolly bodies Basophil stippling	132	Megaloblastic anemia
7	6.8	7840	102.7	22.4	36.7	78,000	0.4	Poikilocytosis Dimorphic anemia	144	-
8	5.17	6370	101.8	23.2	43.1	60,000	0.93	Anispoikilocytosis Macrocytes, Tear drop cells pencil cells	142	Hypercellular bone marrow Megaloblastic erythropoiesis
9	10.72	2850	108.8	22.7	29	1.45 L	0.8	Anisocytosis Macrocytes	138	-
10	7.2	7800	102.8	24.8	37.2	23,000	0.6	Bi-cytopenia Tear drop cells	136	-

(HB - hemoglobin , MCV - mean corpuscular volume , MCH - mean corpuscular hemoglobin, MCHC - mean corpuscular hemoglobin concentration, PBS - Peripheral blood smear) On the basis of the above data mentioned in the 10 cases, low serum vitamin B12 levels and clinical manifestations sustain the diagnosis of

megaloblastic anemia. Injectable, intramuscular vitamin B-12 supplementation was started daily for 1 week followed by weekly for next 3 months in all infants.

Results

This case series included 10 patients out of which 7 were boys and 3 were girls. Presenting complaints of majority of the infants were failure to thrive with severe acute malnutrition (80%). 2 infants also presented with gastrointestinal symptoms like vomiting and loose motions. Neurological symptoms like convulsions and regression of milestones were seen in 7 infants (70%) and 1 patient had infantile tremor syndrome. On investigations, 4 patients had pancytopenia and 8 patients had high MCV value. All infants had low vitamin b12 levels and were subsequently treated with injectable vitamin b12 daily, followed by alternate day to see significant results.

Discussion

Vitamin B12 deficiency has multi system involvement, presenting features being pallor, failure to thrive, gastrointestinal symptoms and neurological manifestations like hypotonia, developmental regression of milestones, seizures, infantile tremor syndrome and irritability. On investigations complete blood count revealed a low value of haemoglobin, increased MCV (>100 fL), normal mean corpuscular haemoglobin concentration (MCHC), thrombocytopenia, and leucopenia. Peripheral blood smear showed macrocytosis, severe anisocytosis, poikilocytosis, hyper segmented neutrophils, Howell Jolly bodies and tear drop cells. Reticulocyte count was low with significant low levels of serum vitamin B12 was observed in all subjects. Bone marrow smear revealed any erythroid hyperplasia, megaloblastosis and hyper segmented neutrophil. In India mainly in rural areas where population tends to be vegetarian, Vitamin B12 deficiency during pregnancy is very common. Use of complementary Vitamin B12 rich food in infancy are rarely consumed in developing countries.The average daily requirement for an infant is 0.5 to 0.6 mcg/day. Vitamin B12 deficiency can cause cerebral atrophy, thinning of corpus callosum which leads developmental delay and regression of milestones. Our study results co-relate with other Indian studies carried out by Jadhav M et. al [2]. and Singh V et. al. [3], which conclude that Vitamin B12 deficiency is commonly observed in infants born to vegan mothers and thus an importance cause of anaemia and reversible developmental delay.

Conclusion

Megaloblastic anemia is a rarely diagnosed anemia in infancy. Isolated vitamin B12 deficiency due to improper weaning and low maternal B12 stores caused due to lack of animal source of protein in diet can be the major predisposing factors for megaloblastic anemia in infancy. In young infants with rapid brain growth, deficiency of vitamin B12 supplementation leads to irreversible brain damage and cerebral atrophy. In this case series we highlight the varied clinical presentations of megaloblastic anemia, and the importance of vitamin B12 supplementation to lactating mothers and infants. Hence early diagnosis in patients with anemia and managment with injectable vitamin B12 can prevent neurological deficits and irreversible brain damage.

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