Case Report

Advances in Neurology and Neuroscience

Case Series on Vitamin B12 Deficiency...Though Rare but a Treatable Disease

Ananya Das[1] and Kalpana Datta[2]*

[1]*Post graduate trainee, Indian Administrative Service, India*

[2]*Professor, Medical college, Kolkata, India*

***Corresponding author**
Kalpana Datta, Post graduate trainee, Indian Administrative Service, India, E-mail: drkalpanadatta@gmail.com

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Introduction

Megaloblastic anemia due to vitamin B12 deficiency is an uncommon problem in childhood that is most frequently associated with decreased ingestion or impaired absorption or utilization of B12 [1,2]. Nutritional B12 deficiency in childhood is rare. Most cases are due to maternal insufficiency, resulting from deficient stores and intake generally among exclusively breastfed infants [3]. B12 deficiency in children often presents with nonspecific manifestations [4,5]. We present two cases of vitamin B12 deficiency in breast fed infants presenting as pancytopenia and gross developmental delay respectively.

CASE 1

A 8-month-old girl presented to the emergency department with severe paleness and lethargy. She had been taking iron medication irregularly for a month because of iron deficiency anemia. On physical examination, the patient was lethargic. Mucous membranes, conjunctivae, palms and soles were severely pale. Tachycardia was present. There was no peripheral lymph nodes, icterus, cyanosis, oedema or clubbing. Apex was normal in position with a ejection systolic murmur in left parasternal region. There was no organomegaly. Other systems were within normal limits.

Her laboratory investigations revealed pancytopenia with Hb-4.6gm/dl,TLC- 1,100/cmm, N17 L_{80},Platelet- 28,000/cmm, RBC-1.1 lakhs/cmm. MCV- 113.6 fl, MCH- 40 pg, MCHC- 35.2 gm/dl, RDW- 17,Reticulocyte count- 2.5% .Her peripheral blood smear showed anisocytosis, hypochromia with occasional macrocytes and spherocytes. Direct coomb's test was negative, G-6 PD was normal, Serum Ferritin: 110ng/ml, HPLC of both parents were normal. TORCH screen was negative. Other tests including renal profile, serum electrolytes and thyroid function tests were within normal limits. Her chest xray and USG whole abdomen was unremarkable. Her routine urine and stool examination was within normal limits .Bone-marrow aspiration study showed hypercellular marrows with increased erythroid precursors were showing megaloblastic maturation. Granulocytes were decreased in number and many giant metamyelocytes and band forms were seen. The megakaryocytes were normal in number. Serum Vitamin B_{12} level was 105 pg/ml (Normal: 211-911 pg/ml). Serum folate level was 12ng/ml (normal-3-20ng/ml).

The levels of serum iron, iron-binding capacity and B12 level in the mother were 27mg /dl (50–120), 390 mg /dl (110–330) and 111 pg /ml (180–914), respectively. Her mother was diagnosed as having a combined iron and B12 deficiency. As a result of these findings, vitamin B12 deficiency due to nutritional inadequacy was diagnosed and our patient was treated with two units of packed cell transfusion. Following this Inj. Methylcobalamin 1mg given intramuscularly once daily for 1 week along with daily folic acid supplementation. After 1 week of treatment her complete haemogram showed:-Hb-9.7g/dl, TLC- 5,400/cmm, N52 L46 Platelet- 1.5 lakhs/cmm, MCV-88fl, MCH- 28.5pg, MCHC- 33.2gm/dl. She was discharged with Oral Tab. Methylcobalamin 1mg to be taken every alternate day for 1 week, then weekly for 1 month and then monthly for 6 months along with tab. Folic acid.During the recovery period iron therapy was initiated.

CASE 2

A 9-month old female child was referred to our hospital with respiratory distress due to viral pneumonia for last one day. Her past history revealed that she was born by normal vaginal delivery at term with her birth weight being 2.7kg. She was on exclusive breast-feeding. Her gross and fine motor development was delayed. She had neck holding at about 5-months of age and is able to roll over since 9months of age and still has bidextrous approach. She has achieved socio adaptive and linguistic developmental milestones as per age. Physical examination revealed that she is alert but apathetic. She was a febrile with mild tachycardia but with severe tachypnea. Pallor was present. She had sparse, fragile hair with hypermelanosis of the fingers and toes. However, her oral mucosa was healthy. Respiratory system examination revealed bilateral rhochi with few crepitations. She had generalised hypotonia with preserved superficial and deep jerks. No other abnormality was noted. Other systems were within normal limit. Laboratory investigations revealed anemia with Hb- 8gm/dl, TLC- 3,400/cmm, N_{43} L_{48}, Platelet- 2.5lakh/cmm, RBC- 3.1 lakhs/cmm. Chest xray showed patchy infiltrates. Antibiotics were started and nebulisation was given. Further investigations showed MCV- 110.6 fl, MCH-38pg, MCHC- 30gm/dl, RDW- 17, Reticulocyte count- 1.5% .Her peripheral blood smear showed anisocytosis, hypochromia with occasional hypersegmented neutrophils. Direct coomb's test was negative, G-6 PD was normal. Serum Ferritin: 110ng/ml, HPLC of both parents were normal. TORCH screen was negative. Other tests including renal profile, serum electrolytes and thyroid function tests were within normal limits. Bone-marrow aspiration study showed

hypercellular marrow with increased erythroid precursors were showing megaloblastic maturation. Granulocytes were decreased in number and many giant metamyelocytes and band forms were seen. The megakaryocytes were normal in number. Serum Vitamin B12 level was 60pg/ml (Normal: 211-911 pg/ml). Serum folate level was 22ng/ml (normal-3-20ng/ml).MRI brain revealed bilateral frontoparietal atrophy.

The levels of serum iron, iron-binding capacity and B12 level in the mother were 98mg /dl (50–120), 220mg /dl (110–330) and 104 pg /ml (180–914), respectively. Her mother was diagnosed as having a vitaminB12 deficiency. As a result of these findings, vitamin B12 deficiency due to nutritional inadequacy was diagnosed and our patient was treated with Inj. Methylcobalamin 1mg given intramuscularly once daily for 1 week .After 1 week of treatment her complete haemogram showed:-Hb- 9.7g/dl, TLC- 5,400/cmm, N_{52} L_{46} Platelet- 1.5 lakhs/cmm,MCV- 88fl, MCH- 28.5pg, MCHC-33.2gm/dl. She was discharged with Oral Tab. Methylcobalamin 1mg to be taken every alternate day for 1 week, then weekly for 1 month and then monthly for 6 months.

Discussion

Nutritional B12 deficiency is treatable disorder of nutritional inadequacy [6].The first report of nutritional vitamin B12 deficiency in early life was published in 1962, when Jadhav et al. described a syndrome of apathy, developmental regression, involuntary movements, and alterations in skin pigmentation in an infant [7]. Exclusively breast fed infants of malnourished or vegan mothers, belonging to poor socioeconomic strata, as well as infants of mothers with undiagnosed or untreated pernicious anemia, are at an increased risk for megaloblastic anemia [8,9]. The average daily requirement for an infant is 0.5-0.6 µg/day. Vitamin B12 is freed from binding proteins in food through the action of pepsin in the stomach and binds to salivary proteins called cobalophilins, or R-binders. In the duodenum, bound vitamin B12 is released by the action of pancreatic proteases. The released vitamin B12 binds to intrinsic factor produced by gastric parietal cells and is transported to the distal ileum. Within ileal cells, vitamin B12 associates with a major carrier protein, transcobalamin II, and is secreted into the plasma. Transcobalamin II delivers vitamin B12 to the liver and other cells of the body, including rapidly proliferating cells in the bone marrow and the gastrointestinal tract. In the absence of intrinsic factor, cobalamin is absorbed only very ineffi ciently by passivediffusion [10] .Megaloblastic anemia due to cobalamin or folate defi ciency is due to ineffective erythropoiesis. Vitamin B12 is necessary for DNA synthesis and its defi ciency prevents cell division in the marrow. Due to deficiency of folate or vitamin B12, red blood cells become large with nuclear or cytoplasmic asynchrony, a characteristic of all megaloblastic anemias. Non specifi c manifestations of megaloblastic anemia include weakness, fatigue, failure to thrive and irritability. Other features seen are pallor, glossitis, vomiting and diarrhea. Neurologic symptoms include hypotonia, developmental delay, seizures, psychiatric changes and subacute combined degeneration of spinal cord [11].

We presented here two cases, one of which, 8months old female, presented with neurodevelopmental delay and the other, 7 months old male, presentated with pancytopenia. Both had hyperpigmentation of fingers and toes and were on exclusive breast feed. In both the cases mothers serum B12 level was low. Since our patients vitamin B12 stores were not sufficient and they had been exclusively breast fed, vitamin B12 deficiency was diagnosed and vitamin B12 supplementation was started which showed a dramatic improvement in both hematological and neurological follow up. If vitamin B12 deficiency in infants is not treated early, it leads to developmental delay, developmental regression and convulsions. Cognitive and developmental delay may persist despite of adequate therapy even though the hematological problems may disappear completely [12].

So evaluation of the B12 status of pregnant and lactating women should be done to prevent newborns and infants from suffering the potentially severe consequences of B12 deficiency. This case shows the importance of vitamin B12 supplementation in pregnancy and lactation especially in case of vegans, whose infants are more likely to be affected than other babies. In a developing country like India, more measures should be taken to diagnose vitamin B12 deficiency and prevent vitaminB12 deficiency in pregnancy by supplementations.

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