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CASE REPORT

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Vitamin B12 deficiency in an infant with neurological and hematological findings: A case report

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Key Clinical Message

It is important for pregnant and breastfeeding women who adhere to a strict vegetarian diet to take appropriate steps to avoid vitamin B12 deficiency in their infants.

Abstract

Vitamin B12 deficiency is rare during infancy. The initial symptoms of this deficiency are subtle and may include irritability, failure to thrive with a decline in growth rate, apathy, anorexia, refusal of solid foods, megaloblastic anemia, and developmental regression. The case presented here involves an 8-month-old male infant who showed neurological symptoms such as decreased activity, increased drowsiness, and reduced interaction with parents, which were ultimately linked to a deficiency of cobalamin (vitamin B12). Early recognition of this condition is critical because it is reversible. Therefore, pregnant and lactating women who follow a strict vegetarian diet should take necessary measures to prevent vitamin B12 deficiency in infants.

KEYWORDS

cobalamin, early childhood, infant, neurological symptoms, vitamin B12

1 | INTRODUCTION

Vitamin B12 (cobalamin) is a group of complex molecule with cobalt-containing corrin ring. It is synthesized only by microorganisms, and it has its principal effect on the hematopoietic and central nervous systems. Vitamin B12 deficiency is uncommon in infancy. The initial manifestations of vitamin B12 deficiency are subtle and include irritability, failure to thrive including decline in growth rate, apathy, anorexia, refusal of solid foods, megaloblastic anemia, and developmental regression. In infants, manifestations of vitamin B12 are usually the result of maternal deficiency, which can be caused by dietary absence or malabsorption syndromes such as pernicious anemia or tropical sprue. This deficiency can occur when babies exclusively breastfed by these mothers.[1] The mechanisms behind the neurological signs of vitamin B12 deficiency include delayed myelination of nerves, alteration in the S-adenosylmethionine: S-adenosyl homocysteine ratio, and accumulation of lactate in the brain.[2] Routine use of complete blood count (CBC) and serum vitamin B12 level is sufficient for appropriate diagnosis. Treatment with

vitamin B12 leads to rapid improvement in symptoms. Long-term deficiency could result in permanent brain damage to the nervous system.[3]

The presented case is an 8-months-old male infant exhibiting neurological symptoms such as decreased activity, increased somnolence, and decreased interactiveness with parents. These symptoms were ultimately attributed to cobalamin deficiency.

2 | CASE PRESENTATION

An 8-month boy, born into a Chaudhary family from western Nepal, was brought to our center with a history of decreased activity and reduced interaction with parents for the past 2 months. The infant's condition was also associated with progressive pallor. According to the mother, the infant sleeps approximately 18–20 h daily. The child had been exclusively breastfed and had recently attempted weaning but refused to take supplementary feedings.

Upon examination, the baby appeared sleepy and pale. His weight was measured at 6.4 kg (<3rd centile), height was 68 cm (25th centile), and head circumference was 43 cm (<3rd centile). No hepatosplenomegaly was noted. During neurological examination, both axial and peripheral muscle tone were found to be decreased. Reflexes could not be elicited.

Laboratory investigations revealed the following results: hemoglobin level of 5.1 (range 10.3–13.5) g/dL, leukocyte count of 11.2×10^9/L (range 5–16×10^9/L), and platelet count of 26×10^9/L (range 200–550×10^9/L). The mean corpuscular volume was 78 fL (range 70–86 fL) and the reticulocyte index was 0.9%. Lactate dehydrogenase (LDH) was 6413 U/L, and liver function tests showed total bilirubin of 2.4 mg/dL and direct bilirubin of 2 mg/dL. The peripheral smear revealed microcytic, hypochromic red blood cells (RBCs) with anisocytosis and poikilocytosis. The leukocytes appeared normal, but platelet count was reduced. The iron profile showed serum ferritin level of 120 ng/mL (range 7–140 ng/mL), serum iron level of 286 mcg/dl (range 50–120 mcg/dl), and total iron-binding capacity (TIBC) of 304 mcg/dl (range 200–400). Glucose-6-phosphate dehydrogenase (G6PD) level was normal. Thalassemia workup was negative (High-Performance Liquid Chromatography: Normal). The sickle cell test was negative. A bone marrow aspiration showed normocellular bone marrow with dyserythropoietic changes and ring sideroblasts. However, a bone marrow biopsy revealed normocellular bone marrow with megaloblastic changes (Figure 1).

Upon further questioning, it was found that the mother followed strict vegetarian diet. Laboratory investigations revealed that the baby had vitamin B12 and a folic acid levels below 159 (range 239–931) pg/ml (lower reporting limit) and above 20 ng/mL, respectively. Additionally, the mother's vitamin B12 level was also less than 159 pg/mL, and folic acid level was 18 ng/mL.

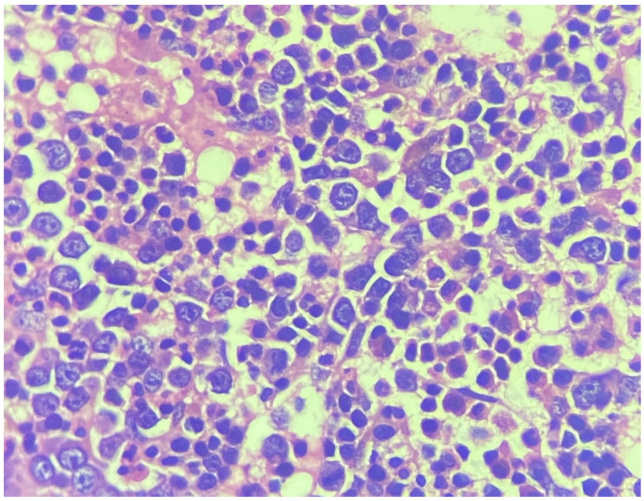

FIGURE 1 Bone marrow biopsy shows trilineage hematopoietic elements. Erythroid series show megaloblastic changes in the form of sieve-like chromatin and prominent nucleoli.

During the early days of hospitalization, he developed epistaxis and fever. Further evaluation showed a total neutrophil count of 630/mm^3 and platelets of 17,000/mm^3. He was managed with broad-spectrum antibiotics, transfusion with packed red blood cells, and administration of granulocyte stimulating factor (filgrastim) as well.

After diagnosis, he received a daily intramuscular injection of vitamin B12 (250 μg) for 2 weeks. In the days following the injection, the appetite and activity of the infant improved significantly. He began crawling and rolling over in bed and was also able to sit without support. Additionally, he started reaching for toys that were out of reach and showed mature pincer grasp. He responded to smiles and started to babble as well. Hematological parameters showed improvement after the 2 weeks of treatment period. He was discharged after 1 month of hospital stay. During a follow-up at the outpatient department (OPD) after 1 year, he is growing appropriately as per his age.

3 | DISCUSSION

Neurodevelopmental delay can be prevented by addressing vitamin B12 deficiency. The estimated vitamin B12 requirements of the growing infant is 0.06–0.1 μg/day and the normal neonatal stores of vitamin B12 is approximately 20–25 μg.[4] This means healthy neonate can have sufficient stores for up to 6–8 months of vitamin B12, even in the presence of inadequate intake. The

average breast milk concentration is 0.4 μg/l.[5] However, breast milk can be deficient in vitamin B12 due to factors such as the mother following a vegan diet, having pernicious anemia, or other malabsorption syndromes. It is important to note that these mothers appear clinically and hematologically normal.[6] Therefore, the dietary history of mother is equally important, while evaluating developmentally delayed infants. Sometimes, it is also important to note the ethnicity as the cultural aspect also guides the pattern of food intake. A study conducted on the diet of people in the Terai region, which is predominantly inhabited by the Tharu ethnic group (Chaudhary), revealed that the common dietary pattern involved a significant consumption of rice with limited amounts of curry or dal as side dishes. The participants in this region were found to have deficiencies in important nutrients including vitamin A, iron, riboflavin, and selenium. It was observed that female patients had lower protein intake per kilogram of body weight than male patients.[7] In our case, it is more attributing toward the strict vegetarian diet of mother resulting in deficiency of vitamin B12.

The clinical features of vitamin B12 deficiency in infancy are predominantly neurological and hematological. Megaloblastic anemia, which is a result of cobalamin or folate deficiency, occurs due to ineffective erythropoiesis. Vitamin B12 is necessary for DNA synthesis and its deficiency inhibits cell division in the bone marrow. Consequently, red blood cells exhibit large size with nuclear or cytoplasmic asynchrony, which is a characteristic of all megaloblastic anemias. Nonspecific manifestations of megaloblastic anemia include weakness, fatigue, failure to thrive, and irritability. Other features can include pallor, glossitis, vomiting, and diarrhea. Neurological symptoms include hypotonia, developmental delay, seizures, and subacute combined degeneration of spinal cord.

Nutritional deficiencies of vitamin B12 in early life can have significant impact on brain development and function, primarily through disruption of myelination. Slower conduction of nerve impulses resulting from myelination damage could result in learning and social interaction.[8] The acquisition of cognitive skills in early life coincide with the pattern of myelination in the central nervous system. Therefore, when myelination is disrupted due to Vitamin B12 deficiency, it ultimately results to delayed acquisition of cognitive skills and even regression of previous learned skills.[9]

Hematological findings in a case of vitamin B12 are anemia, macrocytic RBCs, mild leukopenia, thrombocytopenia, low reticulocyte count, and elevated levels of lactate dehydrogenase. In rare cases, cobalamin deficiency can be associated with increased formation of ring sideroblasts.[10] Pancytopenia can also be a rare manifestation of cobalamin deficiency, as observed in the above case. Mild elevations of aminotransferase are nonspecific findings but are frequently encountered during clinical practice. Elevated levels of methylmalonyl-CoA and homocysteine levels confirm the diagnosis. This test could not be performed on the above case due to economic constraints.

Studies have shown that prolonged low levels of vitamin B12 are associated with severe neurological complications, so early treatment is beneficial to the infant development.[11] It seems that infants treated before the age of 1 year have more favorable outcomes than those treated later. The 2008 WHO technical consultation on vitamin B12 and folate deficiencies determined that vitamin B12 significantly impacts child development and cognitive scores of school-aged children. To address this issue, food fortification and targeted population supplementation have been proposed as the optimal solution.[12]

4 | CONCLUSION

Although vitamin B12 deficiency is uncommon in infancy, it could manifest in infants born from mother who are strict vegetarians. The clinical signs of vitamin B12 deficiency in infancy are generally nonspecific and can include decreased feeding, apathy, and developmental regression. When evaluated, these infants may exhibit megaloblastic changes in RBCs and rarely can also manifest as pancytopenia and sideroblastic anemia as well. Early recognition of these infants is important because this condition is reversible. Therefore, necessary efforts should be done to prevent the deficiency of vitamin B12 in infants by providing adequate supplementation or dietary modifications to pregnant and lactating women who follow strict vegetarian diet.

AUTHOR CONTRIBUTIONS

Niraj Kumar Sharma: Conceptualization; writing – original draft; writing – review and editing. **Madhur Bhattarai:** Writing – original draft; writing – review and editing. **Kushal Baral:** Writing – original draft; writing – review and editing. **Susmita Poudel:** Writing – review and editing. **Nusaiba Farouk Hassan:** Writing – review and editing. **Tulsi Ram Dhakal:** Writing – review and editing. **Rituraj Baral:** Writing – review and editing.

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CONFLICT OF INTEREST STATEMENT

Authors' have no conflict of interest to declare.

DATA AVAILABILITY STATEMENT

All the required information is available in the manuscript itself.

CONSENT

Written informed consent was obtained from the patient to publish this report in accordance with the journal's patient consent policy.

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