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Case Report

Vitamin B12 Deficiency in Infants

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Abstract:

Vitamin B12 is a water-soluble vitamin with essential cellular functions. The main sources for humans are foods of animal origin. Vitamin B12 deficiency is more common in childhood than previously recognised. Clinical symptoms in children are often non-specific and may include megaloblastic anaemia, failure to thrive, muscle hypotonia, irritability or lethargy. Risk factors include families of low socio-economic status, exclusively breastfed infants of vegetarian mothers, and conditions leading to malabsorption.

The authors present a clinical case of a 13-month-old child with malnutrition and vitamin B12 deficiency resulting in megaloblastic anaemia and neurological involvement manifested by apathy and lethargy.

Keywords: vitamin B12 deficiency; megaloblastic anemia; malnutrition; developmental delay

Introduction

Vitamin B12 (B12; also known as cobalamin) is an essential, water-soluble vitamin that plays a crucial role in DNA synthesis, red blood cell formation, and neurological development. Since the human body is incapable of synthesizing B12, its primary sources are foods of animal origin such as meat, fish, and dairy products [1,2]. Deficiency of this vitamin is not only associated with megaloblastic anemia but also with significant neuromotor developmental delays, both of which contribute to serious morbidity during infancy [1].

The etiology of vitamin B12 deficiency in children can be broadly categorized into three groups: decreased intake, abnormal absorption, and inborn errors of vitamin B12 transport and metabolism [3]. The cobalamin stores in newborns are largely dependent on maternal B12 levels during pregnancy. Therefore, maternal deficiencies—whether due to dietary restrictions, unrecognized pernicious anemia, or adherence to vegetarian/vegan diets—can predispose exclusively breastfed infants to B12 deficiency right from birth [1,4,5]. After six months of age, when infants start consuming solid foods, exogenous sources of vitamin B12 become more critical. However, in both developed and developing countries, inadequate dietary intake persists as a significant risk factor, especially among populations with poor socio-economic status [1,4,5].

Recent studies have underscored that the prevalence of vitamin B12 deficiency may be higher than previously thought, even in developed countries. This is particularly evident in populations where exclusive breastfeeding is common and maternal nutritional status is compromised. Beyond hematological manifestations, early deficiency can have long-lasting neurological consequences. Clinical signs often begin between 4 and 12 months of age and may include failure to thrive, lethargy, hypotonia, and regression of developmental milestones, alongside classical features such as megaloblastic anemia [2,5].

Case Presentation

A 13-month-old boy was born from a fifth normal pregnancy and delivery, with a birth weight of 2700 grams and an uncomplicated postnatal period. He has developed normally.

At 11 months of age, the child was admitted to a regional hospital for pneumonia. The tests performed showed a hemoglobin level of 8.8 g/dl, HCT of 0.25, MCV of 96 fl, and serum iron of 17.4 µmol/L, with no deviations in the other laboratory parameters.

One month after discharge, he was readmitted to hospital for acute respiratory infection; laboratory tests showed hemoglobin – 9.3 g/dl; HCT - 0.25; MCV - 103 fl, with normal leukocyte and platelet values.

Twenty days later, the child became lethargic, refused to eat solid foods, had a rash on his body and swelling on his face and limbs. The parents reported that the child did not want to play, stopped smiling, became apathetic and slept most of the time. The child was again admitted to the same hospital. Laboratory tests indicated macrocytic normochromic anemia: hemoglobin of 6.6 g/dl, erythrocytes of 1.8 x10^12/L, HCT- 0.18, leukocytes of 9.2 x10^9/L, MCV of 100 fl, MCH of 36 pg, with normal platelet counts, serum iron of 21 µmol/L, albumin of 3.0 g/dl, total protein of 4.4 g/dl. The child was transferred to a university hospital for further evaluation and treatment.

The child was admitted in an unsatisfactory general condition, presenting with pale skin, visible mucous membranes, markedly reduced skin turgor, and an erythemato-papular rash. There was also oedema on the face and the dorsal surfaces of the hands and feet, and no enlarged lymph nodes were noted. He was lethargic, did not smile, and was generally hypotonic, although he had brisk reflexes and a normal cranial nerve examination. No pulmonary or cardiac abnormalities.

Anthropometric measurements using WHO growth curves indicated severe malnutrition: head circumference of 45 cm (50th percentile), height of 68 cm (3rd percentile), weight of 6600 g (below the 3rd percentile), and a height-weight ratio (z-score) of -3 SD.

Laboratory findings revealed macrocytic normochromic anemia: haemoglobin of 7.7 g/dl, erythrocytes of 2.6 x10^12/L, HCT of 0.24, leukocytes of 4.8 x10^9/L, MCV of 97 fl, MCH of 29.8 pg, reticulocytes of 1.45%, with normal platelet counts. Hypoproteinemia and hypoalbuminemia were also found. Folate levels were normal (5.9 ng/ml; reference range 3.2-19.6 ng/ml), but vitamin B12 levels were low (90 pmol/L; reference range 138-652 pmol/L), with normal serum iron levels.

Additional tests were performed to rule out a secondary cause of malnutrition and vitamin B12 deficiency, revealing normal sweat tests and metabolic screening, and negative microbiological, virological, and parasitological tests. Chest X-ray, abdominal ultrasound, and echocardiography were normal.

A detailed dietary history revealed that the child consumed yoghurt in early infancy, and from the age of 4-5 months was fed mainly carbohydrate food - porridge, without adequate intake of meat and other animal products, and had about 3 meals a day. The mother's diet was similar.

Replacement therapy was initiated, including fresh frozen plasma and erythrocyte transfusion, and intramuscular vitamin B12 for five consecutive days. The child was also put on a balanced diet of five meals a day. Clinical improvement was observed from the second day of vitamin B12 administration, with an improved emotional tone; he was smiling again and was no longer lethargic or hypotonic. Peripheral oedema resolved, anaemia improved, and weight gain was achieved. The child was discharged on day seven, weighing 7000 g.

Discussion

Inadequate nutrition, with improper diet and insufficient protein, energy and micronutrient intake, is a major factor leading to protein-energy malnutrition in infants and the development of vitamin B12 deficiency [2, 6].

Protein-energy malnutrition can be primary, resulting from inadequate food supply caused by socio-economic, political, and environmental factors, and it is most common in low- and middle-income countries, or secondary due to abnormal nutrient loss, increased energy expenditure, or decreased food intake, often in the context of underlying, mostly chronic, diseases [7, 8]. In the case described, secondary causes have been ruled out and the child's malnutrition is attributed to inadequate and inappropriate food intake. The measured anthropometric indicators show a z-score < -3 and the presence of oedema on the dorsal surface of the lower extremities, meeting the WHO criteria for severe primary protein-energy malnutrition [6, 9, 10].

Severe malnutrition leads to biochemical changes based on metabolic, hormonal, and glucoregulatory mechanisms [7]. Micronutrient deficiencies and the development of anaemia are among the major problems in these patients, observed in 78 to 94% of cases [7, 11-13]. Iron-deficiency anaemia is considered the most common type of anaemia [13, 14]. However, many studies have reported a predominance of vitamin B12 deficiency compared with iron deficiency in children with severe protein-energy malnutrition [12, 15, 16]. In a study by Yaikhomba et al., which included 50 children with severe protein-energy malnutrition, anemia was observed in 94% of them. A significantly higher number of these patients had vitamin B12 deficiency (34%) compared with folate and ferritin (iron) deficiency (6% each) [12]. The authors note the correlation between vitamin B12 deficiency and the severity of malnutrition. Chandra et al. also report a predominance of vitamin B12 deficiency (32%) compared with folate deficiency (20%) in children with malnutrition [17]. Our patient was diagnosed with an anaemic syndrome characterised by macrocytic normochromic anaemia with normal serum iron and folate levels but low vitamin B12 levels.

In addition to megaloblastic haematopoiesis and the development of megaloblastic anaemia, vitamin B12 deficiency is associated with neurological manifestations [2, 5, 18]. It should be noted that neurological symptoms may be observed in the absence of accompanying haematological abnormalities [19].

Vitamin B12 is essential for development of the central nervous system, although its exact role in both normal and pathological conditions is not fully understood [20]. Neurological changes are related to disturbances in the myelination of the nervous system [2, 20]. Vitamin B12 deficiency may lead to impaired synthesis of ethanolamine, phospholipids, and sphingomyelin resulting in altered myelin integrity with deficient long fiber tract function and axonal neuropathy [2]. Affected children have normal development during the first 4-6 months of life [19]. The first symptoms appear between 4 and 12 months of age [5], and include irritability, lethargy, apathy, refusal to eat solid food, pallor, and growth retardation. If the condition is not recognized and treated promptly, regression in the neurological development of these children occurs [19]. Approximately half of them show abnormal movements, such as tremors, chorea, or myoclonus, which are not observed in adults with vitamin B12 deficiency (Table 1) [5,19]. The observed apathy, lethargy, and muscle hypotonia in our case are attributed to the neurological manifestations of the established vitamin B12 deficiency, due to the severe protein-energy malnutrition of the child.

Common presenting (neurological) symptoms
Failure to thrive
Aversion or refusal to solid foods
Irritability or increasing lethargy, progressing to obtundation or coma
Swallowing dysfunction
Developmental delay and/or regression
Involuntary movements
Seizures
Common neurologic signs
Microcephaly
Apathy with vacant stare and drooling
Hypotonia
Hypokinesia

Common presenting (neurological) symptoms
Brisk tendon reflexes
Involuntary movements (tremors, myoclonus, choreoathetosis)
Diffuse cerebral atrophy + delayed myelination on neuroimaging

Table 1: Neurology of Nutritional Vitamin B 12 Deficiency in Infants

Measurement of vitamin B 12 levels may be useful in the diagnosis of vitamin B 12 deficiency. Serum vitamin B 12 levels vary depending on the laboratory and the method used, laboratories should determine their own range of results**.** In general, normal serum B12 levels range from 147.6 - 664.2 pmol/L (200-900 pg/ml) [3].

Treatment of vitamin B 12 deficiency depends on its cause. In mild, asymptomatic deficiency, altering the diet or correcting an underlying condition may be appropriate, but in most cases, administration of vitamin B 12 is necessary. Dosage has not been well established in children [3]. Treatment includes intramuscular or oral administration of vitamin B12 (Table 1). For infants and those with neurological involvement, intramuscular B12 is the standard replacement. High oral doses may be effective for lower-risk cases -i.e. older children/adults with no evidence of clinical deficiency [19,21]. Improvement starts early and is generally evident between 48 and 72 hours in most cases. Infants who were previously lethargic and apathetic begin to appear more alert and awake [2, 5, 19, 22], as was seen in our case.

Treatment Approach	Regimen	Indications
Intramuscular vitamin B12 administration	1000 µg i.m. daily for 5-7 days, followed by weekly injections for one month, then monthly maintenance injections	For infants, particularly those with neurological symptoms
Oral vitamin B12 administration	High-dose oral vitamin B12 (1000-2000 µg daily)	For mild or subclinical deficiency, often in older children/adults

Table 2: Treatment Approach for Vitamin B12 Deficiency

The late consequences of prolonged vitamin B12 deficiency in infancy and early childhood are not well studied. There have been reports of low IQ and a psychomotor and linguistic delay, especially in cases of delayed diagnosis and treatment [5, 19, 22, 23]. The long-term prognosis does not depend on serum vitamin levels, but rather on the age at which symptoms appear, their severity, and the duration of the deficiency [5, 23]. It seems that infants diagnosed and treated before the age of 1 year have a better neurological outcome than those treated after this age [5, 23].

Prevention of the late effects of vitamin B12 deficiency includes not only appropriate treatment, but also screening and assessment of children in high-risk groups, nutritional support and long-term follow-up of any complications that occur. This can significantly improve clinical outcomes and reduce the late effects of vitamin B12 deficiency (Table 3) [7].

Category	Recommendations
Screening and Early Diagnosis	- Screen at-risk infants (e.g., exclusively breastfed infants of vegetarian mothers, those from low socio-economic backgrounds). - Perform laboratory tests including complete blood count, serum vitamin B12, folate, and iron levels.
Treatment Approach	- Use intramuscular vitamin B12 (cyanocobalamin or hydroxocobalamin) as the preferred treatment, especially for infants with neurological involvement. - Standard regimen: 1000 µg i.m. daily for 5-7 days, followed by weekly injections for one month, then monthly maintenance as needed.
Nutritional Support	- Ensure a well-balanced diet with sufficient intake of animal-derived foods post-treatment. - Educate caregivers about the importance of dietary sources of vitamin B12.
Long-Term Monitoring	- Conduct regular follow-up to assess growth, neurodevelopmental progress, and overall nutritional status.

Table 3: Recommendations for Clinical Management

Conclusion:

Nutritional vitamin B12 deficiency is a treatable cause of failure to thrive and developmental delay in infants. Screening and investigation of at-risk groups are essential for timely diagnosis and treatment, which determine the long-term prognosis of affected children. Vitamin B12 supplementation, in addition to iron and folic acid, is important in the management plan for these children to prevent haematological and non-haematological manifestations of vitamin B12 deficiency.

Study Limitations:

This case study has several limitations. First, it is based on a single patient, which limits the generalisability of the findings. Secondly, long-term neurodevelopmental outcomes were not assessed due to the short follow-up period. Further studies with larger cohorts and longitudinal follow-up are needed to better understand the long-term effects of vitamin B12 deficiency in infancy.

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