

A case of vitamin B12 deficiency with rapid neurological improvement after treatment

TEDAVİ SONRASI HIZLI NÖROLOJİK DÜZELME GÖRÜLEN VİTAMİN B12 EKSİKLİĞİ OLGUSU

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ABSTRACT

Vitamin B12 deficiency presents with many different clinical manifestations. Its deficiency may cause hematological, neurological, gastrointestinal, dermatological and cardiac findings. Vitamin B12 deficiency develops easier in infants of vegetarian mothers and infants those not having an access to foods containing enough vitamin B12 in the developing countries. In its long-term deficiency, irritability, apathy, loss of appetite and developmental delay may occur in the infant. In this report, we present an infant of vitamin B12 deficiency with a history of hypotonicity and growth retardation. We wanted to draw attention to the rapidly recovering neurological findings of this patient who responded quickly to treatment.

Keywords: infant, neurological sign, vitamin B12 deficiency

ÖZ

B12 vitamini eksikliği birçok farklı klinik belirtiyle ortaya çıkar. Eksikliği hematolojik, nörolojik, gastrointestinal, dermatolojik ve kardiyak bulgulara neden olabilir. B12 vitamini eksikliği, vejeteryan anne bebeklerinde ve gelişmekte olan ülkelerde yeterli miktarda B12 vitamini içeren besinlere erişimi olmayan bebeklerde daha kolay gelişir. Uzun süreli eksikliğinde bebeklerde sınırlılık, ilgisizlik, iştahsızlık ve gelişimsel gecikme görülebilir. Bu yazıda süt çocuğunda hipotonisite ve büyüme geriliği ile ortaya çıkan, tedavinin ardından nörolojik bulguları hızla düzelen bir B12 vitamini eksikliği olgusu sunulmuştur.

Anahtar Sözcükler: süt çocuğu, nörolojik bulgu, vitamin B12 eksikliği

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Vitamin B12 is required for many organ systems. Its deficiency may cause hematological, neurological, gastrointestinal, dermatological and cardiac findings (1). Vitamin B12 cannot be synthesized naturally and it is absorbed from foods (2). Vitamin B12 deficiency develops

easier in infants of vegetarian mothers and those not having access to foods containing vitamin B12 in the developing countries (3). In its long-term deficiency, irritability, apathy, loss of appetite and developmental delay may occur in the infant because of insufficient myelination of

spinal cord and the brain (4). Some B-vitamins, including vitamin B12, were significantly affected by maternal intake. Vegetarians are at a high risk of inadequate intake and status of several nutrients, with vitamin B12 deficiency being a major concern. Although there is no clear data on prevalence, it is possible to reach different data from different countries. In the Czech Republic, younger adults (18–34 years) the proportion of vegetarians and vegans is 10% (5). These data do not identify prevalence of B12 deficiency but provide foresight. There is no prevalence study on this subject in our country. Diagnosis of vitamin B12 deficiency is difficult in the absence of typical macrocytic anemia. However, only the neurological findings can be dominant to neglect the hematological findings (4).

In this article, a 4.5-month-old infant presented with hypotonicity and growth retardation associated with vitamin B12 deficiency and immediate reply to replacement therapy were discussed.

CASE

A 4.5-month-old female infant admitted with inability of suckling and gaining weight. In history, her birth weight was 2500 gr, she was born as mature, she had received exclusively breast fed and the mother was don't able to access meet and other dairy products. She has been hospitalized with bronchopneumonia when she was two months old. She was diagnosed with iron deficiency at the age of 3.5 months with similar complaints. Her 10-year-old sister had hearing loss. In physical examination, her body weight was 500 gr (3-10p), height was 59 cm (10 percentile), and head circumference was as 39.5 cm (10-25 p). Axillary body temperature was 38.1° C and oropharynx was hyperemic. She was not interested with the environment, she was hypotonic, apathetic and she had a pallor. In the laboratory examinations, Hgb: 5.7 g/dL, Hct: 18%, MCV: 91.9 fL, RBC: 2,106,000/ μ L, RDW: 24.5, WBC: 4,800/ μ L, PLT: 290,000/ μ L, Reticulocyte: 1.3%, Vitamin B12: 52.8 pg/mL (126-523), 25-OH Vit D: 37 ng/mL, Folate: 19.8 ng/mL, Ferritin: 4 ng/mL, total iron binding capacity: 308, iron: 80 μ g/dL, transferrin saturation: 6.19 μ g/dL, homocysteine: 184 μ mol/L (0-15). Thyroid function test were in normal range. The peripheral blood smear showed,

anisocytosis, poikilocytosis, tear drop cell, macrocytosis, and hypersegmentation. Vitamin B12 level of the mother was 86 pg/mL. Urine examination, liver function tests, renal function tests, serum electrolytes, calcium, phosphorus, and blood glucose levels were in normal limits. Intramuscular vitamin B12 treatment was started for the both patient and the mother; oral iron treatment was also started for the infant. Treatment plan was made as follows; administration of 100 microgr/day every day for the first five days of the treatment, every other day for the next week, twice a week for subsequent two weeks and then once a month. Muscular tonus of the case, who started to keep her head on the 5th day of the treatment, rapidly returned to normal, her interest to the ambiance and activities increased, her skin color, demand for suckling and nutrition status returned to normal. On the 10th day of the treatment blood count showed the following values: Hb: 7.5 g/dL, Hct: 23%, and MCV: 86.6 fL.

DISCUSSION

Vitamin B12 deficiency is a picture that can be encountered in many different clinic features. The deficiency develops with a disorder in any of the events occurring during the absorption and / or transport of vitamin B12. These are the reasons such as insufficient nutritional uptake, abnormal absorption, defective transport to the cells, and abnormal metabolization of vitamin B12 by the cells (6). It is seen in many pediatric cases as a result of malnutrition and especially in infants fed only with breast milk among vegetarian mothers living in the developing countries. Other reasons are the genetic mutations during the cobalamin absorption, transport, and cellular metabolism. This article represented vitamin B12 deficiency in an infant who was fed exclusively with breast milk and whose mother had inadequate nutrition due to poverty. Low vitamin B12 and high homocysteine levels are defined to indicate the cobalamin dysfunction in the period between birth and the first six 6 months (7). The normal interval is specified as 217-314 pmol/L in the period between the first four 4 days and six 6 months (7). Normal value interval at our laboratory is worked as 126-505 ng/L. According to both reference intervals, vitamin B12 deficiency was present both in the patient and the mother. In their study, Irevall T et al (8), revealed that vitamin B12

deficiency was more than the estimated. This study was conducted by selecting 121 infants at the age of 1 and younger among 11,143 children and vitamin B12 deficiency was found at the rate of 314/100,000 (7).

It is not always easy to diagnose vitamin B12 deficiency by laboratory results. Certain conditions may be associated with spuriously low serum vitamin B12 levels and thus might cause the appearance of vitamin B12 deficiency when the patient is not deficient. Examples include multiple myeloma, HIV infection, pregnancy, oral contraceptive use, and diphenylhydantoin administration. Additional testing for intermediates in vitamin B12 and folate metabolism (methylmalonic acid and homocysteine) can be reserved for cases in which initial test results for vitamin B12 and/or folate levels are borderline (near the lower limit of normal) or inconclusive, or if clinical findings are discordant with initial testing values (eg, low-normal vitamin B12 level in an individual with unexplained macrocytic anemia or unexplained neurologic findings) (9). MMA is elevated in Vitamin B12 deficiency but not in folate deficiency. This is because vitamin B12 is a cofactor in conversion of methylmalonyl-CoA to succinyl-CoA, a reaction that occurs in mitochondria and is catalyzed by methylmalonyl-CoA mutase (10). Homocysteine is elevated in both vitamin B12 and folate deficiencies. This is because both vitamins are required for the metabolism of homocysteine to methionine. The sensitivity of MMA and homocysteine for vitamin B12 deficiency was addressed in a 1994 study that measured these metabolites in a series of 406 individuals diagnosed with vitamin B12 deficiency based on a low vitamin B12 level (<200 pg/mL) plus a clinical finding (diagnostic bone marrow, blood smear, and response to vitamin B12 administration) (11). Of these 406 individuals, 94.5 percent had elevations of both metabolites, and all but one had an increase in at least one metabolite, with a sensitivity of 99.8 percent for the diagnosis of Vitamin B12 deficiency.

Clinical presentation of vitamin B12 deficiency is quite extensive and it affects various organ systems. In pediatric population, neurologic findings vary with the age (12). Vitamin B12 deficiency in infants is in the form of irritability, lethargy, nutritional difficulties (especially rejecting solid foods), paleness, and fatigue. This is

followed by the growth retardation. Other involuntary movements such as tremor and myoclonus have been defined in untreated infants (12). In a large case series published by Goraya et al (13), main physical examination findings were described as apathy, loss of eye contact, abnormal tonus (especially hypotonia), brisk reflexes, and tremor. The underlying cause for the neurological symptoms is suggested to be delayed myelination and demyelination (14). In the present case, hypotonia and apathy were significant findings.

Hematologic indices may accompany the neurologic findings, as well. Classically, megaloblastic anemia develops due to the effect of vitamin B12 on DNA synthesis. While megaloblastic changes are often present, macroscopic anemia is not always present. At the beginning, MCH increases and then MCV increases, macroovalocytosis and hypersegmentation in neutrophils occur. Pancytopenia can be observed together with thrombocytopenia and leukopenia (15). In our case, there was no pancytopenia, but concomitant iron deficiency anemia was present.

There are conditions that may be associated with vitamin B12 deficiency. Decreased absorption (eg, gastrectomy, bariatric surgery, Crohn disease, celiac disease, pancreatic insufficiency, bacterial overgrowth, fish tapeworm infection, gastric atrophy associated with aging), other autoimmune conditions, such as thyroid disease or vitiligo especially in individuals with pernicious anemia, medications and drugs that interfere with absorption or stability (eg, metformin, histamine receptor antagonists, proton pump inhibitors, nitrous oxide) and rare genetic disorders. (16).

These associated conditions should be kept in mind in differential diagnosis. In selected cases, celiac screening and other autoimmune diseases should be examined. We did not perform celiac screening in this case, but thyroid function tests were normal. Early diagnosis and initiation of treatment are important. Treatment is performed by intramuscular injection of vitamin B12 with the doses 0.5-1.0 mg. No side effect is defined. Vitamin B12 is available in several formulations and can be administered by several routes, including intramuscular, deep subcutaneous, oral,

or sublingual. Intranasal administration is generally not used. Transdermal forms of vitamin B12 are available over the counter, but this route of administration has not been validated clinically in the setting of vitamin B12 deficiency and should not be relied upon for treatment. The typical dose for children is 50 to 100 mcg parenterally once per week until the deficiency is corrected and then once per month (cyanocobalamin) or once every other month (hydroxocobalamin); oral doses in children are not well established (17). A 2006 systematic review found data from two randomized trials (108 participants) that compared oral versus intramuscular vitamin B12 and found that oral vitamin B12 was equivalent to or better than intramuscular vitamin B12 for raising serum vitamin B12 levels, correcting anemia, and in one case, resolving neuropsychiatric findings (18,19). It has been reported in the literature that most of the patients return to their basal neurological status after several months of treatment (15). The present case showed a significant recovery on the fifth day of treatment. At the beginning of vitamin B12 treatment, it is recommended to give folate and iron supplements as hematopoiesis will increase. In this period, clinicians should pay attention to the development of hypocalcemia.

In conclusion, we wanted to draw attention to the fact that vitamin B12 deficiency in infants may occur with neurological findings and can be early-diagnosed and treated efficiently.

Informed consent was obtained from the patient.

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