OLGU SUNUMU / *CASE REPORT*

A Rare Finding of Vitamin B12 Deficiency in Infancy: Lethargy

İnfantta Vitamin B12 Eksikliğinin Nadir Bir Bulgusu: Letarji

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ABSTRACT

Vitamin B12 is one of the essential vitamins that affects various systems in the body. Vitamin B12 deficiency can be seen at any age. During infancy, hematological and neurological disorders, including macrositer anemia, neurodevelopmental delay or regression, irritability, weakness, hypotonia, ataxia, apathy, tremor and seizures are caused. Vitamin B12 deficiency in patients with different nonspecific neurological findings should be considered in differential diagnosis. In this article, we present a case of lethargic girl who was referred for eleven months of sleep and awakening. Vitamin B12 levels were found to be low due to the presence of a finding compatible with macrositer anemia in the whole blood count and peripheral spread of the case and because of the backwardness in the neuro motor developmental stages. Following the first dose with Vitamin B12 treatment, the clinical presentation began to improve and the findings disappeared completely over time.

Key words: *vitamin B12 deficiency; lethargy; infancy*

ÖZET

Vitamin B12, vücutta çeşitli sistemleri etkileyen esansiyel vitaminlerden biridir. Vitamin B12 eksikliği her yaşta görülebilir. Süt çocukluğu döneminde sıklıkla makrositer anemi, nörogelişimsel gecikme ya da gerileme, irritabilite, güçsüzlük, hipotoni, ataksi, apati, tremor ve nöbetleri kapsayan hematolojik ve nörolojik bozukluklara neden olmaktadır. Farklı nonspesifik nörolojik bulgularla gelen hastalarda Vitamin B12 eksikliği ayırıcı tanıda mutlaka düşünülmelidir. Bu makalede devamlı uyku hali, uyanamama nedeniyle başvuran Vitamin B12 eksikliği ile ilişkili koma saptanan on bir aylık kız olgu sunulmuştur. Olgunun tam kan sayımı ve periferik yaymasında makrositer anemi ile uyumlu bulgusunun olması ve nöro motor gelişim basamaklarında da gerilik olması nedeniyle bakılan Vitamin B12 düzeyi düşük olarak saptanmıştır. Hastaya Vitamin B12 tedavisi yapılmış ve takipte klinik tablo dramatik olarak tamamen düzelmiştir.

Anahtar kelimeler: *vitamin B12 eksikliği; letarji; süt çocukluğu*

Introduction

Vitamin B12, which is in the form of cobalamin in foods, is mostly of animal origin and can not be synthesized in the human body. The most important function is the synthesis of deoxyribonucleic acid (DNA), which is necessary for cell division and proliferation. Lack of vitamin B12 is associated with megaloblastic anemia, psychiatric and hematological disturbances, and physical and neuro-motor retardation. Due to the demyelination effect, brain and nervous system development is significantly affected. In children with Vitamin B12 deficiency, delays in all motor functions such as head control, sitting, walking, and speaking can be seen with findings such as irritability, apathy, hypotonia, and loss of appetite[1–3]. Especially in developing countries, children in the first 2-year-old group may develop megaloblastic anemia and neurological degeneration due to deficiency in the mother's milk and defective intake[4]. It is important to consider Vitamin B12 deficiency during childhood, to be diagnosed and treated. Although the treatment cost is quite low, delayed treatment can lead to serious complications such as deep anemia, irreversible neurological damage[5]. In this article, we present a case of eleven months old girl with delayed and marked lethargy – sleepy state on her neuromotor developmental stages due to deficiency of Vitamin B12 and her dramatically improved post-treatment findings.

Case Presentation

An 11-month-old girl was admitted to our hospital with complaints of drowsiness-sleepy, anorexia,

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decreased interest in her environment, sleeplessness in her sitting position, and difficulty in awakening.

Cranial computed tomography (CT) at the external center, previously referred to these complaints He was diagnosed with mastoiditis and 1 week with ceftriaxone and 4 days with cefixime due to the presence of mucinous densities in bilateral mastoid cells. The patient applied to our clinic for complaints.

There is no kinship between mother and father. The patient had no pathological features in prenatal, natal and postnatal. It was stated that the vaccinations were made in accordance with the Ministry of Health vaccination schedule. Some steps in neuromotor development have been found to be delayed: head restraint 5–6th month, assisted sitting 8th month, unsupported sitting 9th month, no crawling and stepping, Speech was in 1–2 words in the 8th month.

On physical examination; body weight was measured as 8915 gr (25–50 percentile), height 73 cm (25 percentile), and head circumference 43 cm (3 percentile).

On the neurological examination the general condition was moderate, consciousness was lethargy, no orientation and no cooperative. There was no auditory evoked response, and there was a brief awake state with painful stimuli. Muscle strength was complete and there was no pathological reflex. Pupil reflex bilateral positif, deep tendon reflexes are active in all extremities and plantar responses flexor. The other system examinations of the patient were natural.

In laboratory examinations; In full blood count; hemoglobin 11 g/dL, leukocyte count $7.6\times10^3/mm^3$, mean erythrocyte volume (OEH) 99.7 fL, platelet $436\times10^3/mm^3$ reticulocyte: 8.3% (control: 2.5% and corrected: 2.1%). Erythrocytes hypochromic macrociter in peripheral spread, anisocytosis and poichilocytosis were present. Serum biochemistry, blood gas, thyroid function tests, ammonia, ferritin, folate, urine and blood amino acids, tandem and urine organic acid were normal. Hearing and eye examination were normal. Cranial magnetic resonance imaging (MRI) and cranial computed tomography were reported as normal. MRI spectroscopy was normal. Electroencephalogram (EEG) of the patient had no pathological findings other than mild cerebral dysfunction.

Blood Vitamin B12 level: 83 pg/mL, homocysteine: >50 (N: 0–13) urine methyl malonic acid: 0.481 ng/mL (N: 0–0.4). Vitamin B12 level in the mother's blood was 108 pg/mL.

Based on these results, cyanocobalamin intramuscular therapy was initiated in the patient who was thought to be deficient in Vitamin B12. Vitamin B12 treatment protocol to be applied to the patient; A total of six months of treatment consisting of 100 mcg/day in the first week, 100 mcg in the second week every other day, 100 mcg in the third week every three days, 100 mcg/week in the fourth week and then 100 mcg of intramuscular per month. In follow-up, cyanocobalamin increased the activity of the patient by the second dose, and the prolongation of the wakefulness was seen The sleeping periods continued at the same level as their peers, the interest in the surroundings increased, and the answers began to give appropriate responses to the stimuli. The patient was discharged in this condition. Vitamin B12 level observed after 1 month was 855 pg/mL.

Discussion

Vitamin B12 is a vitamin that plays a role in DNA synthesis and causes a variety of deficiencies that affect all age groups[6]. Vitamin B12, which is not synthesized in humans and primarily in animal origin, is an important cofactor involved in the methylation of homocysteine in methylionine and the conversion of methylmalonil coenzyme A to succinylcoenzyme A. Vitamin B12 deficiency accumulates in these precursors, so measurement of homocysteine and methylmalonic acid levels is helpful in the diagnosis[7]. Her blood methylmalonic acid level was normal but homocysteine level was high.

Vitamin B12 is actively transmitted through the placenta in pregnancy from mother to baby. In healthy newborns, 25–50 μg of total Vitamin B12 is found in the liver and is sufficient until the end of age[7,8]. However, in infants are fed with mother's milk which is deficient in Vitamin B12 or who consume little amounts of animal food, Vitamin B12 deficiency may develop between 6–12 months[3]. The most common cause of vitamin B12 deficiency in our country during infancy is vitamin B12 deficiency during pregnancy[9].

In the study of Koç et al.[10], Vitamin B12 deficiency was found in 72% of pregnancies and 41% of newborns. Vitamin B12 deficiency may be overlooked because anthropometric measurements are not affected if there is a deficiency in the Newborn period[11]. As the child grows and the deficit deepens, clinical signs usually appear between 3–18 months. Vitamin deficiency is thought to be due to low intake due to the infant being fed with breast milk, insufficient intake of

animal food as supplementary food and lack of vitamin B12 in mother. The first clinical finding was delayed in head holding and mild hypotonia. The amount of Vitamin B12 in the mother's milk is related to the intake amount of Vitamin B12 in the diet rather than Vitamin B12 deposits in the mother. Vitamin B12 support to mothers during pregnancy and timely delivery of supplemental nutrients to dairy children prevent signs of vitamin deficiency.

The long-term deficiency of vitamin B12 causes insufficient myelinization in the spinal cord and brain. Many non-specific neurological findings such as lethargy, apathy, weakness, irritability, hypotonia, seizures, developmental retardation, movement disorders, personality changes, memory loss may occur due to Vitamin B12 deficiency, especially in infancy[3]. West syndrome and epileptic cases rarely seen due to Vitamin B12 deficiency have also been reported in the literature[12,13]. It is also emphasized that in a study conducted in adults, Vitamin B12 deficiency may be associated with daytime extreme sleepiness[14]. Hoey et al. [15] reported that vitamin B12 deficiency in a 14-month-old female patient, who was fed only breast-milk, drowsiness, seizures in the eyes, on the face, arms and legs with constant splashes, had a role in the etiology. There were obvious drowsiness in our presence, and there was no orientation and no cooperation. There was no auditory stimulus response and there was a brief awakening with painful stimulus. Also some steps in neuromotor development have been found to be delayed: head restraint 5th–6th month, assisted sitting 8th month, unsupported sitting 9th month, no crawling and stepping.

Although complete blood count is not a diagnostic value alone, Vitamin B12 deficiency should be considered in the presence of macroscopic anemia. In case of accompanying iron deficiency anemia, thalassemia carriage or inflammatory bowel diseases, normocytic and even micrositeritic erythrocytes may be seen in peripheral blood smear. Pancytopenia can also be seen in severe Vitamin B12 deficiencies[16]. In our case, hemoglobin value was in the lower border and mean corpusculer volume (MCV) was high. Hipocrom macrositer erythrocytes, anisocytosis and poichilocytosis were present in the peripheral spread. Elevated levels of homocysteine or serum/urinary methylmalonic acid in patients who are thought to be deficient in vitamin B12 but whose levels are normal are considered significant for diagnosis[17]. Bone marrow aspiration is recommended in cases with diagnostic difficulties. Investigations to investigate etiology are not affected by Vitamin B12 treatment. Therefore, the treatment of the patient should be started before the etiologic investigation is concluded. Determination of etiology is of importance in order to decide the duration of treatment.

Vitamin B12 deficiency is a common condition, especially in developing countries. The majority of Vitamin B12 deficiencies encountered during infancy are due to mothers. Therefore, Vitamin B12 deficiency should be sought in the mothers of infants with a diagnosis of Vitamin B12 deficiency. Vitamin B12 support to mothers during pregnancy and timely delivery of supplemental nutrients to dairy children prevent signs of vitamin deficiency. However, long-term deficiency of Vitamin B12 may cause permanent neurological disturbances as it causes demyelination in the spinal cord and brain. Vitamin B12 deficiency should be kept in mind in patients with nonspecific neurological findings such as sleeping and unconsciousness, apathy, seizures, hypothermia. Early diagnosis and treatment should be avoided complications that may occur.

Conflict of Interest

The authors declare no conflict of interest

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