



# West syndrome due to vitamin B<sub>12</sub> deficiency

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## Abstract

Vitamin B<sub>12</sub> is one of the essential vitamins affecting various systems of the body. Vitamin B<sub>12</sub> deficiency in infants often produces haematological and neurological deficits including macrocytanaemia, neurodevelopmental delay or regression, irritability, weakness, hypotonia, ataxia, apathy, tremor and seizures. In this article, we report the case of a six-month-old male patient diagnosed with West syndrome associated with vitamin B<sub>12</sub> deficiency. Although the patient had no evidence of macrocytic anemia in complete blood count, we measured the level of vitamin B<sub>12</sub> because the patient had hypotonicity and found it to be low. No other problem was found in the other investigations directed to the etiology of West syndrome. He was being exclusively breast-fed and vitamin B<sub>12</sub> deficiency was related with nutritional inadequacy of his mother. Vitamin B<sub>12</sub> deficiency should be considered in the differential diagnosis of patients presenting with different neurological findings. In addition, vitamin B<sub>12</sub> deficiency should be considered as a rare cause in West syndrome which has a heterogeneous etiology. (Turk Pediatri Ars 2015; 50: 251-3)

**Keywords:** Vitamin B<sub>12</sub>, infant, West syndrome

## Introduction

Vitamin B<sub>12</sub> is one of the essential vitamins which affects various systems. Hematological, neurological, psychiatric, gastrointestinal, dermatological and cardiological findings occur in its deficiency (1, 2). Long-term deficiency leads to inadequate myelination in the medulla spinalis and brain and is manifested with irritability, apathy, loss of appetite and developmental delay in infants (2). In the absence of typical macrocytic anemia, it is difficult to make a diagnosis of vitamin B<sub>12</sub> deficiency. However, only neurological findings may be prominent, while hematological findings are normal in individuals with vitamin B<sub>12</sub> deficiency (2). Epilepsy is rarely observed in pediatric and adult patients with vitamin B<sub>12</sub> deficiency (3, 4).

In this case presentation, we presented a six month-old male patient who developed West syndrome related with vitamin B<sub>12</sub> deficiency. Consent was obtained from the family for case presentation.

## Case

A six month old male patient presented with a complaint of having seizure in the form of jumping and huddling

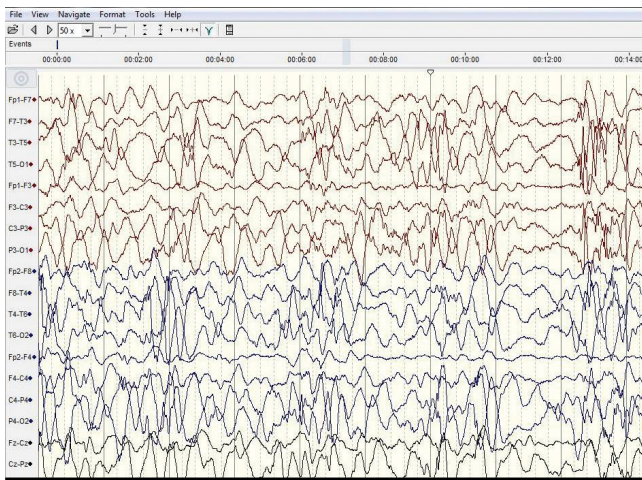
forward which started 10 days ago and recurred numerous during the day. He was born as the second child of his parents who had no consanguinity. Head control occurred at the age of five months and he had just started to sit with support. He was exclusively breastfed since birth and had no known familial history of epilepsy, mental-motor retardation or systemic disease. On physical examination, the head circumference was between the 25<sup>th</sup> and 50<sup>th</sup> percentiles and his weight and height were at the 75<sup>th</sup> percentile. He did not have hepatomegaly. On neurological examination, he had open consciousness, interest for the surroundings, hypotonia, hypoactivity and decreased deep tendon reflexes. He had a seizure in the form of flexor spasm during the examination and was hospitalized with a prediagnosis of West syndrome. Hypsarrhythmia pattern was observed on electroencephalogram (EEG) and synthetic adrenocorticotrophic hormone (ACTH) treatment was initiated (Figure 1). The laboratory findings were as follows: hemoglobin: 12.4 g/dL, mean MCV: 66.9 fL, glucose: 89 mg/dL, ALT: 15 U/L, AST: 17 U/L, urea: 34 mg/dL, creatinine: 0.93 mg/dL, iron: 56 µg/dL, total iron binding capacity: 356 µg/dL, ferritin: 85 ng/mL, ammonia: 0.85 µg/mL, TSH: 2.55 mIU/L, free T4: 1.26 ng/dL. The level of vitamin B<sub>12</sub> was measured, because the patient was hypotonic and was found to be low (74 pg/mL). The ho-

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**Figure 1. Interictal EEG: hypsarrhythmia characterized with burst suppression**

homocysteine level was slightly increased (17  $\mu\text{mol}$ ; normal range: 5-15  $\mu\text{mol}$ ). Since the patient was exclusively breastfed, the mother's vitamin B<sub>12</sub> level was measured and was found to be low (111 pg/mL). In the mother's nutritional history, it was learned that consumption of food of animal origin was low. No pathological finding was found in the investigations performed to elucidate the etiology of vitamin B<sub>12</sub> deficiency in the mother and deficiency was thought to be related with low intake. Cranial magnetic resonance imaging was evaluated to be normal in our patient. Tandem mass spectrometry was found to be normal and mild methylmalonic aciduria was found in urinary organic acid tests. Vitamin B<sub>12</sub> treatment was initiated with a dose of 100  $\mu\text{g}/\text{day}$  for one week and continued with a dose of 100  $\mu\text{g}/\text{day}$  weekly for four weeks and with a dose of 100  $\mu\text{g}/\text{day}$  monthly thereafter. Increased activity was observed beginning from the seventh day of treatment. The patient's seizures were controlled with the second dose of ACTH. Methylmalonic aciduria was not found in urinary organic acid tests performed after vitamin B<sub>12</sub> treatment. Electroencephalogram repeated three months later was evaluated to be normal.

On neurological examination performed at the age of ten months, it was found that the patient had interest for the surroundings, smiled, could speak in monosyllables and sit without support.

## Discussion

West syndrome is an epileptic encephalopathy characterized with spasm type seizures, hypsarrhythmia pattern on EEG and developmental delay or retardation in infants (5). The mean age of onset is four-seven months. In the etiology, cortical dysplasias, neurocutaneous syndromes, hereditary metabolic diseases and prenatal and postnatal

brain damage may be involved (5). It was thought that vitamin B<sub>12</sub> deficiency was involved in the etiology, because our patient had no history of prenatal or postnatal brain damage, cranial magnetic resonance and tandem mass spectrometry were found to be normal, the level of vitamin B<sub>12</sub> was found to be low and mild methylmalonic aciduria found in urinary organic acid tests returned to normal after vitamin B<sub>12</sub> treatment.

Vitamin B<sub>12</sub> is a vitamin which is involved in DNA synthesis and its deficiency leads to various findings affecting all age groups (6). Vitamin B<sub>12</sub> is a significant cofactor which is involved in methylation of homocysteine to methionine and in transformation of methylmalonyl coenzyme A to succinyl coenzyme A and primarily found in food of animal origin. In deficiency of vitamin B<sub>12</sub>, these precursors accumulate. Therefore, measurement of the levels of homocysteine and methylmalonic acid is helpful in the diagnosis of vitamin B<sub>12</sub> deficiency (7). The homocysteine level was found to be increased in our patient and mild methylmalonic aciduria was found in urinary organic acid analysis.

Normally, 25  $\mu\text{g}$  of the total of vitamin B<sub>12</sub> is found in the liver in newborns and this level is sufficient until the age of one year (7). Vitamin B<sub>12</sub> deficiency is observed rarely before the age of four months. Vitamin B<sub>12</sub> deficiency may develop between the ages of six and 12 months in infants who consume food of animal origin in small quantities or are breastfed by mothers who have vitamin B<sub>12</sub> deficiency (2). It was thought that vitamin B<sub>12</sub> deficiency was related with low intake in our patient, because he was exclusively breastfed and the mother had vitamin B<sub>12</sub> deficiency.

In children, neurological findings including weakness, irritability, hypotonia, seizure, developmental delay, movement disorders, personality changes and memory loss may occur in relation with vitamin B<sub>12</sub> deficiency (2). Neurological changes may also be observed without hematological abnormalities (2). Our patient had no finding compatible with macrocytic anemia in complete blood count.

Epilepsy is observed rarely in children and adult patients with vitamin B<sub>12</sub> deficiency (3, 4). The main cause of epileptogenesis related with vitamin B<sub>12</sub> deficiency is not clear. It may be explained with the fact that brain neurons covered with damaged myelin are more sensitive to the stimulating effects of glutamate (4). Generalized tonic clonic and focal seizures related with vitamin B<sub>12</sub> deficiency have been described (8). Kumar (4) reported that vitamin B<sub>12</sub> deficiency was involved in the etiology and very good response was obtained with vitamin B<sub>12</sub> treatment in a 26-year old male patient who had behavioral change for the last one year and did not respond to risperidone and

carbamazepine treatment which was given for complex partial seizures for the last three weeks. Korenke et al. (9) reported a four-month old female patient who presented with the diagnosis of encephalopathy and treatment-resistant seizure. Macrocytic anemia, low vitamin B<sub>12</sub> level, high homocysteine level and methylmalonic aciduria in urinary organic acid analysis were found in the patient. At the 24<sup>th</sup> hour of vitamin B<sub>12</sub> treatment, the patient's seizures stopped, his consciousness opened and he started to respond to stimuli. Hoey et al. (10) reported that vitamin B<sub>12</sub> deficiency was involved in the etiology in a 14-month old female patient who presented with complaints of somnolence and seizures in the form of continuous jerky movements in the eyes, face, arms and legs and who was exclusively breastfed.

A patient with West syndrome which developed as a result of vitamin B<sub>12</sub> deficiency was reported in the literature. Erol et al. (11) reported that mental-motor development which was normal until the age of nine months paused with initiation of seizures in this 10-month-old female patient. No pathology was found on physical examination except for apathy, hypotony and reduced deep tendon reflexes. When methylmalonic aciduria was found in urinary organic acid analysis, vitamin B<sub>12</sub> level was measured and was found to be low. Macrocytic anemia was not observed in this patient similar to our patient. After vitamin B<sub>12</sub> treatment, the patient's somnolence and psychomotor retardation improved markedly and EEG which was performed two months later was found to be normal.

Vitamin B<sub>12</sub> deficiency is commonly observed in developing countries especially because of poor socioeconomic status. The majority of vitamin B<sub>12</sub> deficiency in infancy has maternal origin. Vitamin B<sub>12</sub> deficiency should be considered in the differential diagnosis in patients who present with different neurological signs including seizure and hypotonia, because neurological signs may occur while hematological findings are normal. In addition, vitamin B<sub>12</sub> deficiency should be considered as a rare cause in West syndrome which may develop in relation with various causes.

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