

CASE REPORTS

An occult cause of infantile spasms: Vitamin B12 deficiency. A case report and review of literature

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Abstract

Vitamin B12 deficiency in exclusively breastfed infants is an important problem in developing countries. Vitamin B12 deficiency is associated with a wide spectrum of clinical manifestations. Few cases of vitamin B12 deficiency have been reported as the cause of infantile spasms. We report the case of a 6-month-old boy diagnosed with infantile spasms associated with vitamin B12 deficiency caused by nutritional inadequacy in the mother. He was observed to have head nods and flexor limbs spasms which appeared in clusters. Psychomotor development was normal. The serum vitamin B12 level was low and results of electroencephalography (EEG) indicated modified hypsarrhythmia. His symptoms resolved after synthetic adrenocorticotrophic hormone (ACTH) and vitamin B12 treatment. The EEG was completely normal after the first month and sixth month of treatment. In addition to ACTH and vitamin B12 treatment, following antiepileptic drug treatment was not initiated. During 21 months' follow up he is seizure-free and his neurological development is age-appropriate.

This case of a 6 month-old infant with infantile spasms due to vitamin B12 deficiency seems to be a striking because of only with vitamin B12 and ACTH treatment the patient became seizure-free. Vitamin B12 deficiency may be a treatable cause of infantile spasms and should be considered in the associated cause of infantile spasms especially if nutritional inadequacy in the mother.

INTRODUCTION

Infants of vitamin B12 deficient breastfeeding mothers, or infants receiving low amounts of animal-source foods, may be vulnerable to vitamin B₁₂ deficiency between 6 and 12 months of age.¹

Vitamin B12 deficiency in infant is associated with a wide spectrum of clinical manifestations. These include macrocytic anemia, failure to thrive, irritability, lethargy, hypotonia, developmental delay, psychomotor delay, regression, tremor, convulsions and coma. Less specific manifestations include pallor, vomiting, diarrhea, edema and apathy.² Moreover, neurologic changes often occur in the absence of hematologic abnormalities.³⁻⁵

Few cases of vitamin B12 deficiency have been reported as the cause of infantile spasms. We report the case of a 6-month-old boy diagnosed with infantile spasms associated with vitamin B12 deficiency caused by nutritional inadequacy in the mother.

CASE REPORT

A 6 month-old exclusively breastfed boy was admitted to hospital with brief head nods and symmetric limbs contractions over a period of 10 days. He was the second child of non-consanguineous parents. He was born full term after a normal pregnancy. His birth weight was 2750 gr (25th percentile), length 47 cm (50th percentile) and head circumference was 35 cm (50th percentile).

On physical examination, the child had the following growth parameters; 7.5 kg (10-25th percentile), height 69 cm (25-50th percentile) and head circumference 43 cm (25-50th percentile). He was observed to have head nods and flexor limbs spasms which appear in clusters. Psychomotor development was normal: he was following moving things with eyes and responding to affection. He was achieved trunk control at age 5 months. There were no organomegaly and dysmorphic features.

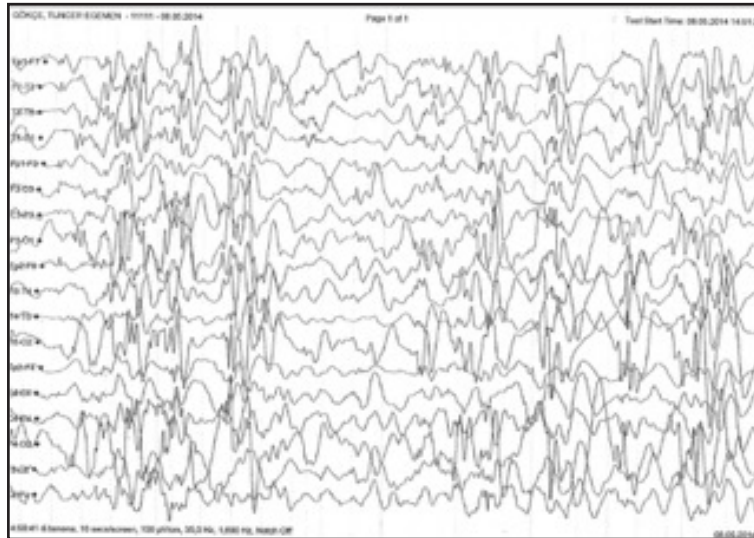


Figure 1. EEG showing modified hypsarrhythmia

Hemoglobin level, leukocyte and platelet counts were 11.5 g/dL, $14 \times 10^3/\text{mm}^3$, and $308 \times 10^3/\text{mm}^3$ respectively. Mean corpuscular volume, red blood cell count, and hematocrit were 76.1 fL, $4.34 \times 10^6/\text{mm}^3$, and 33% respectively. The serum vitamin B12 level was low at 99.76 pg/mL (reference range 191-663 pg/mL). Serum folate level was 16.01 ng/mL (reference range 4.6-18.7 ng/mL). Plasma homocysteine was 3.41 $\mu\text{mol/l}$ (reference range 5-12 $\mu\text{mol/l}$). Iron and ferritin levels, biochemical profile, blood and urine amino acid levels were within normal range. Cranial magnetic resonance imaging was normal.

Results of electroencephalography (EEG) indicated modified hypsarrhythmia (Figure 1) and the patient was diagnosed as having infantile spasms associated with vitamin B12 deficiency.

Serum vitamin B12 level of the mother was low at 40 pg/ml. The mother was also diagnosed to have vitamin B12 deficiency and she was referred to internal medicine physicians.

The patient received intramuscular synthetic adrenocorticotrophic hormone (ACTH) treatment 25 IU twice a week, total of 12 doses and intramuscular vitamin B12 treatment 100 mcg daily for a week, then given 100 mcg every other day for a week, and then given 100 mcg twice a week. After this regimen, he was given 100 mcg monthly for 3 months.

His symptoms resolved after ACTH and vitamin B12 treatment. The EEG was completely normal after the first month and sixth months of treatment (Figure 2). A month after vitamin B12 treatment, vitamin B12 level increased to

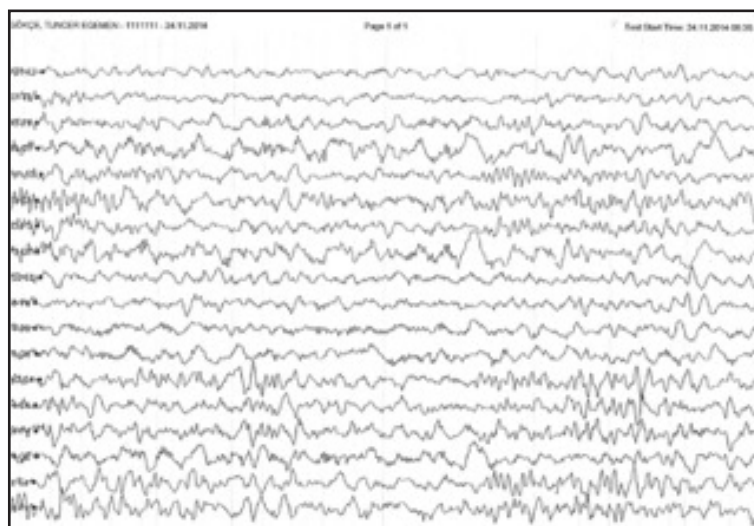


Figure 2. Normal EEG after treatment

normal. In addition to ACTH and vitamin B12 treatment, no other antiepileptic drug treatment was initiated. During 21 months' follow up he is seizure-free and his neurological development is age-appropriate.

DISCUSSION

This case reiterates the association between infantile spasms and vitamin B12 deficiency, and highlights the potential of spasms occurring before other neurological and biochemical abnormalities. In developing countries, vitamin B12 deficiency constitutes a significant problem.⁶ It is very important to be aware that vitamin B12 deficiency can frequently occur in infants born to vitamin B12 deficient mothers and it is a preventable cause of neurodevelopmental delay.

Infantile spasms are a unique form of seizure disorder that their occurrence is almost entirely limited to infancy and they are refractory to conventional anticonvulsant drugs. Infantile spasms involve sudden, generally bilateral and symmetric contractions of muscles of the neck, trunk, and extremities.⁸ The EEG has the characteristics of hypsarrhythmia, a disorganized interictal pattern that consists of random high-voltage slow waves and spikes. In addition to classic EEG pattern, there are several hypsarrhythmia variants, which have been grouped together and termed as "modified hypsarrhythmia".^{9,10}

We reviewed the literature of infantile spasms associated with vitamin B12 deficiency, as given in (Table 1). Erol *et al.*¹¹ described 10 month-old female patient who presented with infantile spasms secondary to vitamin B12 deficiency. When she was 9 months old, she began to exhibit a series of sudden flexions of the head, trunk, arms, and legs. Her neurological examination revealed apathy and profound hypotonia with brisk deep tendon reflexes. Initiation of ACTH treatment, her spasms improved and EEG showed generalized slow activity. After addition parenteral vitamin B12 treatment (1mg daily for 10 days and then 1mg monthly for 3 months), the patient became more awake and reactive to stimuli. EEG was normal at that stage of treatment.

Malbora *et al.*¹² reported two cases of infantile spasms associated with vitamin B12 deficiency. Both of their symptoms started to occur at the age of 6 months, with a series of sudden flexions of the head, trunk, arms, and legs. Neurological examination of both infants revealed apathy and profound hypotonia with

brisk deep tendon reflexes. They had good head control; however, axial and peripheral tone had slightly weakened. The patients were treated with intramuscular cyanocobalamin; 100 mg everyday for 1 week, then 100 mg every week for 4 weeks, and then 100 mg every month for 3 months. In addition, phenobarbital (6 mg/kg/day, twice a day, orally) and synthetic adrenocorticotrophic hormone (ACTH; 40 IU/day) were administered intramuscular twice a week. After 3 months, ACTH and phenobarbital treatments were ended.

Glaser *et al.*¹³ reported a 6-month-old who had been referred due to progressive apathy. The girl was comatose, pale and tachycardic at presentation with generalized muscular hypotonia and lack of tendon reflexes. Vitamin B12 was initiated days after admission, starting with intramuscular injections for 10 days (1 mg/d). On anticonvulsive treatment with sulthiame (100 mg/d) seizures were effectively controlled after 6 weeks. Anticonvulsive therapy was gradually reduced 6 months after admission and finally discontinued.

In contrast to the patients described in the literature, our patient had normal development and neurological examination at presentation. One possible explanation would be the relatively short history of spasms (10 days), compared to the other patients. A more distinct possibility is our patient presented at an early stage on B12 deficiency, prior to increased homocysteine level, which is generally thought to be neurotoxic. It is possible that the low B12 level may be a coincidental finding and that spasms were due to another aetiology such as an occult cortical dysplasia that was not detected by our MRI. However, the fact that the patient clinically responded to vitamin B12 and ACTH and did not require additional anti-epileptic medication seem to support our diagnosis.

There is no consensus on treatment of patients with vitamin B12 deficiency with neurological manifestations. We provide vitamin B12 treatment according to the guidelines of Turkish Society of Hematology.¹⁴ Although five patients, including ours, received different vitamin B12 treatment regimes, all patients became seizure-free and EEG findings became normal. During follow-up all patients have reached age-appropriate milestones.

In conclusion, vitamin B12 deficiency may be a treatable cause of infantile spasms and should be considered in the associated cause of infantile spasms especially if there is nutritional inadequacy in the mother.

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DISCLOSURE

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