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Zekai Avci, Tuba Turul, Sabiha Aysun and Isiil Ünal

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Involuntary Movements and Magnetic Resonance Imaging Findings in Infantile Cobalamine (Vitamin B₁₂) Deficiency

ABBREVIATIONS. EMG, electromyography; Ig, immunoglobulin; MRI, magnetic resonance imaging; vit B₁₂, vitamin B₁₂.

Infantile vitamin B₁₂ (vit B₁₂) deficiency is encountered in malnourished infants or in offspring of strict vegan mothers or mothers with pernicious anemia and accompanied by hematologic and neurologic findings. We present here a 16-month-old infant whose mother had vit B₁₂ deficiency with low socioeconomic level admitted to our hospital. On admission, the patient was apathic, hypotonic, and lethargic. Serum vit B₁₂ level was below detectable limits. On cranial magnetic resonance imaging (MRI), T2-weighted images revealed bilateral frontal and parietal periventricular high-signal symmetric lesions in the white matter (delayed myelination) and frontoparietal cortical atrophy. On day 3 of vit B₁₂ therapy, involuntary movements were observed.

Received for publication Oct 2, 2001; accepted Jan 6, 2003. Reprint requests to (Z.A.) Department of Pediatrics, Fatih University School of Medicine, Alparslan Turkem cad. No: 57, 06510, Biletepe, Ankara, Turkey. E-mail: zekaivci@yahoo.com

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Vit B₁₂ is an essential vitamin and needs to be supplied by diet. Although a vit B₁₂-deficient diet can be tolerated by the adults for years from the endogenous pool, deficiency in infants may become symptomatic in a few months because of the limited hepatic reserve.¹ Infantile vit B₁₂ deficiency is common in malnourished offspring of vegan mothers and mothers with pernicious anemia and has a clinical course of ineffective hematopoiesis and neurodegenerative signs.¹⁻⁵ Here, we present a 16-month-old male infant who had severe vit B₁₂ deficiency accompanied by hematologic, neurologic, and typical MRI findings.

CASE REPORT

A 16-month-old male infant was admitted to our hospital for fever and tendency to sleep. His past medical history revealed that his mental and motor development were normal up to 8 months of age. He subsequently became lethargic and showed developmental regression. He was hospitalized for irritability and apathy during the course of a pulmonary infection.

He was the second child to nonconsanguineous parents with low socioeconomic status. He was delivered at term following an uneventful delivery. His birth weight was 3250 g. He was breast-fed until 16 months of age.

On admission, he was hypotonic, lethargic, and not following objects visually with mild dysmorphic features. He was malnourished; length: 74 cm (<3rd percentile), weight: 9 kg (<3rd percentile), and head circumference: 45 cm (<3rd percentile). He had hyperpigmentation on the dorsum of the hands, fine hair, glossitis, and hepatomegaly. He was able to sit with support and had no head control. He was generally hypotonic but had normal strength and brisk reflexes. Cranial nerve examination was normal.

A complete blood count showed macrocytic anemia (hemoglobin 5.1 g/dL, mean corpuscular volume 103.8 fl). Macrocytosis and anisocytosis were noted. The serum vit B₁₂ level was below detectable limits (limit of detection is 45 pg/mL, normal range: 157–1059 pg/mL) and serum folic acid level was 11.5 ng/dL (normal range: 5.3–14.4 ng/dL). His bone marrow aspiration revealed significant megaloblastic features. A thorough work up including blood gases, direct Coomb's test, electrolyte levels, hemoglobin F, lactic acid, pyruvic acid, ammonium level, biotinidase activity, thyroid function tests, electrocardiography, and echocardiography were normal. The patient had a history of upper respiratory tract infections.

On cranial MRI performed on day 3 of therapy, he developed anisocoria and bilateral periventricular high-signal lesions in the white matter (Fig 1). Bilateral frontal and parietal periventricular high-signal symmetric lesions in the white matter on T2-weighted images (Fig 2).

His mother’s vit B₁₂ level was also low at 125 pg/mL and her folic acid level was normal.

His diet was supported by essential elements (ZnSO₄ 50 µg/day, MgOH₂ 200 µg/day) and he was put on intramuscular vit B₁₂ (100 µg/every other day). On day 3 of therapy, he developed smacking and twitching movements of the lips and marked tremor of the tongue. On the third week he showed tremor of the left arm to tactile stimulation and on arousal. Biperidene hydrochlorate (0.5 mg 3 times daily) was added to control involuntary movements. Involuntary movements decreased after the first week of the biperidene hydrochlorate therapy. Three months later, on examination, it was observed that hypotonia, hipoactivity and involuntary movements, and hyperpigmentation on the dorsum of the hands had already disappeared. MRI findings were observed to be decreased. Today our patient is 3.5 years old and he has near normal mental and motor development.

DISCUSSION

Vit B₁₂ deficiency may have complex clinical presentation associated with hematologic, neurologic,
Infantile vit B12 deficiency was first defined in 6 South Indian infants, ages between 7 and 12 months in 1962. Vit B12 deficiency in children differs from the adults by etiologic factors, clinical presentation, and radiologic findings. It is common in the infants of the mothers with pernicious anemia, mothers who are malnourished because of low socioeconomic condition or who are on a strict vegan diet. Severe neurologic findings ranging from hypotonia, apathy, decreased visual contact, adynamia and lethargy, or even coma may accompany anemia. In contrast to severe neurologic findings in infantile cobalamine deficiency, in adolescents and adults only mild neuropsychiatric symptoms are observed. In a study of adolescents who have no hematologic abnormalities, the cognitive performance of the cobalamine-deficient group who take a vegan diet with marginal vit B12 status was found to be lower than the control group.

Although hypotonia is a frequent sign of vit B12 deficiency in infancy, correlation with EMG findings was rarely reported. Similar to our case, Renault et al reported 2 infants with severe hypotonia and apathy who had peripheral sensory motor neuropathy confirmed by EMG. The mechanism responsible for neuropathy is not clearly understood yet; however, several explanations have been suggested. The reason why he developed involuntary movements during cobalamin therapy is not clear. Similar conditions have been previously reported in the vit B12-deficient infants. Hyperglycinemia causing nonspecific interference with glycine cleavage was suggested to be responsible for abnormal movements. However, normal glycine levels in symptomatic patients excluded this hypothesis. On the other hand, Grattan-Smith et al reported the movement disorder that appeared after treatment is that after a period of severe shortage, the sudden availability of cobalamin resulted in intense stimulation of cobalamin and folate pathways and produced a temporary imbalance of metabolic pathways, with local deficiencies or excesses occurring. A metabolite that has not been demonstrated yet may be responsible for the involuntary movements.

Another distinct finding was the hyperpigmentation of the dorsal sites of the hands in our patient. This distinct finding may be significant in vit B12 deficiency. Generalized hyperpigmentation is a well-defined finding in patients with vit B12 deficiency. To our knowledge, this is the first case reported to have localized hyperpigmentation.

Vit B12 deficiency may lead to low serum IgG and IgM levels as seen in our patient. In a study on rats with vit B12 deficiency, serum IgG and IgM levels were found to be decreased. In our case, serum IgG and IgM levels normalized after vit B12 treatment, so within it was related with vit B12 deficiency.

MRI findings in infantile vit B12 deficiency differ from those of adult form. In adults subacute combined degeneration of spinal cord is detected whereas in infants cerebral atrophy and is seen. In our patient, cranial MRI showed symmetric high-signal lesions in the white matter of both frontal and parietal lobes on T2-weighted images in addition to diffuse cerebral atrophy.
CONCLUSION

Vit B\textsubscript{12} deficiency may be seen in infants and present with distinct clinical and MRI findings.

Zekai Avci, MD
Department of Pediatrics
Fatih University School of Medicine
Ankara, Turkey

Tuba Turul, MD
Sabiha Aysun, MD
Department of Pediatrics
Hacettepe University School of Medicine
Ankara, Turkey

Işıl Ünal, MD
Department of Neurology
Hacettepe University School of Medicine
Ankara, Turkey

REFERENCES

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