Cobalamin Deficiency in a Breast-Fed Infant of a Vegetarian Mother

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Vitamin B12 deficiency in infants is a rare cause of a treatable medical condition that includes failure to thrive, developmental delay, anemia, and a prominent movement disorder [1,2]. The normal newborn has sufficient vitamin B12 stored in his liver to cover all his metabolic needs until the end of the first year of life. Infants born to mothers deficient in vitamin B12 due to nutritional preferences (e.g., vegetarianism) or disease states (e.g., pernicious anemia), and who are exclusively breast-fed may develop vitamin B12 deficiency in the first months of life. The non-specific manifestations of vitamin B12 deficiency in infants may cause a marked delay in the diagnosis and result in deleterious effects on their neurodevelopment. The following case report demonstrates the importance of early recognition and treatment of this serious, treatable nutritional disorder in infancy. Laboratory cobalamin deficiency was previously described in Israel as part of general nutritional deficiencies in infants raised by a cult that practiced vegetarianism [3]; however, we are not aware of previous reports of cobalamin deficiency due to maternal vegetarianism that resulted in reversible neurologic deterioration.

Patient Description

The patient was the first child of non-consanguineous parents of Arab origin who was born following an uneventful pregnancy and normal delivery. Her birth weight was 2,850 g. She appeared to be a very quiet infant, never smiled and showed no interest in her surroundings. Although she began developing the skills of rolling over, pointing to objects and holding toys, they soon waned and she became inactive. During the few weeks before admission she had become apathetic, slept for many hours at a stretch, refused to eat and exhibited some involuntary hand movements. She was exclusively breast-fed and refused all trials of formula or baby food.

She was admitted to the Schneider's Children Medical Center at age 9 months because of fever and further deterioration in her general condition. Her weight was 6.2 kg (below the 5th percentile for her age), head circumference 42.5 cm (5th percentile) and body length at the 50th percentile for her age. She was a normal-appearing, silent baby and demonstrated good head control. Hypotonicity of the trunk and the limbs was prominent. She had fasciculations of the tongue and tremor in the limbs and head, as well as myoclonic jerks of the extremities, some of which resembled shivering attacks. The rest of the clinical examination was normal.

Initial laboratory results including serum glucose, urea, creatinine, electrolytes, calcium, phosphorous and uric acid were within normal limits. Alanine aminotransferase, aspartate aminotransferase, alkaline phosphatase, gamma glutamyl transpeptidase and total bilirubin were within normal limits. Lactic acid, ammonia, albumin, total protein and blood gases were normal. Lactate dehydrogenase was 3,400 IU, hemoglobin 8.0 g/dl, mean cell volume 96.2 U (normal 70–78), mean cell Hb concentration 36.4 U (normal 30–33), and reticulocytes 0.5%. The serum iron level was 21 g/dl, transferrin 182 mg/dl (normal 95–385 mg/dl), Hb F 5.4% and Hb A2 2.8%. Hypersegmented neutrophils and macrocytes were present in the peripheral blood smear. Bone marrow aspiration revealed hypercellular marrow with an increased proportion of promegaloblasts and the presence of giant metamyelocytes.

The serum vitamin B12 level was 13 pmol/L (normal 138–781), plasma homocysteine 118 μmol/L (normal 4–11), methionine 3 nmol/ml (normal 8–47), and urinary homocysteine 95 μmol/mmol creatinine (normally undetected). Urinary excretion of methylmalonic acid was 200 mmol/mol creatinine (normal <5).

The electroencephalogram was abnormal, showing an encephalopathic pattern with high amplitude delta waves and the absence of normal sleep activity with no epileptic discharge. A computed tomography scan of the head showed marked dilatation of the cerebral ventricles and prominent cerebral sulci and extra-axial cerebrospinal spaces compatible with brain atrophy. An auditory brain-evoked response examination showed bilateral prolonged conduction time between the nerve and the auditory brain stem (interpeak latencies I-V), compatible with a demyelination process. Her hearing was normal bilaterally.

After the laboratory results revealed the presence of severe vitamin B12 deficiency, further questioning revealed that the mother had been a strict vegetarian ("vegan") for the past 5 years. The mother had no obvious gastrointestinal disease or any neurologic abnormalities. Her hemoglobin level was 12.1 g/dl, white blood cell count 5.6 K/l, MCV 87.4 fl (normal 70–78), but her blood smear failed to show any abnormalities. Her plasma vitamin B12 concentration was 56 pmol/L (normal 138–781), and urine MMA 8 mmol/mol

MCV = mean cell volume
MMA = methylmalonic acid

creatinine (normal <5). The rest of her biochemical profile was within normal limits. No antiparietal cell antibodies were detected.

The child had a stormy clinical course that was complicated by *Klebsiella* sepsis with signs of acute hemolysis, severe leukopenia and disseminated intravascular coagulation. She recovered following treatment with antibiotics, packed cells and plasma transfusions. She was treated with daily parenteral vitamin B12 (1 mg/day) starting on the 12th day of her hospitalization when cobalamin deficiency had been confirmed. Her appetite improved gradually, and she was discharged when she had reached the point of eating appropriate amounts of infant formula. The mother was referred to her primary physician for further workup, which revealed no additional problem. She discontinued her former strict vegetarian practices and underwent parenteral cobalamin therapy. The baby gradually became more alert, began to smile and communicate and gained weight. Although the movement disorder was slow to improve, there were no signs of it at the age of 10 months. At follow-up at the age of 2 years, the child was on a normal diet and had normal cognitive and motor development. Her head circumference was 48 cm (50th percentile).

Comment

Our patient had the full-blown hematologic and neurologic manifestations of infantile vitamin B12 deficiency, which was confirmed by low serum levels of the vitamin, increased excretion of MMA and increased serum levels of homocysteine. She had weakness, anorexia, developmental delay, anemia, macrocytosis, and hypersegmentation of the neutrophils. She also had some silent feature of the condition, such as high LDH levels, low reticulocyte count and large numbers of fragmented red blood cells on the blood film that characteristically accompany cobalamin deficiency. In addition, she had a peculiar movement disorder that included tremor, twitches and myoclonic jerks that are typical for infantile cobalamin deficiency [4].

About one-half of the infants who develop signs and symptoms of vitamin B12 deficiency in the first year of life present with an unusual movement disorder [4]. These include tremor, twitches, chorea, or myoclonus that may involve the limbs, the head and the tongue in a nonuniform pattern. This movement disorder can present before treatment or several days following the initiation of vitamin B12 therapy when the infant shows general signs of improvement. The duration of the movement disorder can range from 10 to 30 days. von Schneck et al. [5] summarized the clinical description of 26 infants who had been reported up to 1997 and found that 24 of them had neurologic abnormalities at infancy; of the 16 infants for whom a follow-up was available 6 still had an abnormal neurodevelopmental status years after the correction of the cobalamin deficiency. These were the infants who were diagnosed much later (mean age 13 months) than those who improved when treatment was administered within an acceptable time frame (mean age 10 months).

Infants who are born to well-nourished mothers have about 25 μg of vitamin B12 stored in their liver at birth. The recommended daily allowance of vitamin B12 is 0.3 μg/day, while the World Health Organization recommendation is even less (0.1 μg/day for therapeutic effect). The stored vitamin B12 should be adequate to maintain the infant cobalamin status until the end of the first year of life. In mothers with vitamin B12 deficiency, the amount of vitamin B12 transferred to the infant during pregnancy and during breast-feeding is markedly decreased and, if no supplementary formula is added to the child's diet, may lead to clinical signs of cobalamin deficiency late in the first year of life, when the relationship between the maternal nutritional status and a normally born infant seems to be remote [2].

There are many causes of vitamin B12 deficiency in lactating mothers, among them abnormal absorption, inborn errors of cobalamin transport and metabolism, and decreased intake. Since the main source for cobalamin in the diet comes from meats, eggs and diary products, a prolonged, strict vegetarian diet inevitably causes a marked decrease in cobalamin liver stores and low plasma vitamin B12 concentrations that are associated with poor breast milk cobalamin concentrations. This was shown in different ethnic and religious populations that practice vegetarianism. In addition, it has been shown that folic acid, which is abundant in the vegetarian diet, may delay the development of vitamin B12 deficiency manifestations in the vegetarian patient.

Vegetarianism has a long history of association with alternative medicine and with radical and often altruistic causes, ranging from feminism, nuclear disarmament or environmental issues to animal rights. In addition, the consumption of red meat decreased in Western Europe during the last decade due to the bovine spongiform encephalopathy scare. It is not surprising that vegetarianism appeals to younger age groups, and that it puts the infants of a young vegetarian mother who has been practicing the restricted diet for prolonged periods at high risk for nutritional, developmental and hematologic disadvantages. While the trends of adopting vegetarianism in western societies seems to increase the risk of poor vitamin B12 status in infants, the rarity of the clinical syndrome may result from several possibilities, such as "partial" vegetarianism that permits consumption of other sources of vitamin B12 (diary products, fish or eggs), or the awareness of the need to supplement the diet with vitamin B12. Moreover, the availability of diverse infant formulas that can be used as a supplement to the poorly growing baby may halt the progression of the full clinical spectrum of infantile cobalamin deficiency.

We recommend that dietary assessment of pregnant and lactating women be accompanied by appropriate education and monitoring of mothers and their offspring. This will minimize the risks of poor dietary practices that can lead to infantile nutritional deficiency such as vitamin B12 deficiency.

LDH = lactate dehydrogenase

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References

1. Rasmussen SA, Fernhoff PM, Scanlon KS. Vitamin B12 deficiency in children and adolescents. *J Pediatr* 2001;138:10–17.
2. Rosenblatt DS, Whitehead VM. Cobalamin and folate deficiency: acquired and hereditary disorders in children. *Semin Hematol* 1999;36:19–34.
3. Shinwell ED, Gorodisher R. Totally vegetarian diets and infant nutrition. *Pediatrics* 1982;70:582–6.
4. Grattan-Smith PJ, Wilcken B, Procopis PG, Wise G. The neurological syndrome of infantile cobalamin deficiency: developmental regression and involuntary movements. *Mov Disord* 1997;12:39–46.
5. von Schenck U, Bender-Gotze C, Koletzko B. Persistence of neurological damage induced by dietary vitamin B-12 deficiency in infancy. *Arch Dis Child* 1997;77:137–9.

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