CASE REPORT

Vitamin B_{12} deficiency presenting as acute ataxia

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SUMMARY

A previously healthy 7-year-old Caucasian boy was hospitalised for evaluation of acute ataxia and failure to thrive, initially suspicious for an intracranial mass. Weight and body mass index were below the third percentile and he demonstrated loss of joint position and vibratory sense on examination. Laboratory studies revealed megaloblastic anaemia while an initial MRI of the brain showed no evidence of mass lesions or other abnormalities. A dietary history revealed the child subscribed to a restrictive vegan diet with little to no intake of animal products or other fortified foods. The child was diagnosed with presumed vitamin B_{12} deficiency and was treated with intramuscular B_{12} injections. Neurological symptoms resolved promptly within several days after starting therapy. This case underlines the importance of assessing nutritional status in the evaluation of neurological dysfunction in the pediatric patient.

BACKGROUND

Childhood cerebellar ataxia can be seen in a variety of disorders, including mass lesions (posterior fossa neoplasms in particular), vascular malformations, infections, genetic disorders and nutritional deficiencies. We describe a case of a vitamin B_{12} deficiency as a cause of cerebellar ataxia, a very rare and under-reported association generally seen in adulthood.

Vitamin B_{12} or cobalamin deficiency is an uncommon but treatable cause of failure to thrive and developmental delay in children. Vitamin B_{12} plays a major role in human metabolism. It is required for the conversion of methylmalonyl-CoA to succinyl-CoA, a compound metabolised by the Krebs cycle to produce energy. It also ensures activity of methionine synthase, an enzyme that catalyzes the methylation of homocysteine to form the essential amino acid methionine.[1]

In developed countries, deficiency can result from either an inborn error of absorption and metabolism or, more frequently, nutritional problems. A deficiency of this essential nutrient results in accumulation of methylmalonic acid and homocysteine in blood and urine, and the onset of clinical haematological, neurological and psychiatric manifestations.[2] The most frequent inborn error is cobalamin C disorder, which is caused by a mutation of the *MMACHC* gene, which encodes a protein critical to the metabolic pathway that leads to the formation of methionine and succinyl-CoA.[3] Vitamin B_{12} deficiency, however, most commonly occurs in infants who are exclusively breast-fed by mothers who are vegetarians or have undiagnosed pernicious anaemia, leading to low stores of vitamin B_{12} at birth and inadequate amounts of this nutrient in the breastmilk.[4]

In cases of vitamin B_{12} deficiency, haematological, neurological, psychiatric and gastrointestinal symptoms may arise. The most common symptoms in the paediatric population include failure to thrive, hypotonia, irritability or lethargy, anorexia, glossitis, developmental delay and even developmental regression.[5] Brain atrophy, delayed myelination, polyneuropathy and movement disorders have even been reported.[6] Associated laboratory findings include macrocytic megaloblastic anaemia, increased urinary levels of methylmalonic acid (U-MMA) and elevated levels of plasma homocysteine (P-HCY). Elevation of transaminses can be a common non-specific laboratory finding as well.[7] Adults with vitamin B_{12} deficiency may present with subacute combined degeneration of the spinal cord, dementia, depression and megaloblastic anaemia. This impairment of the mature nervous system develops over a period of months to years. In the pediatric population, who undergo extensive growth and development of their brains, cobalamin deficiency can cause severe impairment in just weeks to months.[4] Supplementation with cobalamin can correct the haematological and metabolic disturbances, but early recognition and treatment of this nutritional deficiency is key to preventing long-term neurodevelopmental sequelae.

We present the case of a vegan 7-year-old Caucasian boy with megaloblastic anaemia, ataxia and failure to thrive as a result of nutritional vitamin B_{12} deficiency. This case highlights the importance of recognising the varied clinical symptoms of poor nutritional status in paediatric and adolescent populations who subscribe to an alternative dietary regimen.

CASE PRESENTATION

A 7-year-old previously healthy boy presented to the emergency room with a 3-month history of progressively unsteady gait. Over the course of several months, he had progressed from intermittent clumsiness, to intermittent falling and by the date of presentation, a widened gait. In addition to the reported changes in gait, the parents noticed a change in the patient's behaviour over the preceding couple of months. He would engage in obsessive–compulsive behaviours, including lining up his toys, repetitive stair climbing and difficulty with concentration. Given the chronicity of symptoms, they were not aware of the progression of the motor and cognitive symptoms until several family members and friends had brought it to their attention. His medical history includes chronic intermittent abdominal pain for 2 years, poor dentition requiring

multiple tooth extractions and an extensively strict vegan diet since birth. He took no medications and his immunisations were up to date without any preceding illness.

On presentation his vital signs were as follows: weight 18 kg (3rd percentile), height 120 cm (26th percentile), temperature 36.1°C, pulse 62, blood pressure 86/61. General examination revealed a thin-appearing boy in no acute medical distress with poor dentition evidenced by numerous extractions. Respiratory and cardiovascular examinations were within normal limits. Abdominal examination revealed a soft, thin, non-tender abdomen with no palpable masses and normal bowel sounds. Neurological examination revealed normal mental status and cranial nerve examination. Motor examination was positive for decreased muscle bulk throughout with normal tone and strength. Sensory examination was normal to light touch, pin-prick and cold temperature throughout. Reflexes were 1+ in both upper and lower extremities. On vibratory testing, the patient had absent vibratory sense at the ankles, knees and wrists using a 128 Hz tuning fork. He had absent joint position testing of the fingers and toes up to 45°. Gait examination revealed a wide-based gait, with positive Rhomberg and difficulties with tandem straight-line ambulation. Initial laboratories were significant for a haemoglobin level of 11.8 g/dl with a mean corpuscular volume (MCV) of 107 fl. An MRI of the brain and spine were performed that revealed no abnormalities.

His neurological examination findings, elevated MCV and strictly vegan diet since birth were consistent with vitamin B_{12} deficiency that was confirmed with laboratory testing. Given the extensive neurological involvement of depressed reflexes, abnormal gait, absent joint position/vibratory sense and changes in his behaviour, a diagnosis of subacute combined degeneration was made in spite of negative MRI findings.

INVESTIGATIONS

Vitamin B_{12} level at time of initial presentation—109 pg/ml (normal 250–1205 pg/ml)

TREATMENT

- Parenteral vitamin B_{12} supplementation
- Dietary modification

OUTCOME AND FOLLOW-UP

The patient was treated with vitamin B_{12} injections at a dose of 0.2 µg/kg intramuscular for 2 days, then 1000 µg intramuscular daily for 7 days, then 100 µg intramuscular weekly for 4 additional weeks. Dosage has not been well established in children. Because hypokalaemia has been observed during treatment initiation in adults with severe anaemia, low initial cyanocobalamin doses (0.2 µg/kg, given subcutaneously for 2 days) have been recommended for children with severe anaemia. These low initial doses are followed by 1000 µg/day for 2–7 days, then subsequent weekly doses of 100 µg subcutaneously for a month.[8] Size and frequency of doses need to be carefully titrated in relation to clinical response and laboratory values.

The patient and his family received extensive counselling on proper nutritional supplementation required to maintain a healthy, well-balanced diet in the context of their vegan preferences. Repeat vitamin B_{12} testing and complete blood count were normal. After 2 months of therapy, the patient had near complete resolution of joint position vibratory sense, normal reflexes and improved cognition.

DISCUSSION

The popularity of vegetarian or other similar diets in Western culture has increased greatly over the past few decades. A 2012 Gallup survey revealed that 5% of adults in the USA are self-described vegetarians, while 2% consider themselves to be vegans.[9] Approximately 2% of American 6-year-old to 17-year-old children were identified as vegetarians, while 0.5% of this group claims to be strictly vegan.[10] Vegetarians and vegans acknowledge multiple influences over their dietary choices, including concern for the environment, long-term health benefits, religious beliefs and economic concerns.[11] The rise in vegetarianism may also be attributed to the growing ethnic diversity of the population at large. Restaurants and commercial food industries have responded in kind to this interest in alternative diets, increasing the variety of products offered to meet demand. There are several studies that have been carried out in both adult and pediatric populations that show important benefits of vegetarian diets and a relation with reduced risk for diseases like diabetes, obesity, heart disease and several types of cancers.[12] However, the exclusion of animal products in a vegetarian and vegan diet may affect cobalamin (vitamin B_{12}) status and cause elevation in plasma homocysteine levels.[13 14] The risk of nutritional inadequacy as a result of these diets increases with the number and degree of restrictions on the food groups that are consumed. The patient's willingness to use fortified foods or nutritional supplements and to accept medical advice is also an important factor to consider.

Vegan and vegetarian diets in children can be healthy if they are well balanced and include a diverse array of foods. Adequate energy intake is crucial in the pediatric population because of the intensity of growth and development during childhood and adolescence. The vegetarian diet contains less total protein than an omnivorous diet, but intake is usually satisfactory provided that total energy intake is adequate. The quality of protein intake can be of concern, as plant proteins are limited in some amino acids, like lysine, cysteine and tryptophan.[15] While vegetarian diets tend to be high in folic acid because of high intake of fruits and vegetables, they can, as evidenced in the case of our patient, be low in vitamin B_{12}, which is found in its bioavailable form only in meat and animal products.[16] Cobalamin deficiency may take years to develop, as the body is able to store sufficient quantities of this vitamin. Furthermore, high folic acid levels that occur as a consequence of the vegetarian or vegan diet can mask B_{12} deficiency megaloblastic anaemia, delaying detection of this problem until after the onset of neurological symptoms.[17]

It is not known how cobalamin deficiency causes neurological problems. In infants, the chief components of neurological syndrome of cobalamin deficiency are developmental regression and involuntary movements. Movement disorders are not a feature of cobalamin deficiency in older children and adults; rather, these patients present with axonal neuropathy and myelopathy. Some authors suggest that cobalamin deficiency leads to impaired synthesis of ethanolamine, phospholipids and sphingomyelin, resulting in alterations to myelin integrity.[18] Data on the prognosis of these patients is limited. The reported long-term dysfunctions of prolonged cobalamin deficiency in infants are diminished IQ and psychomotor delay. It would appear that long-term prognosis is more dependent on the overall duration of deficiency and severity of symptoms, rather than on serum levels of vitamin B_{12}.[19]

Efforts should be directed to preventing this dietary inadequacy, given the relationship between prognosis and duration of the deficiency. In patients who subscribe to a diet in which

consumption of animal products is restricted, supplementation or intake of fortified food is essential. Lactating women and exclusively breastfed infants of vegan mothers require supplementation, as do vegan and vegetarian children. Appropriate sources of B_{12} can include yeasts, fortified soy and nut beverages, and cereals. As breast milk of strictly vegan mothers can be low in B_{12}, their exclusively breastfed infants require supplementation.[20] Infants, children and adolescents who adhere to a vegan or vegetarian diet should be regularly assessed regarding the adequacy of their intake of fortified foods or supplements. It is recommended that at least three servings of food rich in vitamin B_{12} be included in the daily diet or supplementation provided at 5–10 μg per day.[21 22]

The patient we describe in this case presented with neurological sequelae of his nutritional deficiency. He was also malnourished, indicating that both the quality and quantity of his dietary intake were not conducive for normal growth and development. The subtle and complex nature of the patient's presentation suggested a broad differential diagnosis, as findings on examination mimicked those seen in oncological and infectious processes. While our patient ultimately exhibited clinical symptoms and laboratory findings consistent with a diagnosis of subacute combined degeneration, it is important to note that he did not have the characteristic MRI findings of increased signal intensity in cerebral white matter and posterior spinal columns typically seen on T2-weighted images.[23] This suggests that in the pediatric population, this myelopathy cannot be ruled out on the basis of normal imaging. Furthermore, the rapid reversibility of our patient's symptoms following institution of therapy emphasises the need for early detection to facilitate full clinical recovery.

Our patient's case highlights the importance of taking a dietary history, as the information gathered here allowed us to recognize and initiate treatment for this patient's vitamin deficiency and to address his poor growth. Appropriate dietary education and follow-up over time remain essential to ensure good growth and development.

Learning points

- Vitamin B_{12} deficiency is an uncommon but treatable cause of neurological dysfunction and failure to thrive in the pediatric population.
- Early recognition and treatment of the neurological manifestations of vitamin B_{12} deficiency is essential in ensuring full clinical recovery in developing children.
- Dietary assessments are crucial in the medical evaluation of all pediatric patients.

Competing interests None.

Patient consent Obtained.

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