Neuroregression in infants has diverse aetiologies, and vitamin B₁₂ deficiency is a rare one. Infantile vitamin B₁₂ deficiency is usually secondary to maternal pernicious anaemia or maternal vegetarian diet. We report a 10-month-old infant with developmental regression secondary to vitamin B₁₂ deficiency. Her mother was a strict vegetarian and the patient was exclusively breastfed. Clinical symptoms normalised after vitamin B₁₂ supplementation.

Case report

A 10-month-old female child, firstborn to non-consanguineous parents, presented with a history of regression of milestones, namely inability to sit with support, roll over or hold her neck. The mother also complained of the child having abnormal movements, especially in the upper limbs. She attained milestones appropriate for her age until 6 months of age. Birth history was normal, and the child was exclusively breastfed for 6 months. On examination, the patient looked apathetic and exhibited lassitude. She could neither hold her neck up nor reach for objects, but recognised her mother’s face. There was no pallor or hyperpigmentation of her oral cavity, and she could not control her movements, including holding her head. She was also unable to sit without support and stand with support. Repeat serum vitamin B₁₂ level was 936 pg/mL and serum homocysteine level was 10 µmol/L. She is now on a regular follow-up schedule on an outpatient basis.

Discussion

In a paediatric population, vitamin B₁₂ deficiency can be associated with haematologic, neurologic and psychiatric symptoms. Infantile vitamin B₁₂ deficiency was first reported in six South Indian infants, who presented at 7 - 12 months with megaloblastic anaemia, developmental regression and skin hyperpigmentation.[2] Infantile vitamin B₁₂ deficiency is a rare but treatable cause of developmental delay and regression, affecting exclusively breastfed infants born to vitamin-B₁₂-deficient mothers. Infant cobalamin status is determined by the cobalamin content in the breastmilk and the maternal cobalamin concentration during lactation. Maternal factors such as pernicious anaemia, vegan diet and malabsorption contribute to infant cobalamin deficiency.[3] Humans are unable to synthesise vitamin B₁₂, and their only dietary sources are products of animal origin, such as meat, liver, fish, eggs or milk. The average body store of vitamin B₁₂ in healthy adults is ~3 mg, compared with 25 µg in neonates, so adults can tolerate deficient diets for many years without visible symptoms, whereas neonates born to a vitamin-B₁₂-deficient mother can develop symptoms within a few months.[4] In our patient, vitamin B₁₂ deficiency was attributed to the maternal vegetarian diet.

Vitamin B₁₂ deficiency principally affects the central nervous system (CNS) and those tissues with rapid mitotic activity, such as digestive tract epithelium and haematopoietic cells. CNS symptoms generally appear between 2 and 12 months of age, and include vomiting, lethargy and feeding problems. Hypotonia, optic atrophy, adynamia, developmental regression and abnormal movements such as tremors or myoclonus are other hallmarks of the disease.[4] In contrast to severe neurological findings in infantile vitamin B₁₂ deficiency, in adolescents and adults only mild neuropsychiatric symptoms with vitamin B₁₂ deficiency can be associated with haematologic, neurologic and psychiatric symptoms. Infantile vitamin B₁₂ deficiency was first reported in six South Indian infants, who presented at 7 - 12 months with megaloblastic anaemia, developmental regression and skin hyperpigmentation.[2] Infantile vitamin B₁₂ deficiency is a rare but treatable cause of developmental delay and regression, affecting exclusively breastfed infants born to vitamin-B₁₂-deficient mothers. Infant cobalamin status is determined by the cobalamin content in the breastmilk and the maternal cobalamin concentration during lactation. Maternal factors such as pernicious anaemia, vegan diet and malabsorption contribute to infant cobalamin deficiency.[3] Humans are unable to synthesise vitamin B₁₂, and their only dietary sources are products of animal origin, such as meat, liver, fish, eggs or milk. The average body store of vitamin B₁₂ in healthy adults is ~3 mg, compared with 25 µg in neonates, so adults can tolerate deficient diets for many years without visible symptoms, whereas neonates born to a vitamin-B₁₂-deficient mother can develop symptoms within a few months.[4] In our patient, vitamin B₁₂ deficiency was attributed to the maternal vegetarian diet.

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 Movements is not well understood. Hyperglycinaemia causing vitamin B12 deficiency results in the accumulation of precursor propionyl-CoA, which in turn leads to odd-chain fatty acid synthesis, resulting in incorporation of large amounts of unusual C15 and C17 fatty acids in nerve sheets with altered nerve functions. Neuroimaging studies did not reveal any abnormalities in our patient.

Abnormal movements such as tremors or myoclonus have been described in vitamin-B12-deficient infants before or during treatment with vitamin B12. The reason for these abnormal movements is not well understood. Hyperglycinaemia causing nonspecific interference with glycine cleavage was suggested to be responsible for abnormal movements. However, normal glycine levels in symptomatic patients excluded this hypothesis. Grattan-Smith et al. reported that the movement disorder that appeared after treatment is due to the swift availability of cobalamin resulting in intense stimulation of cobalamin and folate pathways, producing a short-term imbalance of metabolic pathways, with local deficiencies or excesses occurring. A metabolite yet to be demonstrated may be responsible for the involuntary movements. Our patient had myoclonic jerks that disappeared after 2 months of treatment with vitamin B12.

Vitamin B12 supplementation results in rapid clinical improvement with complete resolution of structural and EEG abnormalities; however, there is a concern for long-term prognosis. Pearson and Turner followed up a child with vitamin B12 deficiency diagnosed at 32 months and found an IQ of 60 at the age of 6 years. Graham et al. identified mild cognitive impairment in 2/4 patients with cobalamin deficiency. Von Schenck et al. observed that when a diagnosis is made within 10 months of age, it has been associated with a favourable outcome compared with permanent neurological abnormalities in children whose diagnoses were made after 1 year of age.

It is important to emphasise that vitamin B12 supplementation during pregnancy should be provided for strict vegans and mothers with pernicious anaemia to avoid irreversible neurological damage in exclusively breastfed babies.

References