Vitamin B_{12} deficiency presenting with solid food aversion and global developmental delay in a child

Introduction

Vitamin B_{12} is a water-soluble vitamin which is found exclusively in food of animal origin such as meat, fish, eggs and milk (Quentin et al, 2012). It acts as an important coenzyme in the conversion of homocysteine to methionine (folate-dependent reaction) and the conversion of L-methylmalonyl coenzyme A to succinyl-CoA (Quentin et al, 2012). Dietary vitamin B_{12} deficiency is relatively common in the elderly but is rare in children. It is almost exclusively seen in infants of breastfeeding mothers who eat a strict vegetarian diet (Agrawal and Nathani, 2009; Ide et al, 2011).

Vitamin B_{12} deficiency in children can present with reversible megaloblastic anaemia, oedema (caused by hypoalbuminaemia), neurological manifestations such as irritability, apathy, developmental delay, ataxia, paraesthesia, hyporeflexia, hypotonia, tremor, seizures, loss of acquired motor abilities and coma (Reghu et al, 2005). An interesting observation seen in infants with vitamin B_{12} deficiency is difficulty in weaning on to solid foods (Reghu et al, 2005; Ide et al, 2011). This article describes a young child with vitamin B_{12} deficiency who presented with failure to wean on to solid foods and developmental delay.

Discussion

This case demonstrates the need to consider vitamin B_{12} deficiency in a young child who presents with difficulty in weaning on to solid foods and developmental delay. Delay in diagnosis of vitamin B_{12} deficiency often occurs because of its manifestation with non-specific symptoms and signs (Demir et al, 2013).

Neuroregression caused by vitamin B_{12} deficiency has been extensively reported and persistent neurological deficits are known to occur in cases in which diagnosis and treatment is delayed (beyond 12 months of age) (Incecik et al, 2010; Quentin et al, 2012; Stabler, 2013). Radiological findings of frontoparietal cortical atrophy on cranial magnetic resonance imaging (T2 weighted) images have been described in such cases (Agrawal and Nathani, 2009). A study in Turkey involving 41 children with severe vitamin B_{12} deficiency needing hospitalization demonstrated that children who made full neurological recovery had a mean age at diagnosis of 11.7 months while those with partial recovery had a mean age at diagnosis of 12.9 months (Demir et al, 2013). *Table 1* summarizes the clinical findings from two studies of children with vitamin B_{12} deficiency.

Vitamin B_{12} deficiency in infants occurs either as a result of maternal pernicious anaemia or as a result of a strict vegetarian diet in breastfeeding mothers (Reghu et al, 2005). It is important to elicit the dietetic history of a breastfeeding mother when a child presents with vitamin B_{12} deficiency. A review by Pawlak et al (2013) identified vitamin B_{12} deficiency rates and its prevalence in specific populations: 62% among pregnant women, from 25–86% among children, 21–41% among adolescents and 11–90% among the elderly. The same review (Pawlak et al, 2013) further highlighted that deficiency rates were reported to be higher among vegans compared to vegetarians and among individuals who had

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Case Report

An 18-month-old Caucasian boy of non-consanguineous parents was referred by his GP with a history of severe aversion to solid foods, faltering weight gain (was 91st centile at 6 months of age), repetitive involuntary movements of upper limbs and regression of his developmental milestones. At presentation he was exclusively breastfed. For a short period at 7 months of age he had eaten small amounts of baby rice and rusk. His mother reported having been on a strict vegetarian diet for the preceding 20 years and was not taking any vitamin supplements. There was no relevant family history; his older sisters aged 10 and 6 years were healthy and developing normally.

At presentation his weight was 10.5 kg (25th centile), height 79 cm (9th centile) and head circumference 46.5 cm (25th centile). He appeared pale, had low tone but normal reflexes. Global development delay was detected, being just able to sit unsupported with a hunched back, showing little interest in toys and demonstrating limited social skills. Laboratory investigations revealed a megaloblastic anaemia (haemoglobin 8.8 g/dl, mean cell volume 107 fl) and serum albumin, folate, ferritin, creatinine kinase and thyroid-stimulating hormone within normal limits. His vitamin B_{12} level was extremely low at <50 ng/litre (range 150–900 ng/litre). The maternal vitamin B_{12} level was 165 ng/litre and haemoglobin was 12.8 g/dl. Intramuscular hydroxycobalamin injections were started.

Marked improvement in his overall condition was noted soon after the first dose of vitamin B_{12}. Four further intramuscular injections of hydroxocobalamin at a dose of 1 mg on alternate days were administered at home. His vitamin B_{12} level normalized within 6 weeks (>7500 ng/litre). He had started eating a varied (solid) diet and made definite developmental progress – beginning to walk unaided and becoming more vocal and socially interactive. Formal assessment at 30 months of age revealed persistence of developmental delay (skills consistent with 18 months of age); this is likely to be the result of irreversible neurological damage subsequent to late treatment with delayed diagnosis of vitamin B_{12} deficiency. His latest haemoglobin and vitamin B_{12} levels were normal.

adhered to a vegetarian diet since birth compared to those who had adopted such a diet in later life.

Vitamin B_{12} deficiency is an easily treatable condition and is best diagnosed by measurement of serum methylmalonic acid, homocysteine or both (in untreated patients); an elevated level of methylmalonic acid is more sensitive and specific than vitamin B_{12} level itself for the diagnosis (Ganesan et al, 2013).

Conclusions

It is important that clinicians consider a diagnosis of vitamin B_{12} deficiency in young children presenting with solid food aversion and developmental delay as prompt recognition and treatment is likely to prevent permanent neurological damage. Delay in diagnosis of vitamin B_{12} deficiency often occurs because of its manifestation with non-specific symptoms and signs. The possibility of this diagnosis should be particularly considered in breastfed infants presenting with unexplained developmental problems, neuroregression along with failure to wean on to solids (food aversion) even in the absence of an obvious risk factor such as a history of a vegan diet in the mother. In cases where the diagnosis has been made early, improvement in clinical condition is generally seen following initiation of vitamin B_{12} treatment, but long-term neurological (and developmental) follow up is required. BJHM

Table 1. Clinical findings of children with vitamin B_{12} deficiency

Honzik et al (2010) (40 breastfed infants, average age at diagnosis 4.4 ± 2.5 months)	Anaemia – 63% (megaloblastic in 28% of all children)
	Failure to thrive – 48%
	Hypotonia – 40%
	Developmental delay – 38%
	Microcephaly – 23%
	All but one patient (98%) had methylmalonic aciduria, 80% of infants had hyperhomocysteinaemia and 87% had increased aminotransferases
Demir et al (2013) (41 hospitalized children with severe vitamin B_{12} deficiency; mean age at diagnosis 12 ± 6 months)	Growth retardation – 78%
	Hyperpigmentation of the skin – 78%
	Diarrhoea – 63.4%
	Convulsion – 14.6%
	Weakness, reluctance to eat, vomiting, irritability and tremor were found in all the patients, in addition to hypotonia, motor retardation and pallor

LEARNING POINTS

- Inability to wean a breastfed infant on to solid foods together with stagnation or regression of developmental milestones could be regarded as a red flag for potential vitamin B_{12} deficiency.
- It is important to take a maternal dietetic history, including whether any supplements are being taken.
- Marked improvement is often seen following initiation of treatment, but long-term follow up is essential.
- Neurological damage in children diagnosed late with vitamin B_{12} deficiency is likely to be irreversible.

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