Vitamin B₁₂ neuropathy in a 6 year old

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SUMMARY Gross neuropathy consequent upon selective malabsorption of vitamin B₁₂ was diagnosed in a 6 year old Bangladeshi girl brought to Great Britain for further investigation of an unexplained illness of three years' duration. The initial peripheral blood count was normal. Treatment with vitamin B₁₂ has led to substantial recovery.

Case report

The patient had lived in Bangladesh throughout infancy and childhood. Her grandparents were second cousins. She had been well until 3 years of age when her tongue became red and painful. Treatment with a multivitamin preparation produced temporary improvement but the symptoms recurred over the next three years. During this time she also suffered episodes of unexplained anaemia associated with a dimorphic blood picture, her haemoglobin concentrations ranging between 4.0 and 9.0 g/dl. She received repeated courses of iron and folic acid. Episodes of vomiting and weight loss occurred which were treated with intravenous fluids, high dose corticosteroids, and on one occasion blood transfusion. From the age of 3 years there was a gradual development of generalised muscular weakness and from age 5½ years a coarse tremor of the legs, hands, and face was noted.

The initial examination showed a thin, unhappy child who was unable to walk, sit, get out of bed, or feed unaided. She was below the third centile for weight and the 10th centile for height. There was generalised muscle wasting, hypotonia, and areflexia. She had absent corneal reflexes, difficulty in swallowing, she drooled from the side of her mouth, and her speech was slurred. Light touch sensation was preserved but other sensory modalities could not be reliably tested because of her general debilitated state. As far as we could ascertain her intellectual development had been normal. The child's tongue was red, atrophic, and showed gross fasciculation.

Initial assessment suggested the possibility of a brain stem lesion. Computed tomography showed moderate hydrocephalus with no obvious cause. Repeat tomogram after lumbar puncture and the introduction of niopam showed no focal lesion but a

general decrease in the size of the medulla, pons, and cerebellar hemispheres. Her electroencephalogram and cerebrospinal fluid were normal.

No abnormalities were detected in plasma urea, creatinine, electrolytes, calcium, phosphate, magnesium, glucose, serum creatinine kinase, copper, caeruloplasmin, lead, and thyroxine concentrations. Routine urine analysis and amino acid screening were normal.

Although the initial peripheral blood picture was normal, a repeat blood sample taken during a febrile episode showed a pancytopenia (haemoglobin 8.5 g/dl, white cell count $2.0 \times 10^9/l$, platelets $112 \times 10^9/l$, mean corpuscular volume 92.1 fl, and mean corpuscular haemoglobin 31.9 pg). The child's bone marrow was grossly megaloblastic with a seemingly complete block on red cell production. Serum vitamin B₁₂ was only 55 ng/l (low range of normal 110 ng/l). Serum folate was normal at 4.6 µg/l.

Urinary excretion was 1% and 0.1% in parts one and two respectively of the Schilling test but near maximum recovery of the labelled vitamin B₁₂ in a five day faecal collection after the test indicated near total failure to absorb vitamin B₁₂ even with exogenous intrinsic factor. Intrinsic factor antibody and autoantibody screen were negative. Resting stomach pH was 1.42 with normal acid output after intramuscular pentagastrin (6 µg/kg). Histology of gastric and duodenal mucosa and barium meal were normal. Faecal fat excretion was 5.2 g/day. Nerve conduction studies showed a mixed peripheral neuropathy, predominantly sensory. Her electro-myogram was normal.

The patient was treated initially with intramuscular hydroxocobalamin (1 mg daily) and supplementary iron and folic acid. Haematological response was rapid and after 7 days of treatment the haemoglobin concentration, white cell count, and platelet counts had risen to 10 g/dl, $9.3 \times 10^9/l$, and $323 \times 10^9/l$ respectively and the reticulocyte count to its maximum value of 18%. After 14 days the haemoglobin was 12.2 g/dl and the reticulocyte count had fallen to 6%. Repeat bone marrow aspiration one month after starting treatment was normal. Steady clinical improvement has continued to the present. Growth acceleration has been remarkable—height increasing to the 25th centile and weight to greater than the 25th centile in 16 weeks. She has become a happy, active child and is

now able to walk and run unaided. There are no involuntary movements. There is, however, a residual peripheral sensory neuropathy with generally slight reduction of power and absent tendon reflexes.

Discussion

Vitamin B₁₂ deficiency is rare in childhood; it usually occurs in breast fed infants of vitamin B₁₂ deficient mothers within the first year of life¹ or in childhood pernicious anaemia.² It may also be associated with extensive ileal resection, blind loops, and Crohn's disease.³ In our patient vitamin B₁₂ deficiency due to failure of active uptake of the vitamin B₁₂ intrinsic factor complex by the ileal mucosa was diagnosed by exclusion. This condition is commonly associated with proteinuria (Imerslund-Grusbeck syndrome),³ though this was absent in our patient.

Jadhav¹ describes florid, neurological manifestations of vitamin B₁₂ deficiency in infants, with involuntary movements and tongue fibrillation similar to that of our patient. To our knowledge, however, there is no other report documenting such severe neurological deterioration in childhood vitamin B₁₂ deficiency. Lambert,² reviewing the clinical signs in juvenile pernicious anaemia, found no central nervous system abnormality in 7 of 9 patients and only absent reflexes and diminished vibration sense in the remaining two. He concluded that only anaemia, anorexia, vomiting, and diarrhoea were common to all patients.

There are neurological manifestations of vitamin B₁₂ deficiency in up to 90% of untreated patients. The peripheral neuropathy tends to be predominantly sensory. Computed cranial tomography may show non-specific atrophy but in most cases is normal.⁴ Necropsy studies show patchy degenera-

tion of nerve fibres in both the brain and in the spinal cord.⁵

Folate may induce temporary haematological remission in vitamin B₁₂ deficiency but may also precipitate sudden and rapid neurological deterioration.⁶ Our patient received large doses of supplementary folate while in Bangladesh and this may have contributed to the severity of her illness.

In adult pernicious anaemia early treatment with parenteral vitamin B₁₂ within the first three to 6 months of the onset of symptoms leads to resolution of most of the neurological deficit, improvement occurring largely within the first 6 months.⁴ Our patient has shown steady improvement since diagnosis. There is no evidence of mental retardation, although this has been reported.² Her potential for continuing recovery is possibly greater than that of the classic, adult patient with pernicious anaemia despite the late introduction of treatment and the previous folate treatment.

Investigation of obscure neurological disease in childhood should include a vitamin B₁₂ assay even when the blood count is normal.

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Achalasia of the oesophagus presenting as foreign body obstruction

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SUMMARY A 15 year old boy with profound weight loss was found to have foreign body obstruction of the lower oesophagus. Achalasia was subsequently diagnosed and there was rapid gain in weight and height after oesophagomyotomy.

Achalasia of the oesophagus is a rare disease in children. The overall incidence is approximately 1/100 000¹ with only some 4 to 5% reporting symptoms under the age of 14 years.^{2,3} Almost all patients with achalasia present with dysphagia.⁴ Regurgitation, retrosternal pain, weight loss, and