Selective cobalamin (vitamin B_{12}) malabsorption in adolescence

A case report

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Summary
Selective cobalamin (vitamin B_{12}) malabsorption has been well described as a familial phenomenon, but severe pancytopenia in adolescence as a result of this defect has not previously been documented.

Familial selective malabsorption of cobalamin was first reported by Imerslund and was later confirmed by Gräsbeck et al. The disorder is autosomal, and usually presents in the first 2 years of life. Although occurrence in children older than 10 years has been documented, the haematological results have not been severe. Proteinuria occurs regularly but has occasionally been absent.

A case of severe pancytopenia due to selective cobalamin malabsorption in a black adolescent is reported.

Case report
A 17-year-old black youth was admitted to hospital with mental obtundation. Although no history was available initially, it was later established that he was the sixth of 9 children. He was born and schooled in Kwazulu. Lethargy and nonspecific body weakness had been absent. In the last month he had been working in Johannesburg. Meat and fresh vegetables were consumed on average 5 days per week. There was no history of head trauma, previous illnesses or weight loss. His siblings were apparently healthy. He was admitted to hospital because he had vomited yellow fluid and fainted.

On examination the patient was found to be delirious and somewhat obtunded. His general appearance was good with no evidence of malnutrition. He was pyrexial (38.5°C) with a collapsing pulse of 120/min and a blood pressure of 90/0 mmHg. Marked pallor was noted but there was no bleeding into the skin, mucous membranes or retina. He was not jaundiced. His neck was supple. No lymphadenopathy or hepatosplenomegaly was present.

The cardiorespiratory system was normal and the abdomen was non-tender. Apart from the obtundation, the neurological examination was normal. A chest radiograph was also normal. Urinalysis revealed no proteinuria. The white cell count was 2.8 x 10^9/l with a differential count of 11% polymorphonuclear cells, 87% lymphocytes and 2% monocytes. The haemoglobin concentration was 3.3 g/dl with a mean cell volume of 106 fl. The platelet count was 37 x 10^9/l and the Westergren erythrocyte sedimentation rate 5 mm/h. The blood smear revealed normochromia, anisocytosis, oval macrocytes, punctuate basophilia and fragmentation. Toxic granulation of the leucocytes was seen. The severe pancytopenia was shown on bone marrow aspirate and trephine biopsy to be due to severe megaloblastic anaemia. The serum vitamin B_{12} measurement was less than 100 ng/l, while the red cell folate level was normal (129 μg/l packed red cells). The serum ferritin value was 452 ng/ml (normal 12-400) and the serum folate level was normal (7 μg/l). Liver function tests and urea and electrolyte measurements were normal. The lactate dehydrogenase was > 1110 U.

The patient responded well to intravenous antibiotics, folic acid and intramuscular vitamin B_{12}. Supportive therapy, including platelet transfusions, was added when fundal haemorrhages were noted. The reticulocyte count rose to a peak of 48.2% after 5 days of treatment. Three weeks after admission the white cell count was 8.8 x 10^9/l and the differential count was normal.

The haemoglobin concentration had risen to 11.9 g/dl and the platelet count to 305 x 10^9/l. Stool examination was normal except for the presence of hookworm ova. These cleared when the patient was treated with mebendazole.

The Schilling test was abnormal, with less than 1% of an oral dose of 1 mg cobalt-57-labelled vitamin B_{12} being excreted in the urine. There was no improvement when the labelled vitamin B_{12} was fed together with intrinsic factor. A gastroscopy was normal as was a gastric biopsy. Antibodies to intrinsic factor were not documented. Further investigations were done to assess the absorptive function of the small intestine. A lactulose hydrogen breath test was normal, which suggested that there was no overgrowth of organisms in the small bowel. A radiographic study of the small bowel was also normal. Despite this negative finding metronidazole was given for 7 days and labelled vitamin B_{12} was again given together with intrinsic factor. Excretion of the vitamin remained less than 1%. Vitamin B_{12} binders were within normal limits. No methylmalonic acid was found in the urine and there was no increase in amino acids in the plasma. These findings appeared to exclude methylmalonic aciduria.

Before a small-bowel biopsy could be performed, the patient absconded and could not be traced; no further tests on him or his family were therefore possible.

Discussion
Cobalamin, formerly known as vitamin B_{12}, is essential for normal cell division. It cannot, however, be synthesised by mammalian tissues and must therefore be assimilated from the food chain. Nutritional deficiency of cobalamin in man occurs only in strict vegetarians who eat no meat, eggs or milk. In this patient the diet appeared to be normal and absorptive function was therefore studied.

A gastric cause seemed unlikely since gastroscopy and a gastric mucosal biopsy were normal. Furthermore, there was persistent cobalamin malabsorption despite intrinsic factor supplementation. Insofar as the small bowel was concerned, hookworm ova were isolated from the faeces. There is considerable controversy whether hookworm infection can result in malabsorption. A poor correlation has been found between the worm burden and malabsorption in most studies and Brasitus concluded in a recent review that hookworm infestation does...
not cause malabsorption in man. The fact that the Schilling test remained abnormal 1–2 weeks after the clearing of the ova suggested that the hookworms were not causing the intestinal malabsorption. The question then arose whether tropical or coeliac sprue might be present. However, these disorders are usually associated with other features of malabsorption, and in the present case the severe pancytopenia due to cobalamin deficiency would be expected to have been associated with weight loss, steatorrhoea, and low serum folate and albumin concentrations.

The transileal transport of cobalamin is poorly understood. Transcobalamin II, which is necessary for the transport of cobalamin across and out of the ileal cell, was not deficient. In addition, the cobalamin-binding proteins, which are important in plasma transport, storage and excretion, were within normal limits.

Selective cobalamin malabsorption as described by Imerslund and Gräsbeck et al. is usually familial, and presents in children and is accompanied by mild proteinuria. The patient reported is thus not typical in that he had severe pancytopenia presenting in adolescence and had no proteinuria. It was not possible to establish whether other family members were affected since none was available for study. The exact relationship of the disorder present in our patient to the previously reported cases is therefore uncertain. Whether this defect is due to loss of receptors, to abnormal receptors or to an abnormal internalisation of the ileal receptor-intrinsic factor-cobalamin complex is not clear.

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REFERENCES


Wegener’s granulomatosis in an 11-year-old child

A case report

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Summary

Early diagnosis and treatment of Wegener’s granulomatosis with cyclophosphamide has considerably improved the prognosis in this previously fatal disease. Experience with this disease in an 11-year-old child is reported.

Wegener’s granulomatosis is a necrotising granulomatous vasculitis affecting the upper and lower respiratory tract and the kidney. It is uncommon in young patients, with only 42 cases thus far reported in children, adolescents and young adults. This disease is much more common in older patients, the peak age being the 4th decade. Early diagnosis and treatment is essential for prolonged survival because, if untreated, 82% of patients die within 1 year.

Case report

An 11-year-old Indian girl presented with a 7-week history of loss of appetite, loss of weight, purulent discharge from both ears and an unresolving sinusitis. Examination revealed a pyrexial and ill-looking child with bilateral purulent otitis media, pansinusitis and several punched-out mouth ulcers. The haemoglobin was 11,3 g/dl, total white blood cell count 10,7 x 10^9/l, platelets 650 x 10^9/l with a hypochromic microcytic anaemia, left shift and toxic granulations. Urea and electrolyte values and immunoglobulin and complement measurements were normal. The erythrocyte sedimentation rate (ESR) was 104 mm/1st h (Westergren) and the purified protein derivative (tuberculin) test was negative. Two right apical

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