Failure to thrive associated with the Imerslund-Grasbeck syndrome

A. N. CAMPBELL†
M.B. B.S., M.R.C.P.

J. INGLIS**
M.B., Ch.B., M.R.C.P.

A. S. PAYNTER*
M.B. B.S., M.R.C.P.

*Departments of Child Health, †Newcastle General Hospital,
*Royal Victoria Infirmary, Newcastle, **Doncaster Royal Infirmary*

Summary

Two siblings are described who presented with failure to thrive and in whom a diagnosis of Imerslund-Grasbeck syndrome was made. Following treatment with i.m. hydroxocobalamin there was a good and rapid increase in weight and their haematology returned to normal.

Introduction

Vitamin B₁₂ deficiency in childhood is rare. Imerslund (1960) and Grasbeck *et al.* (1960) described a disorder due to selective vitamin B₁₂ malabsorption associated with proteinuria. The malabsorption is not correctable by administration of intrinsic factor.

Case report

A boy was born at full term by forceps delivery with a birth weight of 2.29 kg. He made good neonatal progress and continued to grow along the 3rd centile for weight. At the age of 18 months he began to show symptoms of lethargy, anorexia and generalized ill health. On admission, when 2 years old, his weight was below the 3rd centile at 9.0 kg.

On examination he was strikingly pale and had a loud precordial systolic murmur. There were no other physical signs. His Hb was 5.4 g/dl; WBC $9.5 \times 10^9/l$; platelets $80 \times 10^9/l$. A blood film showed a picture consistent with megaloblastic anaemia with gross anisocytosis, poikilocytosis and macrocytosis. An iliac crest bone marrow biopsy showed megaloblastic anaemia with very active erythropoiesis. Serum chemistry was normal apart from an alkaline phosphatase of 784 i.u./l. The 24-hr urinary protein excretion was 300 mg with a marked albumin band on electrophoresis. There were no intrinsic or parietal cell antibodies present in his serum. Serum vitamin B₁₂ was 80 ng/l; serum folate 11.9 µg/l; serum iron 62.1 µmol/l with a total iron binding

capacity of 67 µmol/l. A xylose absorption test showed a venous blood concentration of 1.8 mmol/l at one hr and 2 sweat sodium tests were within normal limits. A breath hydrogen test using a loading dose of lactulose showed no evidence of small bowel overgrowth, and a barium meal and follow-through was normal. A whole body radioactive scan using a tracer dose of (⁵⁷Co) cyanocobalamin showed less than 1% absorption of the vitamin at one week (normal 27-47% of dose) and a repeat using intrinsic factor failed to increase absorption.

During the investigations he received 220 ml of packed red cells increasing the Hb to 15.2 g/dl. After the diagnosis had been made he received 4×250 µg hydroxocobalamin i.m. and was discharged home on the same (3 monthly) dose.

Follow-up studies have shown him to have maintained a normal Hb and serum total vitamin B₁₂ concentration, and he has thrived, becoming more energetic and with a good appetite. One year after starting treatment his weight is now 13 kg on the 10th centile, with a height of 90 cm.

During his admission his sister, aged 15 months, was seen. She had no physical abnormalities although her weight was 8.6 kg on the 10th centile. Her Hb was 7.7 g/dl and the blood film macrocytic. Megaloblastic anaemia was confirmed on bone marrow aspiration. She was also found to have proteinuria and her serum vitamin B₁₂ concentration was borderline at 120 ng/l. A whole body cyanocobalamin study showed no absorption of vitamin B₁₂ with or without intrinsic factor. She was started on hydroxocobalamin 250 µg i.m. and since then has thrived. Her weight is now on the 75th centile, her height 86 cm, and Hb 12.1 g/dl.

The mother of these siblings has a normal Hb and serum vitamin B₁₂ concentration, but unfortunately the father was not available for investigation.

Discussion

These 2 siblings show features of Imerslund-Grasbeck syndrome with a specific malabsorption of vitamin B₁₂ leading to a severe megaloblastic anaemia associated with proteinuria. They also showed a marked failure to thrive which has responded well to treatment with parenteral hydroxocobalamin. No small bowel biopsy was performed as it was not considered justified, but xylose absorption was normal and a breath hydrogen test excluded blind loop syndrome. The fact that there was a rapid increase in weight apparently due to the parenteral hydroxocobalamin suggests that specific malabsorption of cobalamins was responsible for the failure to thrive.

Walters and Koch (1972) reported a similar case in a 16-month-old infant who gained weight from the 3rd to the 10th centile after treatment. Studies by McKenzie *et al.* (1972) suggest that the abnormality of vitamin B₁₂ absorption lies in the attachment of the vitamin to the receptors in the ileum and is not

associated with a morphologically identifiable lesion. The mild but persistent proteinuria is unassociated with other evidence of renal dysfunction and has been found in previously reported cases.

Acknowledgment

We thank Dr C. E. Cooper, Consultant Paediatrician, Newcastle General Hospital, for permission to report this case.

References

- GRASBECK, R., GORDIN, R., KANTERO, I. & KUHBACK, D. (1960) Selective vitamin B₁₂ malabsorption and proteinuria in young people. *Acta medica scandinavica*, **167**, 289.
- IMERSLUND, O. (1960) Idiopathic chronic megaloblastic anaemia in children. *Acta paediatrica scandinavica*, **49** (Suppl 119), 1.
- MACKENZIE, I.L., DONALDSON, R.M., TRIER, J.S. & NATHAN, V.I. (1972) Ileal mucosa in familial selective vitamin B₁₂ malabsorption. *New England Journal of Medicine*, **286**, 1021.
- WALTERS, T.R. & KOCH, H.F. (1972) Generalized malabsorption, failure to thrive and megaloblastic anemia. *American Journal of Diseases of Children*, **124**, 766.