

# Imerslund-Grasbeck Syndrome: A Case Report

A Cakmak, A Atas, M Soran, A Koc

## Citation

A Cakmak, A Atas, M Soran, A Koc. *Imerslund-Grasbeck Syndrome: A Case Report*. The Internet Journal of Pediatrics and Neonatology. 2007 Volume 9 Number 1.

## Abstract

To present a case thought to be Imerslund-Grasbeck syndrome because of vitamin B12 deficiency, proteinuria and glossitis. A 5-year-old girl presented at our clinic with fever, poor weight gain, pallor and findings of frequent infection. On examination, megaloblastic anaemia, glossitis and proteinuria were determined in the girl and the mother also had vitamin B12 deficiency anaemia. With these findings, the patient was diagnosed with Imerslund-Grasbeck syndrome. Vitamin B12 treatment was started and the clinical findings were corrected. The patient was followed up by the clinic for one year. Imerslund-Grasbeck syndrome should be considered for patients presenting with retarded growth development, anaemia and proteinuria. Early detection of this disorder would enable screening and genetic counselling for asymptomatic family members.

## INTRODUCTION

Familial selective malabsorption of vitamin B12 associated with proteinuria was first described by Imerslund (1960) and Grasbeck et al (1960) (Imerslund-Grasbeck syndrome) (1,2). Inherited as an autosomal recessive trait, Imerslund-Grasbeck syndrome is characterized by the onset of megaloblastic anemia and asymptomatic proteinuria during the first 2 years of life (3). It is the most common cause of cobalamin deficiency in children, and varying manifestations include an insidious debut with infections and failure to thrive, hematological and neurological symptoms, and slight general malabsorption. Mild proteinuria is frequently, but not always present, and its incidence seems to be diminishing. Genealogical studies show consanguinity and clustering of the origins of grandparents (4).

We aimed to present a case thought to be Imerslund-Grasbeck syndrome because of vitamin B12 deficiency, proteinuria and glossitis

## CASE

A 5-year-old girl presented with fever, poor weight gain and pallor. There was a 3-month history of increasing paleness, weakness, loss of weight, abdominal pain and vomiting. The patient was evaluated by a complete history, physical examination, complete neurological examination and a laboratory work-up that included a serum vitamin B12 level, urine analysis, and complete blood count. The patient's mother showed vitamin B12 deficiency anaemia with a vitamin B12 level of 124 ng/L.

Physical examination showed glossitis and the neurological examination was normal. She revealed no sign of hypotonia or hyperreflexia and her mental status was also normal. Diagnostic imaging showed a normal abdominal ultrasound. The peripheral blood smear showed hyper segmented neutrophils and macrocytic red blood cells with marked anisocytosis and poikilocytosis. No parasite was found on stool examination. The laboratory values were consistent with vitamin B12 deficiency (Table 1). A 24-hr urine collection showed an abnormal excretion of protein at 200 mg/dl and the urinalysis showed 2+ protein. The patient was started on a high daily dose of vitamin B12 of 1000 µgr IM and the treatment continued with 100µgr weekly/ IM. The anaemia and proteinuria resolved after the vitamin B12 treatment.

**Figure 1**

Table 1: Hematological Values

WBC ( $\mu$ l)	5450
Neutrophils ( $\mu$ l)	2000
Platelet count ( $\mu$ l)	206000
Reticulocytes (%)	0.73
Hemoglobin (g/dl)	5
Hematocrit ( % )	13.5
Vitamin B12 (pg/mL) (Normal: 120-700)	50.4
Total bilirubin (mg/dl)	1.2
Folate (ng/L) ( normal:4-30)	4
LDH (U/l)	4125
Ferritin (20-210 pg/l)	226

**DISCUSSION**

Imerslund syndrome, a recessive autosomal disease, is associated with megaloblastic anemia and proteinuria. The diagnosis should be considered when the three typical features are present: macrocytic anemia, decreased serum B12 level and proteinuria (5).

The pathogenesis of vitamin B12 malabsorption in this syndrome remains unknown. In one study, the uptake of IF-B12 complex in vitro by homogenised ileal biopsy specimens from one patient was found to be normal and it was therefore postulated that the defect lay at a later stage after the attachment of the IF-B12 complex to the surface of the ileal cell (6). In another detailed study of two brothers with the syndrome, IF-B 2% uptake in the ileum in vivo was examined by sub cellular fractionation of ileal biopsy specimens (7). No uptake of vitamin B12 was detected in the ileal tissue (8).

The presence of megaloblastic anemia in children should be followed by investigation of proteinuria, due to the existence of this rare disorder that has a simple diagnosis and an effective treatment (3).

Anaemia and proteinuria were determined in our patient from the clinical findings of pallor, weakness, weight loss, abdominal pain, glossitis and vomiting together with the laboratory results. The applied treatment resulted in the correction of the clinical and laboratory findings.

Vitamin B12 deficiency is a well-known cause of recurrent aphthous stomatitis, although the mechanism by which this deficiency causes the stomatitis is not well understood (9). Broides et al. demonstrated that serum vitamin B12 deficiency is associated with a neutrophil chemotactic defect and recurrent aphthous stomatitis in Imerslund-Grasbeck patients. They reported 3 infants with vitamin B12 deficiency due to Imerslund-Grasbeck, who presented with borderline or normal hemoglobin concentrations, recurrent aphthous stomatitis, and a neutrophil function defect. Vitamin B12 therapy led to an immediate resolution of aphthous stomatitis and full correction of neutrophil function (9).

The glossitis shown by our case was resolved with the vitamin B12 treatment.

In conclusion, Imerslund-Grasbeck syndrome should be considered when cases present with general symptoms together with especially retarded growth development, pallor, frequent infections, anaemia and proteinuria in the urine. This rare disorder has a simple diagnosis and can be treated effectively.

**References**

1. Imerslund O. Idiopathic chronic megaloblastic anaemia in children. *Acta Paediatr Scand* 1960;119:1-115.
2. Grasbeck R, Gordin R, Kantero I, Kuhlback B. Selective vitamin B12 malabsorption and proteinuria in young people. A syndrome. *Acta Med Scand* 1960; 167: 289-96.
3. Bonfin C, Strapasson E, Delle LA, Malvezzi M, Moreira VA, Netto AG, Martins FL, Bitencourt MA, Pasquini R. [Imerslund-Grasbeck syndrome: report of two cases] *J Pediatr (Rio J)*. 1999; 75: 477-80. [Article in Portuguese]
4. Dugue B, Ismail E, Sequeira F, Thakkar J, Grasbeck R. Urinary excretion of intrinsic factor and the receptor for its cobalamin complex in Grasbeck-Imerslund patients: the disease may have subsets. *J Pediatr Gastroenterol Nutr*. 1999;29:227-30.
5. Flechelles O, Schneider P, Lesesve JF, Baruchel A, Vannier JP, Tron P, Schaison G. [Imerslund's disease. Clinical and biological aspects. Apropos of 6 cases] *Arch Pediatr*. 1998;5:344-5. [Article in French]
6. Mckenzie IL, Donaldson RM, Trier JS, Mathan VI. Ileal mucosa in familial selective vitamin B12 malabsorption. *N Engl J Med* 1972;286:1021-5.
7. Burman JF, Jenkins WJ, Walker-Smith JA, Phillips AD, Sourial NA, Williams CB, Mollin DL. Absent ileal uptake of IF-bound vitamin B1, in vivo in the Imerslund-Grasbeck syndrome (familial vitamin B1, malabsorption with proteinuria). *Gut* 1985; 26:311-314.
8. Lin SH, Sourial NA, Lu KC, Hsueh EJ. Imerslund-Grasbeck syndrome in a Chinese family with distinct skin lesions refractory to vitamin B12 *J Clin Pathol* 1994;47:956-958.
9. Broides A, Yerushalmi B, Levy R, Hadad N, Kaplun N, Tanner SM, Chapelle Ade L, Levy J. Imerslund-Grasbeck syndrome associated with recurrent aphthous stomatitis and defective neutrophil function. *J Pediatr Hematol Oncol*.

2006; 28:715-9.

**Author Information**

**Alpay Cakmak**

Assistant Professor of Pediatrics, Department of Pediatrics, Harran University School of Medicine

**ALi Atas**

Assistant Professor of Pediatrics, Department of Pediatrics, Harran University School of Medicine

**Mustafa Soran**

Assistant Professor of Pediatrics, Department of Pediatrics, Harran University School of Medicine

**Ahmet Koc**

Professor of Pediatrics, Department of Pediatrics, Harran University School of Medicine