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SPECIAL REVIEW

Marathon of eponyms: 9 Imerslund–Grasbeck syndrome (Juvenile pernicious anaemia)

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The use of eponyms has long been contentious, but many remain in common use, as discussed elsewhere (Editorial: Oral Diseases. 2009: 15; 185). The use of eponyms in diseases of the head and neck is found mainly in specialties dealing with medically compromised individuals (paediatric dentistry, special care dentistry, oral and maxillofacial medicine, oral and maxillofacial pathology, oral and maxillofacial radiology and oral and maxillofacial surgery) and particularly by hospital-centred practitioners. This series has selected some of the more recognized relevant eponymous conditions and presents them alphabetically. The information is based largely on data available from MEDLINE and a number of internet websites as noted below: the authors would welcome any corrections. This document summarizes data about Imerslund–Grasbeck syndrome.

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Also known as

Enterocyte cobalamin malabsorption
Enterocyte intrinsic factor receptor defect
Gräsbeck–Imerslund disease
Imerslund anaemia
Imerslund syndrome
Imerslund–Najman–Gräsbeck anaemia
Imerslund–Najman–Gräsbeck syndrome
Imerslund–Najman–Gräsbeck disease
Juvenile megaloblastic anaemia
Megaloblastic anaemia 1
MGA 1
Recessive megaloblastic anaemia
Selective vitamin B12 (cobalamin) malabsorption with proteinuria

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The condition

Imerslund–Grasbeck syndrome (IGS) is a rare autosomal recessive syndrome caused by selective malabsorption of vitamin B12 resulting in megaloblastic anaemia (juvenile pernicious anaemia). Under normal physiological conditions, digestive enzymes liberate vitamin B12 from food and it subsequently binds to the glycoprotein haptocorrin (R-protein or cobalophilin), present in leukocytes, saliva and other secretions. In the small intestine, pancreatic enzymes and pH changes dissociate vitamin B12 from haptocorrin, and the vitamin then binds to intrinsic factor (IF) secreted by the gastric parietal cells. The resulting vitamin B12–IF complex then attaches to a specific receptor in the distal small intestine (ileum). The cubilin–amnionless complex is called cubam and is considered to be essential for intestinal vitamin B12 uptake and renal protein reabsorption. Subsequently, the complex is internalized by the ileal enterocyte, vitamin B12 is liberated and transferred to blood transcobalamin (also called transcobalamin II) synthesized in the intestine (probably in the vascular endothelium) and elsewhere. From the blood, the transcobalamin–cobalamin complex delivers vitamin B12 to the tissues and liver stores.

In IGS, there is mutation in the ileal enterocyte receptor that binds the vitamin B12–IF complex. Typically, there is mutation in either the cubilin (CUBN) gene on chromosome 10 or the amnionless (AMN) gene on chromosome 14.

In IGS, clinical features include fatigue, weakness, pallor, failure to thrive and grow, infections, neurological damage, gastrointestinal disorders with diarrhoea and vomiting, jaundice, heart murmur and a benign non-specific proteinuria (with no signs of renal disease) which does not resolve following B12 therapy. The syndrome may be associated with a neutrophil function defect, glossitis and mouth ulceration. Both genders are affected and the onset is typically in the second year of life. In contrast, transcobalamin deficiency and errors in the biosynthesis of vitamin B12 coenzymes result in severe illness shortly after birth. Some cases similar to IGS may be due to defects in the gastric intrinsic factor gene (GIF).

Commonly used diagnostic tests for IGS are determination of the serum total vitamin B12 or transcobalamin-bound vitamin (holo-transcobalamin) concentrations. Measurements of the metabolites methylmalonate and homocysteine are also used: in principle, methylmalonate accumulates in vitamin B12 deficiency, but not in folate deficiency. Vitamin B12 absorption tests show low absorption, not corrected by administration of IF.

Imerslund–Grasbeck syndrome symptoms are responsive to parenteral vitamin B12 therapy.

Background to eponym

A typical case of this condition was first reported by Emil Najman and B. Brausil in 1952, but most of the work has been done by Imerslund and Grasbeck. The syndrome was first fully described in Finland and Norway where the prevalence is about 1:200 000.

The main persons

Olga Imerslund was born in Norway, on 9 April 1907, and graduated in Medicine at the University of Oslo in 1936. During the next 5 years, she worked in hospitals in Halden, Stavanger and Trondheim. During World War II, she was an assistant physician at Göteborg Barnsjukhus in 1941–1942, and worked in Edinburgh at a hospital run by the Norwegian health authorities during 1943–1945. After the war, she returned to Norway to work in the children's department at Ullevål sykehus, Oslo (1947–1948), Rikshospitalet, Oslo (1948–1950), Haukeland sykehus, Bergen (1950–1951) and then again at Rikshospitalet (1951–1955). In 1956–1957, she visited the USA on a scholarship. During 1959–1961, she was head physician at the Scandinavian Teaching Hospital in Korea. She died on 23 August 1987.

Emil Najman was professor of paediatrics in Zagreb, Croatia, from 1956.

Armas Ralph Gustaf Gräsbeck was born in 1930 in Finland and, from the early 1970s, was director and professor of the Minerva Foundation Institute for Medical Research, University of Helsinki and now is on the Board of Directors.

Associated persons

Armas Ralph Gustaf Gräsbeck (born in 1930)
Olga Imerslund (1907–1987)
Emil Najman

Source internet sites (accessed 21 February 2009) and further reading

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