Selective Vitamin B\textsubscript{12} Malabsorption (Imerslund-Gräsbeck Syndrome)

Studies on Gastroenterological and Nephrological Problems

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Abstract. In a girl 10 years of age with selective vitamin B\textsubscript{12} malabsorption associated with proteinuria and residual symptoms of funicular myelosis an extensive study of the intestinal and nephrologic functions was done. Repeated Schilling tests pointed to a malabsorption pattern of vitamin B\textsubscript{12}. Gastric acid and intrinsic factor secretion as well as gastric morphology were normal. There were no antibodies against intrinsic factor and parietal cells in serum. Ileal mucosa showed on light- and electron-microscopy no pathologic changes. Pancreatic exocrine function as well as pH and calcium concentrations in the lumen of the gut were within the normal range. A general malabsorption syndrome could be excluded.

A high selective glomerular proteinuria was found through different methods. Inulin clearance was slightly reduced, PAH clearance, however, markedly so. There was no further evidence for renal tubular dysfunction. Renal biopsy showed a minimal proliferative intercapillary glomerulonephritis (minimal changes). In electron-microscopic studies a fusion of a part of the foot processes of the podocytes was found.

No familial history of the syndrome could be demonstrated in our patient.

Key words: Vitamin B\textsubscript{12} – Selective vitamin B\textsubscript{12} malabsorption – Proteinuria – Imerslund-Gräsbeck syndrome – Funicular myelosis.

Zusammenfassung. Bei einem zum Zeitpunkt der Untersuchung 10 Jahre alten Mädchen mit selektiver Vitamin B\textsubscript{12}-Malabsorption und Proteinurie wurden eingehende gastroenterologische und nephrologische Untersuchungen durchgeführt. Die Patientin wies auch nach mehrjähriger, regelmäßiger Vitamin B\textsubscript{12}-Substitution noch Restzeichen einer funikulären Myelose auf, die durch elektrodiagnostische Untersuchungen objektiviert werden konnten. Die wiederholte Prüfung der Vitamin B\textsubscript{12}-Resorption mit dem Schilling-Test zeigte eine Vitamin B\textsubscript{12}-Malabsorption. Antikörper gegen Intrinsic-Faktor und Parietalzellen konnten im Serum nicht nachgewiesen werden. Die Mukosa des terminalen Ileums wies licht- und elektronenmikroskopisch keine pathologi-
schen Veränderungen auf. Die exokrine Pankreasfunktion sowie das pH und die Calcium-Konzentrationen im Duodenalsaft waren im Bereich der Norm. Ein generelles Malabsorptions-Syndrom konnte ausgeschlossen werden.


In 1960 Imerslund [26] and Gräsbeck et al. [17] described independently a syndrome in which megaloblastic anemia develops in early childhood due to selective vitamin B₁₂ malabsorption. Persistent, benign, “idiopathic” proteinuria was associated. The syndrome was assumed to be congenital with a recessive autosomal transmission. Most of the published cases are from Norway, Finland, and Israel; the remainder are sporadic from several different countries [13]. In Western Germany up to now 9 cases have been described [4, 22, 28, 16, 36]. So far there is little known about the pathophysiology of the syndrome. Several steps of the biochemical mechanism of vitamin B₁₂ absorption are poorly understood. Furthermore the renal defect has not been differentiated satisfactorily, neither morphologically nor functionally. Therefore the association between vitamin B₁₂ malabsorption and proteinuria remains unexplained from the pathogenetic point of view. This report summarizes the results of extensive gastroenterologic and nephrologic studies in a new case of Imerslund-Gräsbeck syndrome.

Materials and Methods

Vitamin B₁₂ absorption was measured with the urinary excretion test described by Schilling [42]: Doses of 0.5 µCi ⁵⁷Co-labeled cyanocobalamine were administered either as free vitamin or with 50 mg hog intrinsic factor added. Gastric acid secretion and fasting serum gastrin concentrations were estimated as described previously [1]. In the pooled 1-h output of gastric juice after stimulation with pentagastrin the unsaturated and specific vitamin B₁₂ binding capacity were measured. The methods applied are summarized with the procedure for the identification of binding and blocking antibodies against intrinsic factor in serum by Genth [15], modifying the methods described by Irvine [27]. Parietal cell antibodies were determined by means of indirect immunofluorescence using fresh rat kidney as substrate. For the assay of vitamin B₁₂ in serum a radioassay was used [29]. Serum folate acid was estimated by a microbiological method by means of Lactobacillus casei [49]. Gastroscopy and gastric biopsies were performed with a pediatric gastroscope (Olympus model GIF type P). A biopsy specimen of the terminal part of the ileum was taken with the pediatric Watson capsule. The capsule was passed overnight and the position was determined by injection of radiopaque contrast material. Light- and electron-microscopic studies were performed by standard techniques. The evaluation of pancreas exocrine function after stimulation with 2 IU/kg secretin and subsequently with 21U/kg pancreozymin included the determination of volume, bicarbonate [39], amylase [10], lipase [25], trypsin and chymotrypsin [40], protein, bilirubin, calcium, potassium, and sodium.