Fat accumulation in enterocytes: a key to the diagnosis of abetalipoproteinemia or homozygous hypobetalipoproteinemia

Fig. 1 A 20-year-old woman was referred by her ophthalmologist to investigate the reason for her hypovitaminosis A and secondary night blindness. A macroscopic image taken during gastroscopy shows a pale duodenal mucosa.

Fig. 2 Videocapsule image illustrating the pale yet pronounced aspect of the villi.

A 20-year-old woman was referred by her ophthalmologist to investigate the reason for her hypovitaminosis A and secondary night blindness. She had no other symptoms of deficiencies in fat-soluble vitamins, no abdominal complaints, and no weight loss.

Laboratory examination revealed a deficiency in vitamin A ($<12\mu\text{g/dL}$, normal range 30–80) and vitamin E ($<0.30\text{mg/dL}$, normal range 0.5–1.8), a very low prothrombin time (30%), and very low levels of cholesterol (30mg/dL), triglycerides (4mg/dL), and LDL-cholesterol (below the

Fig. 3 Microscopic image showing vacuolization, especially on the top of the villi. Vacuolization causes a paler aspect because of fat dissolving during the process of embedding the tissue in paraffin wax ("empty" vacuoles instead of fat accumulation).

Fig. 4 Negative periodic acid-Schiff staining shows no microorganisms nor accumulation of glycogen, supporting the assumption that the vacuolization is due to lipid accumulation.

level of detection). Her level of 25-hydroxy vitamin D appeared to be normal, but at the time of her first admission, vitamin D substitution had already been started. A slightly raised alanine aminotransferase was also detected (33U/L).

Further work-up excluded cystic fibrosis, exocrine pancreas insufficiency, and celiac disease. Gastroscopy revealed a very pale duodenal mucosa; the villi, however, could be easily recognized (● Fig. 1). Videocapsule endoscopy revealed a pale small bowel mucosa with extremely pronounced villi (● Fig. 2, ● Video 1). Biopsies of the duodenal mucosa revealed areas of extended supranuclear vacuolization of the cytoplasm in the villi. These areas were interspersed with normal areas (● Fig. 3 and ● Fig. 4).

These findings suggested a diagnosis of either abetalipoproteinemia or homozygous hypolipoproteinemia, disorders that are caused by mutations in both alleles of the microsomal triglycerides transfer protein (MTP) or in the APO-B gene, respectively [1–2]. This results in the failure of APO B-100 synthesis in the liver and APO B-48 synthesis in enterocytes, leading to fat accumulation in the small intestine. This diagnosis can be con-

Video 1

Videocapsule endoscopy in a 20-year-old woman suffering from hypovitaminosis A and secondary night blindness revealed a pale small-bowel mucosa with extremely pronounced villi.

firmed by sequencing the MTP and APO-B genes [1].

This disorder can be treated by a low-fat diet, supplementation of essential fatty acids, and high oral doses of fat-soluble vitamins [1]. Follow-up is necessary to monitor potential ophthalmologic, neurologic, hematologic, and hepatologic complications [1–2].

This patient illustrates that the disorder is sometimes diagnosed in adulthood when the phenotype is mild [1–3]. The prognosis is variable but adherence to the treatment regime can restore neurological function and prevent subsequent disease progression [1–2].

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