Abetalipoproteinemia: a case report

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Abetalipoproteinemia is a rare autosomal recessive disorder characterized by steatorrhea, poor weight gain, acanthocytosis and retinitis pigmentosa. Here we peresent a six-month-old patient with abetaliporoteinemia.

He had a history of chronic diarrhea from the first month of life. He was cachectic and his motor development was delayed. Microscopic examination of the stool revealed fat. Mild anemia with reticulocytosis, acanthocytosis, low triglyceride, low cholesterol, low-density lipoprotein, high-density lipoprotein, and apolipoprotein A and B were detected. Ophthalmological examination was normal. Peroral jejunal capsule biopsy revealed normal villi and significant lipid deposition in the cytoplasm of affected cells. The patient was given large doses of vitamins E and A.

Key words: abetalipoproteinemia, acanthocytosis, steatorrhea.

Abetalipoproteinemia (ABL) is a rare autosomal recessive disorder in which patients are unable to produce the apolipoprotein B moiety of the beta-lipoprotein. This results in an inability to transport lipid material out of the intestinal epithelial cells, and a foamy lipid material accumulates within the cell cytoplasm[1]. It was first described in two siblings of consanguineous parents who developed progressive ataxia in association with fat malabsorption, atypical retinitis pigmentosa and abnormally formed red cells which were later termed acanthocytes[2]. This rare disorder is characterized by steatorrhea, poor weight gain, acanthocytosis and retinitis pigmentosa[1,3]. The first Turkish case was reported by Özsoylu et al.[4] in 1985. We present here an infant with ABL to emphasize the diagnostic role of peripheral smear, serum triglyceride, and cholesterol levels in patients with failure to thrive and steatorrhea.

Case Report

A six-month-old male infant was admitted to our hospital with a history of chronic diarrhea characterized by green and foul smelling stool since the first month of his life. He was the second child of healthy nonconsanguineous parents. Family history was unremarkable. After two months of breastfeeding, a commercially available formula was introduced because of failure to gain weight. His body weight was 3330 g, length was 58 cm (both below 3rd percentile), ratio of midarm circumference to head circumference was 0.20 (severe malnutrition), and relative weight was 65%. His motor development was delayed and ophthalmological examination was normal. He had no organomegaly.

Laboratory tests revealed: hemoglobin 8.8 g/dl and mean corpuscular volume 75 fl. A slight reticulocytosis was detected (4%). In peripheral blood smear acanthocytosis was observed (Fig. 1). His blood biochemistry revealed low triglyceride (8 mg/dl) cholesterol (48 mg/dl), low-density lipoprotein (LDL) (20 mg/dl, normal: 65-150 mg/dl), high-density lipoprotein (HDL) (34 mg/dl, normal: 35-60 mg/dl), apolipoprotein A (apo A) (84 mg/dl, normal: 94-199 mg/dl) and B (apo B) (< 35 mg/dl, normal: 49-109 mg/dl). Prothrombin time was 16 seconds. Serum aspartate aminotransferase and alanine aminotransferase levels were 95 U/L and 82 U/L, respectively. Serum albumin was within normal limits. Sweat test was negative. Stool was positive for fat. Peroral jejunal capsule

biopsy samples were prepared as frozen sections, and stained with hematoxylin-eosin (HE) and Sudan black. On light microscopy, the villi were of normal height; the cells lining the crypts and those in the lamina propria were normal. Epithelial cells covering the villi were columnar, with basal nuclei surrounded by vacuolated, foamy cytoplasm (Figs. 2-4). Frozen sections stained with Sudan black showed significant lipid deposition in the cytoplasm of affected cells. Thus, cytoplasm of columnar cells covering the tips of the villi reacted strongly with the Sudan black (Fig. 5). In order to make the diagnosis of homozygous hypobetalipoproteinemia, LDL and apo B levels of the mother were studied and were within normal limits.

The patient was given large doses of vitamins E and A (200 mg/kg/day and 20,000 IU/day, respectively) and a diet containing 180 kcal/kg/day energy.

Fig. 3. Villus is intact. Epithelial cells have many vacuoles in their cytoplasm (arrow). Nuclei which are located basally are seldom observed. Lamina propria containing blood vessels (b) is observed beneath the epithelium (HE X 20).

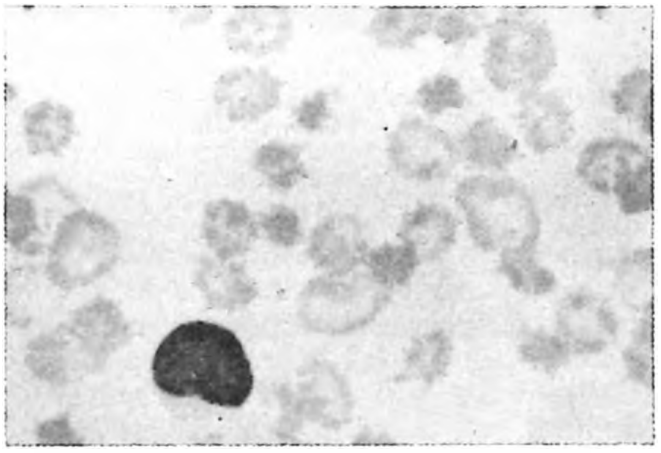

Fig. 1. Peripheral blood smear contains numerous acanthocytes (Wright-Giemsa, oil immersion X 100).

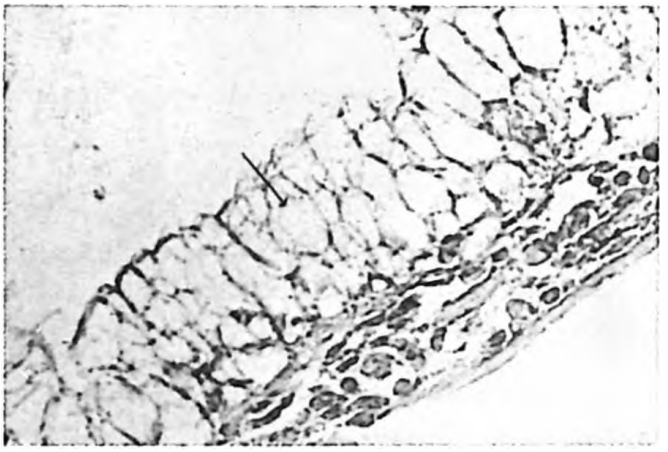

Fig. 4. Cytoplasms of the epithelial cells have foamy appearance. Nuclei are not observed in most of cells (HE X 40).

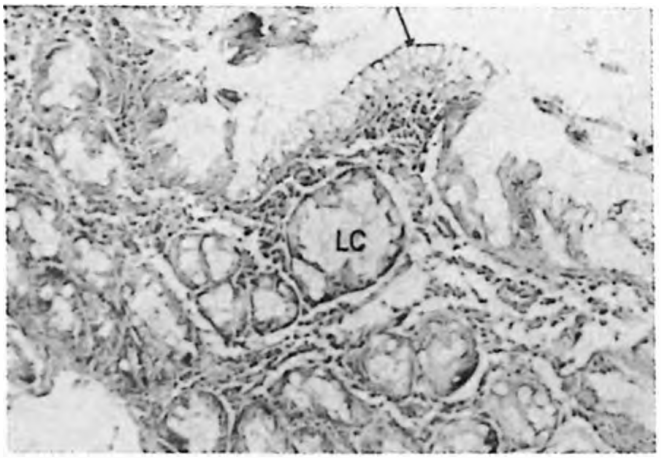

Fig. 2. Simple columnar epithelium composed of cells containing many clear vacuoles (arrow) in their cytoplasm. Lieberkühn's crypts (LC) in the lamina propria are seen (HE X 10).

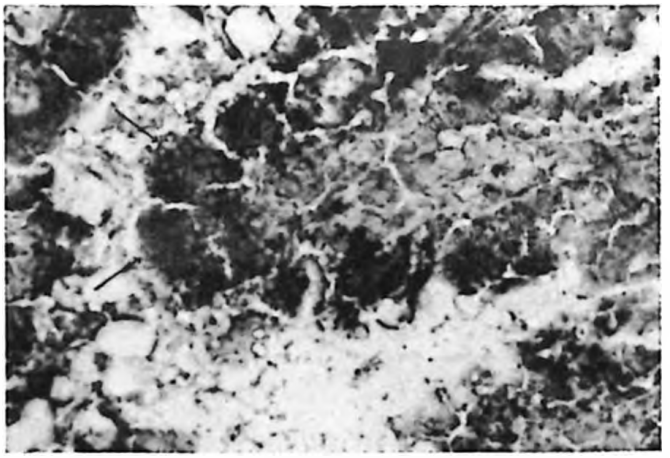

Fig. 5. Cytoplasm of the cells covering the villi react strongly with Sudan black (arrow). These cells have lipid deposition in their cytoplasm. Lipid droplets stained blue-black are observed (Sudan black X 20).

Discussion

Clinical findings of ABL are usually a result of the low absorption and transport of lipids, especially the fat soluble vitamins, A, D, E, and K[1,5]. Malabsorption of fat is common in ABL and often begins in infancy with steatorrhea and poor weight gain. Children with ABL have often been misdiagnosed as having celiac disease[3,5]. In addition to ABL, cystic fibrosis, combined immune deficiency, Wolman's disease and chylomicron retention disease should be kept in mind in infants with steatorrhea beginning in the first months of life[1].

The most prominent and debilitating symptoms are neurological and usually begin in the second decade. The first sign of disease is usually the loss of deep-tendon reflexes, followed by decreased distal lower extremity vibratory and proprioceptive senses and cerebellar signs[3,5]. Although our case was only six months old, his motor development was delayed. Patients with ABL develop atypical retinitis pigmentosa, but it is not seen until the adolescent period[1,3,6]. The ophthalmological examination of our case was normal. Oral vitamin E was given because of its preventive role[7].

Acanthocytosis is widely recognized as a typical feature of ABL in over 50% of red cells[8]. The total content of phospholipids in acanthocyte membranes is normal but their distribution is distinctly abnormal[8]. We observed acanthocytosis in our patient. The most dramatic finding may be the lipid and lipoprotein profile with a total cholesterol level from 20 to 50 mg/dl, low triglyceride levels, and negligible levels of VLDL, LDL, and apo B[3,9]. In the patient with ABL, most of the cholesterol and triglyceides are present in HDL; however, even the HDL levels are lower than normal[1,3].

Recently, it was reported that the lack of synthesis of apo B-48 is not due to the absence of the gene on chromosome 2[1,10]. The microsomal triglyceride transfer protein (MTP) is a heterodimer composed of the multifunctional enzyme, protein disulfide-isomerase, and a unique large, 97-kDa, subunit. It is found as soluble protein within the lumen of the endoplasmic reticulum of the liver and intestine and is required for the assembly of VLDL and chylomicrons[11]. Chromosome 4 includes the MTP gene (4q22-24). Mutations in the 97-kDA subunit of the MTP which result in an absence of MTP functions have been shown to cause ABL[12,13]. Jejunal biopsy is diagnostic in ABL. The appearance of the jejunal biopsy herein described was essentially similar to those in previous reports[1,14]. Treatment consists of high doses of vitamins A and E.

We present this rare genetic disease to emphasize the dignostic role of peripheral smear, serum triglyceride, and cholesterol levels in patients with failure to thrive and steatorrhea.

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