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A Rare Cause of Fat Malabsorption in Children: Chylomicron Retention Disease: A Case Report

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Abstract

***Background*:** Chylomicron retention disease is an autosomal recessive disorder causing malabsorption of intestinal fat. It is extremely rare. This report is presented because although the condition is rare in cases presenting with fatty diarrhea, inability to gain weight, and abdominal distension, it should nevertheless be considered.

***Case Presentation*:** A four-month-old girl presented due to diarrhea, inability to gain weight, and lack of appetite since birth at Çukurova University, Pediatric gastroenterology outpatient clinic, Adana, Turkey. No blood or mucus was present in stool. Her general condition was average, she appeared pale and lethargic, the abdomen was distended, and no organomegaly was present. Duodenal pathology was normal but electron microscopy revealed that the enterocytes were filled with fat globules. Causes leading to fat malabsorption were investigated, and homozygous mutation was determined in the SAR1B, chylomicron retention disease, gene.

***Conclusion*:** The patient was treated with a low-fat diet and fat-soluble vitamin supplementation resulting in significant improvement. Although it is rarely seen in patients presenting with chronic diarrhea, chylomicron retention disease should be kept in mind in the differential diagnosis.

***Key Words*:** Children, Chylomicron Retention Disease, Malabsorption, SAR1B gene.

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1- INTRODUCTION

Chylomicron retention disease is an autosomal recessive disorder causing malabsorption of intestinal fat. Chylomicron retention disease is caused by mutations in the SAR1B gene (1). Identification of the SAR1B gene mutation through genetic testing is necessary for a confirmatory diagnosis (2). It is extremely rare, with approximately 50 cases being reported worldwide (3). The diagnosis of Chylomicron retention disease is often delayed because of their nonspecific signs and symptoms. Chylomicron retention disease causes chronic fatty diarrhea, failure to thrive and hypocholesterolemia starting from the neonatal period (4). This report is presented because although the condition is rare in cases presenting with steatorrhea, inability to gain weight, and abdominal distension, it should nevertheless be considered.

2- CASE REPORT

A four-month-old girl presented due to diarrhea, inability to gain weight, and lack of appetite since birth. We learned that she was born at 35 weeks weighing 2800 g, that diarrhea had been present since birth, that she produced 5-6 fatty stools a day, and that weight gain was inadequate. No blood or mucus was present in stool. The patient's weight was 4830 g (<3p), and length 58 cm (<3p). Her general condition was average, she appeared pale and lethargic, the abdomen was distended, and no organomegaly was present. Cardiovascular system, respiratory system and neurological examination were normal. Second-degree consanguinity was present between the parents. Hemoglobin, leucocyte count, platelet count were normal. Biochemical values were AST: 126 IU, ALT: 152 IU, triglyceride; 166 mg/dl, total cholesterol: 82 mg/dl, HDL: 16.2 mg/dl, LDL: 33 mg/dl, VLDL:33 mg/dl, Apo A: 62.5 (108-225), and Apo B: 49.3 (51-165). Lipoprotein electrophoresis was presented in table I. Abdominal USG, immunodeficiency panel, and the sweat test were normal; while the esophagus and stomach were normal at upper gastrointestinal system endoscopy. Upper gastrointestinal endoscopy showed completely milky white appearance of duodenal mucosa. Duodenal pathology was normal (**Figure.1**), but electron microscopy revealed that the enterocytes were filled with fat globules (**Figures 2, 3**).

Abetalipoproteinemia and hypobetalipoproteinemia genetic tests were normal. Causes leading to fat malabsorption were investigated, and homozygous mutation was determined in the SAR1B, chylomicron retention disease, gene. The fat-soluble vitamin support the patient was receiving was maintained. Diet was adjusted to a medium-chain fatty acid-rich one. The patient is currently hospitalized, normally producing 4-5 fatty stools a day and with diarrhea attacks every two months, during which fatty diarrhea is produced 10-12 times daily. She is presently 14 months old, weighs 7400 g, and is under observation in Çukurova University, Pediatric gastroenterology clinic, Adana, Turkey.

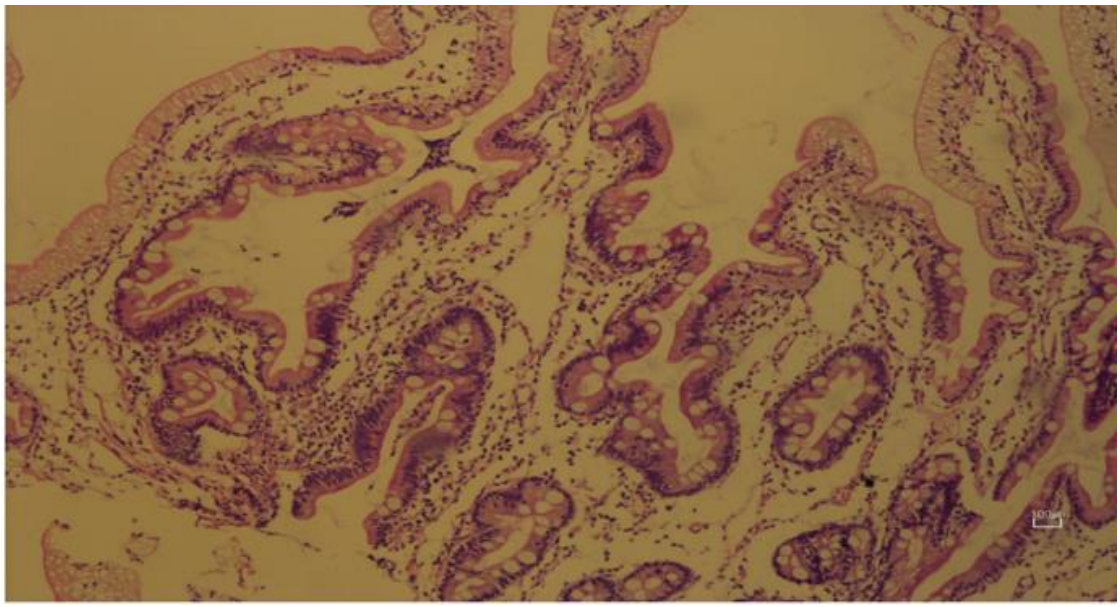

Fig.1: The intestinal biopsy: normal villi.

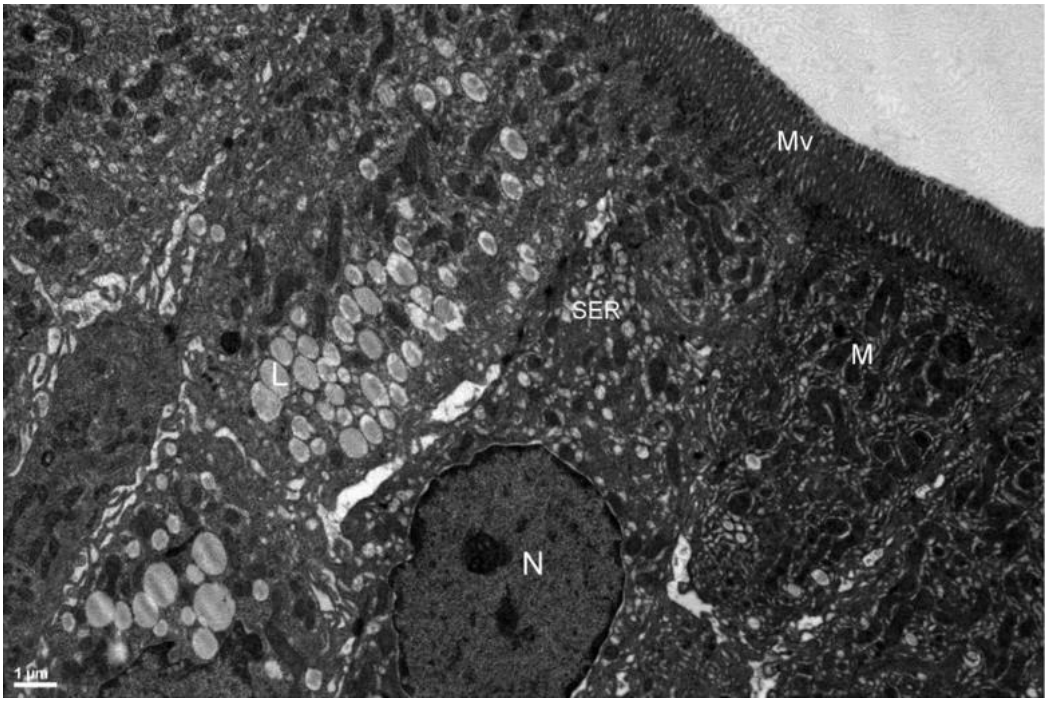

Fig.2: The columnar epithelial cells (enterocytes) of the intestinal mucosa are shown. The microvilli (Mv) on the apical surface, nucleus (N), mitochondria (M), smooth endoplasmic reticulum (SER), and lipid droplets (L) in the cytoplasm are indicated. Bar= 1µm.

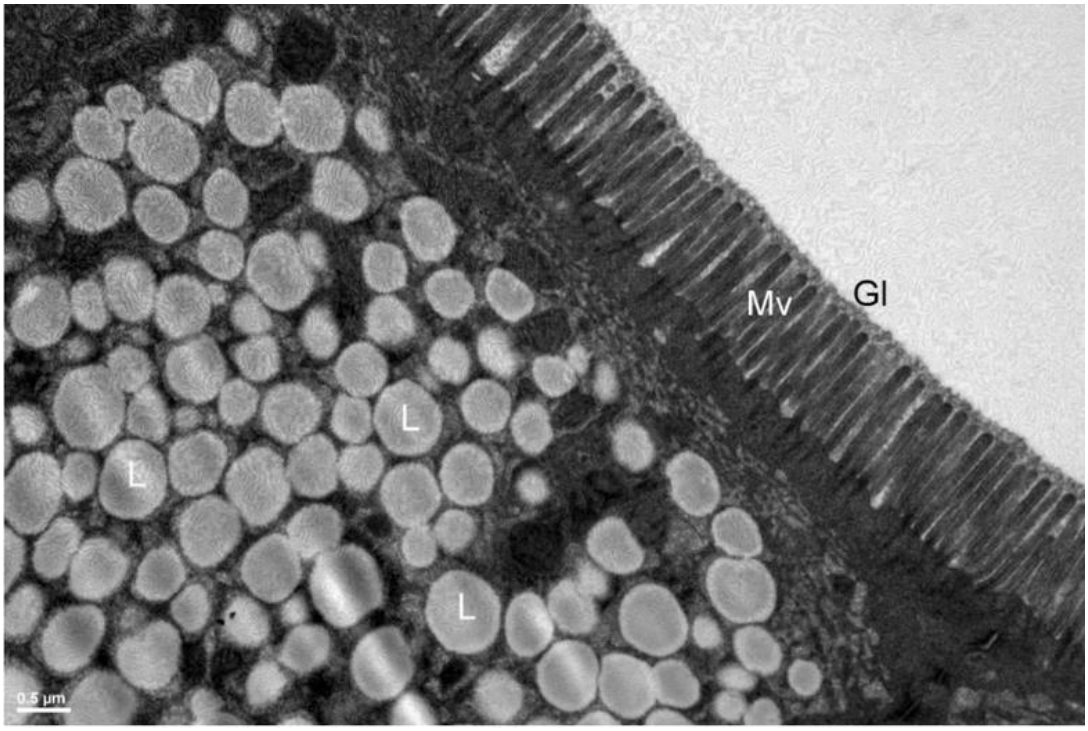

Fig.3: The enterocyte reveals normal microvilli (Mv) and the glycocalyx (Gl) on the apical surface, but many of the lipid droplets (L) are shown in the apical cell cytoplasm. Bar= 0,5 µm.

3- DISCUSSION

Chylomicron retention disease is an autosomal-recessive condition caused by mutations in the SAR1B gene (4). Different mutations has been identified, although it seems that there is no genotype-phenotype correlation (1). As it was previously reported by Sassolas et al. (5), until 2012, mutations in the SARB1B gene has been established in 43 patients, respective to 17 mutations. Since then, as far as we know, 5 new diagnosis were reported in the literature (6-8). Failure to thrive, chronic diarrhea, and hypocholesterolemia emerge in early infancy, between one and six months (4). Similarly, to our patient, most infants present with an unremarkable birth history followed by vomiting, steathorrea and failure to thrive (9). Hepatomegaly, high transaminases and steatorrhea are determined in approximately 15% of cases. Hepatomegaly and elevated transaminases are frequently seen and are secondary to steatosis. No case of cirrhosis has been reported (4, 5). The diagnosis is supported by the presence of white duodenal mucosa upon endoscopy, the presence of cytosolic lipid droplets and lipoprotein-sized particles in the enterocytes biopsy and by the identification of a mutation in SAR1B gene (5, 9). Mild villous atrophy may be present in some patients, and if lipid vacuoles are missed in that situation, the condition may be confused with celiac disease. Duodenal pathology was normal in our case. We think that since we placed the duodenal biopsy specimen into formalin during upper GIS endoscopy, as we do in all cases, the fats inside the enterocytes dissolved and were not observed. Duodenal biopsy specimens should be placed into physiological fluid in such cases, and sent directly to the pathology lab. Treatment is aimed at preventing nutritional deficiencies and optimizing growth. Nutrition rich in essential fatty acids and medium chain triglycerides and poor in fat should be provided in treatment.

Severe complications such as sensory neuropathy, ataxia, and proprioceptive abnormalities may occur due to vitamin E deficiency. Various ophthalmological complications may occur in association with vitamin A deficiency, and osteopenia may develop due to vitamin D deficiency (4). All patients must receive fat-soluble vitamins via the oral route. Vitamin E (50 IU/kg/day), A (15,000 IU/day), D (800-1.200 IU/day), and K (15 mg/week) replacement must be administered (10, 11). In addition to fat-soluble vitamins, folic acid and iron can also be given if required. Dose adjustment must be performed based on plasma levels. Serum vitamin levels almost never reach normal ranges, despite sufficient amounts and durations of vitamin support and symptom stabilization (10).

Treatment should not therefore be guided by serum vitamin levels alone, and the clinical picture should be considered. We readjusted the doses of these vitamins that our patient had received previously. Transaminase control at every examination and ultrasonography every three years are required due to hepatosteatosis and rarely seen steatohepatitis. One study performed in France and Canada investigated 16 children with a mean age of 12 years, mean time since diagnosis of two months, and follow-up times ranging between four and 10 years. Normal prenatal and natal history, growth retardation, chronic steatorrhea, low plasma cholesterol levels, normal plasma triglyceride levels, and low vitamin E levels despite high-dose vitamin E support were determined in all cases. Hypoalbuminemia was reported in 80% of cases, ALT elevation in 75%, and hepatomegaly and hepatosteatosis in 25% (9). Muscle pains and cramps, decreased deep tendon reflexes, creatine kinase elevation, decreased ejection fraction at echocardiographic examination, and lipid vacuoles at muscular biopsy have been reported in adult patients (11). Hypoalbuminemia, transaminase elevation, low plasma cholesterol levels, and normal triglyceride levels were also determined in our case. Since treatment was initiated promptly, no ophthalmological or neurological complications have to date been observed in our patient.

4- CONCLUSION

Fat malabsorption is one of the important causes of congenital diarrhea. Cystic fibrosis is the first condition to be considered in the context of fat malabsorption. However other, albeit rare, causes of fat malabsorption should be remembered. Chylomicron retention disease is a rare familial hypocholesterolemic syndrome characterized by lipid malabsorption.

5- CONFLICT OF INTEREST: None.

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