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Case Report

A rare case of abetalipoproteinemia

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ABSTRACT

The disease studied here abetalipoproteinemia (ABL) is a very rare autosomal recessive disorder which is caused by microsomal triglyceride alteration in protein gene mutation. ABL is defined by a lack of lipids and apolipoprotein B in the plasma, as well as fat malabsorption and a variety of clinical symptoms. We report a 21-year-old male with a history of persistent diarrhea, steatorrhea, and growth retardation who was born to consanguineous parents. The patient was diagnosed with ABL and was treated with dietary changes and fat-soluble vitamin replacement, as well as being monitored on an outpatient basis.

Keywords: Apolipoprotein B, ABL, Fat malabsorption, Steatorrhea, Growth retardation

INTRODUCTION

Absence of plasma apolipoprotein B and (apo B)-containing lipoproteins characterises ABL, a rare hereditary autosomal recessive metabolic condition of fat and fat-soluble vitamin malabsorption caused by microsomal triglyceride transfer protein (MTP) deficiency.[1,2] MTTP is a chaperone protein found in the endoplasmic reticulum of enterocytes and hepatocytes. It has three structural domains (N-terminal -barrel, -helix, and C-terminal) as well as three functional domains (transfer activity, membrane interaction and the lipid binding).

Bassen and Kornzweig were the first to report a link between peripheral blood acanthocytosis and atypical retinitis pigmentosa and ataxia in 1950.[3] According to the signs and absence of lipoproteins, the illness was later called "ABL" by Salt and colleagues.[4]

A total absence of plasma apolipoprotein (apo) B-containing lipoproteins, chylomicrons, VLDL, and LDL was determined to constitute a biochemical abnormality.

ABL is caused by a defect in apo B post-translational processing and secretion, which is linked to a lack of MTP function. Patients with ABL are most common in their second to fourth decades, with a few in their first and sixth decades. A more severe phenotype causes earlier presentation. Chronic diarrhoea develops, which subsides with time as patients learn to avoid fatty foods. Fat soluble vitamin insufficiency develops during childhood and is exacerbated by a high-fat diet. Vitamin E at high doses raises serum vitamin levels to 30 percent of the lower limit. Serum levels can be normalized with high doses of vitamin A treatment. The transport of vitamin A in the blood by retinol-binding protein is unaffected in ABL. Demyelination affects both the central and peripheral nervous systems.

The disease usually appears in the first or second decade of life.

Multiple prior research have found that vitamin E therapy improves neurological dysfunction in the long run, and that early treatment before the age of 16 months avoids neurological dysfunction.

In the course of the disease, myositis, and retinitis pigmentosa are also found. Large doses of vitamins E and A, as well as a low-fat diet, were provided to the patient.

The molecular basis of this disorder is the inheritance of two mutations in the MTTP gene, which is located on chromosome 4q23 and encodes the large subunit of MTTP, which is a 97-KDa protein with 894 amino acids that forms a heterodimer with the endoplasmic reticulum enzyme protein disulphide isomerase and accelerates the transfer of lipids onto apolipoprotein B, in the liver and intestine, apo B is assembled and secreted, leading in the production of VLDL and chylomicrons, respectively.[5,6]

The history and clinical symptoms of a patient with ABL who was referred to our institution with chronic diarrhoea, cachexia, ataxia, and visual abnormalities are described in this paper.

CASE REPORT

A 21-year-old man was admitted to our hospital with severe diarrhoea and weight loss. He describes passing 3-6 episodes of bulky, oily, greasy, watery stools with no concomitant blood or mucus, no history of tenesmus, urgency, or incomplete evacuation, and no history of nocturnal episodes.

He exhibited an ataxic stride, nodded his head, and had a visual deficiency that required finger counting from 6 meters when he presented. He'd lost a lot of muscle mass. On the day of the presentation, his weight was around 40 kg and my height was 150 cm.

Table 1: Laboratory tests.

Tests	Results
CBC	
Hb	9.4 gm/dl
MCV	79 fl
TLC	7700
DLC	N 64/L 28/ M6/ E02
Platelets	2.88 lakhs/cumm
Peripheral smear	Showed acanthocytes and few fragmented RBC
Stool routine	
Stool RE/ME	Pus cells occasional
RBC	Absent
Fat globules	Present
Lipid profile	
Cholesterol	34 mg/dl (130-200)
TG	9 mg/dl (<150)
VLDL	1.8 mg/dl (5-51)
LDL	1.2 mg/dl (<130)
HDL	31 mg (30-70)
Random blood sugar	
RBS	90 mg/dl
USG	
Abdomen	Thickening of jejunal loops

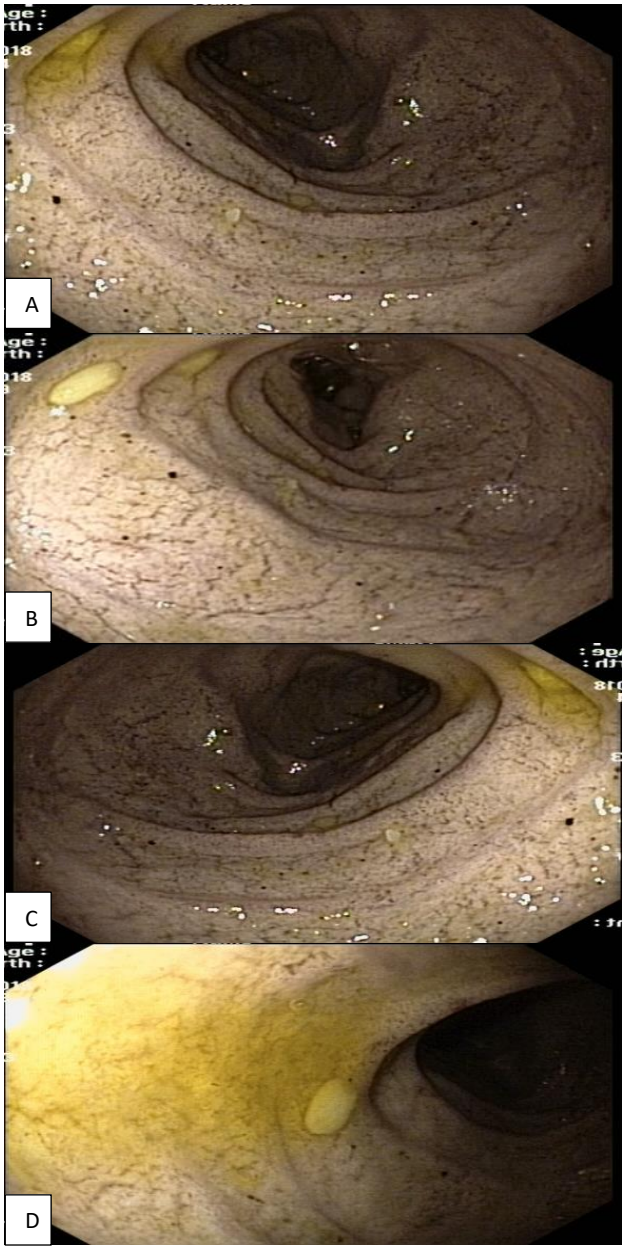

Figure 1 (A-D): Gastroscopy-normal mucosal pattern till D2.

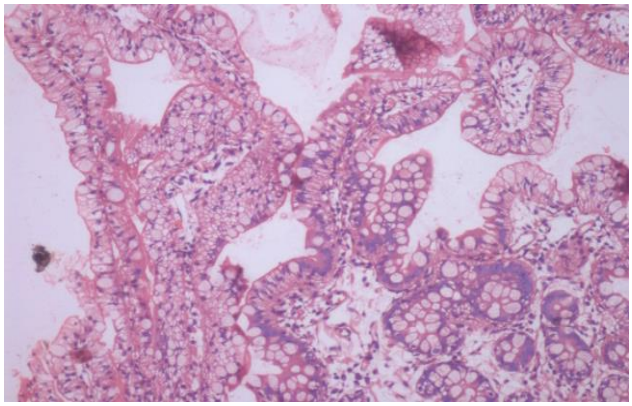

Figure 2: Biopsy showed lymphoplasmacytic infiltration and vacuolated cytoplasm.

The parents lipid profiles were completely normal. It would have been beneficial to perform molecular diagnosis but unfortunately the parents did not agree to do genetic study.

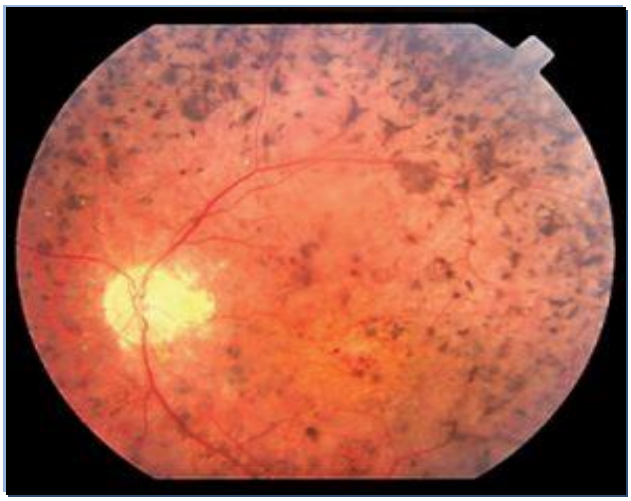

Figure 3: Fundoscopic examination revealed presence of retinitis pigmentosa.

Cystic fibrosis (CF) and celiac disease were the most likely differential diagnoses in the presence of symptoms, but severe hypocholesterolemia and hypotriglyceridaemia suggested ABL, homozygous familial hypobetalipoproteinaemia (FHBL) with dominant transmission (mutations in the APOB gene), and chylomicron retention disease (CMRD) with recessive transmission (mutation in SAR1B gene).

Celiac disease and CF were ruled out by normal levels of tissue transglutaminase antibodies and a sweet chloride test, as well as microscopic examinations. The lipid profile of the family proved helpful in distinguishing between various illnesses.

The presence of fat globules in the stool and undetectable quantities of plasma apo B and low-density lipoproteins ruled out CMRD, while acanthocytes in the peripheral smear and acanthocytes in the peripheral smear validated the diagnosis of ABL.

Dietary changes and high-dose fat-soluble vitamin supplements were part of the treatment. Our patient was given Caprilon formula, 1 cc/kg/day medium-chain triglycerides (MCT) oil, 400 IU/kg/day vitamin A, 150 mg/kg/day vitamin E, 1000 IU/day vitamin D, 5 mg daily vitamin K, and additional dietary supplements such as iron and folic acid.

Every six months, he was weighed and showed that he had gained the proper amount of weight. After 6 months of dietary changes, his weight had gained to 43 kg. Liver aminotransferases were increased (AST 160 and ALT 250 U/L), but after enforcing a strict fat-restricted diet, these enzyme levels returned to normal during follow-ups.

DISCUSSION

Absence of apoB-containing lipoproteins in plasma characterises ABL, a relatively rare recessive metabolic condition. Malabsorption of fat and fat-soluble vitamins causes a variety of clinical phenotypes, beginning with steatorrhea and failure to flourish in early childhood and progressing to multi-system disorders as the patient grows older.[7] The majority of individuals are diagnosed in their second to fourth decades, with only a handful in their first and sixth decades. Early onset of symptoms could indicate a more severe phenotype that is more resistant to medical therapy, leading to poor results. On the other hand, due to the implications of fat-soluble vitamin insufficiency, later presentation and a longer duration of untreated disease may be associated with bad results.

The majority of ABL patients experienced lipid malabsorption, abnormally low serum lipid levels, and gastrointestinal symptoms such as diarrhoea, steatorrhea, and oral fat intolerance. Fat-soluble vitamin insufficiency has also been linked to retinitis pigmentosa, myopathy, and spinocerebellar ataxia in the majority of individuals. Some of the patients had liver involvement.[8-9]

Fat intolerance, diarrhoea, steatorrhea, growth retardation, developmental delay, and low TG and cholesterol levels were all signs and symptoms of early onset ABL in our patient. In addition, typical signs of the intestinal biopsy were detected. Ina study by Zamel et al the majority of described individuals had gastrointestinal signs such as fat intolerance, diarrhoea, and steatorrhea.

Retinitis pigmentosa was discovered during a fundoscopic examination. Sobrevilla et al studied that both the central and peripheral nerve systems can be damaged by ABL, which is the most significant clinical symptom. The fundamental pathology is gradual demyelination of the neurological system, which is caused by aberrant lipid peroxidation of the highly unsaturated phospholipid of myelin, which is proven to be caused by a long-term vitamin E shortage.[10] Several studies have shown that starting high-dose vitamin E therapy (100 IU/Kg) before the age of two years can help to avoid increasing neurological dysfunction and reduce neurological sequelae.[11]

ABL manifests itself in the eyes in a variety of ways. The most common problem associated with ABL is retinitis pigmentosa. Pigmentary retinal degeneration is a form of macular degeneration that involves slowly growing annular scotomas. Early on in the course of the disease, patients may experience impaired night vision or colour vision. Preventing the formation and progression of retinopathy with high dosage vitamin E therapy or a combination of vitamin E and vitamin A therapy before the age of two has been shown in previous research.[12-14]

The hematologic manifestation of ABL is red cell acanthocytosis, which has been reported in multiple cases

in a study conducted by Zamel et al and is also evident in our patient.

Fat malabsorption generates a mixture of unabsorbed fatty acids and calcium ions in the intestinal lumen, resulting in increased absorption of dietary oxalate and kidney stone development in patients with ABL. [15] Dietary fat limits, fat-soluble vitamin supplements, a particular formula, and polycitrate were used to treat the patient's issue.

Although our patient did not have hypothyroidism, a link between ABL and subclinical hypothyroidism has been reported in a few investigations previously.[16]

In some cases, hepatic involvement was documented, including hepatosteatosis and cirrhosis.[17] Our patient's hepatic involvement was increased serum transaminases, which were likely caused by hepatosteatosis and cleared with proper treatment.

CONCLUSION

ABL may exhibit specific symptoms in addition to the standard signs and symptoms. To avoid the difficulties that can arise from fat-soluble vitamin deficiency, it's critical to have a proper diagnosis and therapy as soon as possible.

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