

Case Report

Abetalipoproteinemia a rare case of malabsorption disorder with diagnostic insights: a case report

Behnaz Darban¹ · Mina Rabbani² · Salar Golmohammadzadehkhiaban² · Fereshteh Karbasian³ · Mohammad ali Molavi¹

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Abstract

Background Abetalipoproteinemia (ABL) is a rare autosomal recessive disorder marked by significantly reduced or absent levels of plasma cholesterol, low-density lipoproteins (LDLs), and very-low-density lipoproteins (VLDLs). This condition is also referred to as Bassen-Kornzweig syndrome. Patients with ABL commonly exhibit symptoms affecting the neurological, hematological, and gastrointestinal systems, arising from deficiencies in fat-soluble vitamins and impaired absorption of fat. This case report presents the unique challenges of diagnosing and managing ABL in an infant, emphasizing the importance of early recognition to prevent neurological complications.

Case presentation We hereby report a case involving a 7-month-old male infant of Middle Eastern descent, who was admitted to Khalij Fars Hospital for evaluation of poor weight gain and frequent loose, bulky stools. Upon further investigation, the patient was diagnosed with Abetalipoproteinemia (ABL) and subsequently managed with dietary modifications and oral fat-soluble vitamins, resulting in improved growth and developmental progress.

Conclusions This case underscores the need for timely recognition and tailored management of ABL to mitigate developmental and neurological complications, ultimately improving quality of life and outcomes. It also highlights the importance of screening in consanguineous populations to enable early diagnosis.

Keywords Abetalipoproteinemia (ABL) · Fat malabsorption · Microsomal triglyceride transfer protein (MTTP) · Medium-chain triglycerides (MCT) · Case report

1 Introduction

Abetalipoproteinemia (ABL) is a rare autosomal recessive disorder caused by pathogenic mutations in both alleles of the MTTP gene on chromosome 4q23. These mutations lead to dysfunction of the microsomal triglyceride transfer protein (MTTP; OMIM 157147) [1]. The disease is linked to over 33 identified mutations. Most mutations are frameshift, nonsense, and splice-site mutations in the MTTP gene, resulting in truncated forms of MTTP and a complete loss of function [2, 3]. The MTTP gene is responsible for producing microsomal triglyceride transfer protein (MTTP), which is a dimeric lipid transfer protein that comprises protein disulfide isomerase and a unique 97-kDa subunit. MTTP plays a crucial role in the

✉ Mina Rabbani, rabbani.mina73@gmail.com; Behnaz Darban, Darban.sm@gmail.com; Salar Golmohammadzadehkhiaban, salarkhiabani76@gmail.com; Fereshteh Karbasian, Karbasian.md@gmail.com; Mohammad ali Molavi, shayanmolavi@yahoo.com |

¹Department of Pediatrics, Clinical Research Development Center of Children's Hospital, Hormozgan University of Medical Science, Bandar Abbas, Iran. ²School of Medicine, Iran University of Medical Sciences, Tehran, Iran. ³Department of Paediatric, Gastroenterology and Hepatology, Ali-Asghar Children's Hospital, Iran University of Medical Sciences, Tehran, Iran.



transfer of lipids, including triglycerides and phospholipids, between membranes, which is essential for the formation of lipoproteins.. Recent findings [4, 5] indicate that mutations in the gene encoding the 97-kDa subunit of the microsomal triglyceride transfer protein lead to abetalipoproteinemia, a hereditary condition characterized by the impaired synthesis of chylomicrons in the intestine and very low-density lipoproteins in the liver [4, 5].

Clinically, ABL manifests with both gastrointestinal and neurological symptoms due to impaired lipid absorption and vitamin deficiencies." Abetalipoproteinemia has yielded significant insights into the physiological mechanisms underlying lipoprotein assembly and vitamin E metabolism [4]. Additionally, research on ABL patients has highlighted the crucial role of hepatic secretion of VLDL in delivering vitamin E to peripheral tissues [6]. These findings emphasize the critical function of vitamin E in supporting optimal physiological performance across various tissues [7].

One common symptom of abetalipoproteinemia is the inability to absorb fats, which can lead to signs such as failure to thrive, diarrhea, and vomiting, usually appearing in infancy. Acanthocytosis, anemia, and hemolysis may also occur, leading to increased levels of bilirubin in the blood [2].

Other symptoms may involve hepatomegaly, loss of night and color vision, acquired atypical pigmentation of the retina, as well as spinocerebellar ataxia and myopathy [2, 8].

2 Case report

A 7-month-old male infant of Middle Eastern descent, born to consanguineous parents, was referred to Khalij Fars Hospital(South of Iran) in March 2023 due to poor weight gain. The patient's parents are first cousins, increasing the likelihood of inheriting autosomal recessive disorders like ABL. At birth, his weight was 3860 g, height 50 cm, head circumference 34 cm, and chest circumference 36 cm. The patient's mother noted that he had not been weighed since he was 5 months old. This case underscores the importance of regular pediatric check-ups, especially in infants with consanguineous parental backgrounds.

During the initial assessment, it was noted that the patient's weight was 5 kg and height was 64 cm. All growth parameters were below the 3rd percentile on the growth chart. Additionally, the patient had been experiencing loose bulky stools for the 3 weeks before presentation and had a history of being hospitalized for 10 days due to suspected congenital pneumonia.

In the case study, the patient presented with no reported family history of similar medical issues. Upon physical examination, abdominal distention and tympanic resonance were observed, The patient had dry skin and dry eyes. The conjunctiva appeared pale, and there were no signs of scarring or eczema. Examination revealed hepatomegaly, with the liver palpable three centimeters below the costal margin and having a soft consistency. No splenomegaly or other signs of organomegaly were observed. The liver edge nodule was not palpable, and auscultation of the liver was normal but no evidence of organomegaly. Additionally, there was no history of chronic liver disease or bloody diarrhea.

Additionally, hyporeflexia and decreased deep tendon reflexes (DTR) were noted, while all other examinations yielded normal results. Hyporeflexia and decreased deep tendon reflexes (DTRs) were noted, likely due to vitamin E deficiency, which can lead to peripheral neuropathy and spinocerebellar involvement if untreated."

Laboratory findings are summarized in Table 1. Key results included significantly low cholesterol (49 mg/dL) and triglyceride (24 mg/dL) levels, elevated liver enzymes (AST 98 U/L, ALT 98 U/L), and peripheral blood smear findings indicative of anemia and hemolysis (anisocytosis 1+, hypochromia 2+, target cells 1+, microcytosis 2+, schistocytosis 3+).

Stool exam: consistency loose, color yellow, fat 2+, mucus negative, RBC negative, WBC negative, no occult blood.

The retinal fundoscopy revealed no abnormalities, and echocardiogram (Echo) appeared normal.

The microscopic findings during the endoscopy revealed normal mucosa in the esophagus and stomach while showing dilated lacteals of the lymphatic vessel in the duodenum.

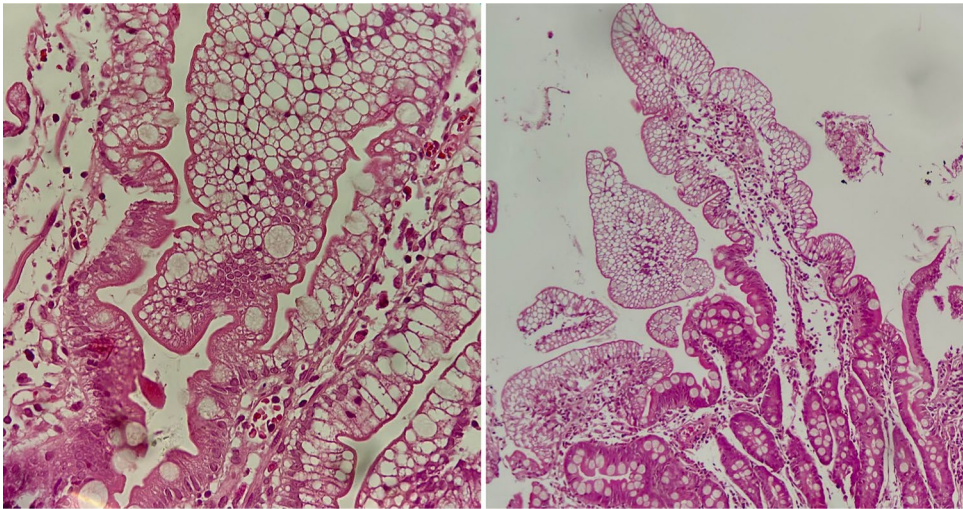
"Pathology reports preserved villi, mild excess Lymphoplasmacytic cell infiltration in lamina propria intraepithelial, less than 20/100 enterocytes, and cytoplasmic epithelial villi vascularization compatible with the diagnosis of abetalipoproteinemia, as shown in Fig. 1. The presence of dilated lacteals in the duodenum and lymphoplasmacytic infiltration in the lamina propria are consistent with fat malabsorption, supporting the diagnosis of ABL.

Dietary changes were implemented alongside high-dose oral supplementation of fat-soluble vitamins as part of the treatment plan. The patient followed a medium-chain triglyceride-rich diet and received vitamins E, A, D, and K at dosages suitable for correcting infant deficiencies, including vitamin A at 10000 IU/day, vitamin D at 800 IU/day, vitamin E at 1000 IU/day, vitamin K at 5 mg daily, vitamin B12, medium-chain triglycerides (MCT) oil at 1 cc/kg/day, and Caprilon formula.Regular blood tests were conducted to monitor for potential toxicity or deficiencies related to

Table 1 Laboratory findings

Test	Result	Reference range
Cholesterol	49 mg/dL	120–200 mg/dL
Triglyceride	24 mg/dL	30–150 mg/dL
AST (aspartate aminotransferase)	98 U/L	10–40 U/L
ALT (alanine aminotransferase)	98 U/L	7–56 U/L
Total protein	6.4 g/dL	6.0–8.3 g/dL
Albumin	4 g/dL	3.5–5.0 g/dL
T4 (Thyroxine)	10.2 nmol/L	5.0–12.0 nmol/L
TSH (thyroid stimulating hormone)	2.45 mIU/L	0.5–5.0 mIU/L
Peripheral blood smear	–	–
- Anisocytosis	1+	Negative
- Hypochromia	2+	Negative
- Target Cells	1+	Negative
- Microcytosis	2+	Negative
- Schistocytosis	3+	Negative
Stool examination		
- Consistency	Loose	Normal (formed)
- Color	Yellow	Brown
- Fat	2+	Negative
- Mucus	Negative	Negative
- RBC (red blood cells)	Negative	Negative
- WBC (white blood cells)	Negative	Negative
- Occult blood	Negative	Negative

Fig. 1 Duodenal Mucosa Biopsy showing dilated lymphatic vessels (lacteals) within the lamina propria (H&E stain, 400× magnification), a characteristic histological finding in abetalipoproteinemia (ABL) due to impaired fat absorption



high-dose fat-soluble vitamin supplementation [4, 9]. We conducted regular check-ups every 6 months, observing appropriate weight gain and performing ophthalmological and neurological evaluations. Regular follow-up included ophthalmological and neurological evaluations, hepatic ultrasonography, bone mineral density measurements, and echocardiography every 3 years to monitor for potential complications. Additionally, we recommended hepatic ultrasonography, bone mineral density measurement, and echocardiography every 3 years for further evaluation. The patient was not hospitalized and received outpatient treatment. At the 3-month follow-up, the patient showed significant improvement in weight gain and developmental milestones. Improvements in weight gain and developmental milestones were assessed through regular pediatric evaluations and parental reporting. The family reported adherence to the dietary and supplementation plan, with no adverse effects noted [2, 10].

The patient's family expressed relief at the improvement following diagnosis and treatment, particularly as they were concerned about the patient's developmental delays.

3 Discussion

Abetalipoproteinemia (ABL; OMIM 200100), is an extremely rare autosomal recessive disorder of lipoprotein metabolism, estimated to occur in fewer than 1 in 100,000 individuals with a strong association with consanguineous marriages. This condition exhibits an autosomal recessive inheritance pattern, necessitating the presence of mutations in both alleles of the gene for the manifestation of the disease. Furthermore, the prevalence of this disorder is uniform across both sexes, affecting females and males equally [7, 11].

Differential diagnoses for ABL include conditions with overlapping features such as fat malabsorption, growth failure, and neurological deficits. These include celiac disease, an autoimmune disorder triggered by gluten characterized by diarrhea and villous atrophy on biopsy; Crohn's disease, an inflammatory bowel condition presenting with chronic diarrhea and granulomas on biopsy; and familial hypobetalipoproteinemia (FHBL), a genetic lipid disorder causing low LDL levels, typically milder and later-onset than ABL. In this case, hallmark findings such as severely low cholesterol levels, fat-soluble vitamin deficiencies, consanguinity, and specific histological features confirmed ABL, excluding other diagnoses.

When a person is conceived, each sibling of an individual with a genetic condition has a 25% likelihood of being affected, a 50% likelihood of being an asymptomatic carrier, and a 25% likelihood of being unaffected and not a carrier. Carrier testing is a viable option for at-risk relatives, and prenatal as well as preimplantation genetic testing can be performed if the pathogenic variants in the MTTP gene within the family have been identified [12, 13].

The symptoms of Abetalipoproteinemia (ABL) typically manifest during infancy and are often observed following breastfeeding. Common symptoms include vomiting, steatorrhea due to fat malabsorption, and failure to thrive. Affected individuals may attempt to mitigate these gastrointestinal symptoms by avoiding dietary fat [13]. Upon endoscopic examination, the intestinal mucosa may exhibit a distinct snowy appearance, known as snow-white duodenum, which is caused by the accumulation of undigested fats due to impaired chylomicron assembly [10, 14].

The primary concern of the mother, who visited the hospital, was loose, bulky stool 3 weeks before the appointment. This symptom aligns with abetalipoproteinemia (ABL), as individuals with this condition often experience steatorrhea, which presents as loose, bulky stools. ABL is the result of mutations in the MTTP gene, causing malabsorption of dietary fats due to an impairment in chylomicron assembly [15]. The undigested fats are expelled in the stool, indicating an underlying issue with lipid transport and absorption. Thus, it is essential to address fat malabsorption through tailored dietary interventions to effectively manage the condition and avert complications [2].

In the presented patient, we noticed a decrease in deep tendon reflexes. Thus, The decreased deep tendon reflexes (DTRs) in ABL patients are primarily due to the neurodegenerative effects of prolonged vitamin E deficiency. Early diagnosis and adequate vitamin E supplementation are critical to prevent or slow the progression of neurological damage, including peripheral neuropathy and spinocerebellar ataxia, resulting in peripheral neuropathy and, in some cases, spinocerebellar involvement. These neurological impairments are a hallmark of the disease and emphasize the critical need for early and adequate vitamin E supplementation to prevent or slow the progression of neurological damage [8].

Ensure adequate caloric intake to promote healthy growth; maintain a low-fat diet consisting of 10%-20% of total calories from fat; consider oral essential fatty acid supplementation, such as up to 1 teaspoon per day of oils rich in polyunsaturated fatty acids; Tailored dietary modifications and supplementation of fat-soluble vitamins are critical in managing ABL to prevent neurological and developmental complications, as detailed in the case report. Mild anemia typically does not require treatment, although in some cases, vitamin B12 or iron therapy may be necessary [4, 7].

This case emphasizes the diagnostic complexities of abetalipoproteinemia in infancy, especially in consanguineous populations. Early diagnosis and tailored treatment with vitamin supplementation can improve prognosis and quality of life, reducing the risk of severe neurological impairment.

Those who do not receive treatment may experience unusual pigmentation of the retina, leading to a gradual loss of night vision and/or color vision in adulthood. Untreated individuals may also show neuromuscular symptoms such as progressive loss of deep tendon reflexes, reflexes, vibratory sense, and proprioception; muscle weakness; dysarthria; and ataxia typically appearing in the first or second decades of life [9, 16].

4 Conclusion

In summary, abetalipoproteinemia is a rare but clinically significant disorder, especially in populations with a high prevalence of consanguineous marriages. Early diagnosis and tailored management, including vitamin supplementation and dietary modifications, are critical in preventing severe neurological and developmental complications. This case highlights the importance of raising awareness about ABL among clinicians to ensure timely recognition and intervention. Future research should focus on the long-term outcomes of high-dose vitamin therapy in ABL patients and the development of genetic screening programs for at-risk populations to facilitate early diagnosis and intervention and also focus on exploring the long-term outcomes of high-dose vitamin therapy in ABL patients and developing genetic screening programs for at-risk populations. Such initiatives could pave the way for earlier diagnosis and improved management strategies, ultimately reducing the burden of this condition.

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Author contributions B.D. and M.A.M. identified the case and initiated the hospital's initial clinical management. F.K. conducted a detailed investigation and oversaw the treatment process. M.R. and S.G. were responsible for data collection and drafting the manuscript. All authors critically reviewed and approved the final version of the manuscript, ensuring its accuracy and integrity.

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Data availability The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate This study was approved by the Medical Ethics Committee of Iran University of Medical Sciences. Informed consent for participation in the study was obtained from the patient's legally authorized representatives (parents).

Consent for publication Written informed consent for publication of this case report and any accompanying images and data was obtained from the patient's legal guardians. A copy of the written consent is available from the corresponding author upon reasonable request.

Competing interests The authors declare no competing interests.

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