# Rickets and dysmorphic findings in a child with abetalipoproteinemia

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## ABSTRACT

يتميز نقص البروتين الدهني بيتا في الدم (Abetalipoproteinemia) بظهور كريات الدم الحمراء الشائكة (acanthocytosis)، والإسهال الدهني المزمن، ونقص الكوليسترول في الدم.

نستعرض في هذا المقال حالة طفل مُصاب بنقص البروتين الدهني بيتا وكان يبلغ من العمر 18 شهراً، وقد صاحب هذا النقص بعض الشذوذ في جسم الطفل وكساح. لقد تم تحويل المريض لعمل الفحوص اللازمة بسبب معاناته من تأخر في النمو وإسهال دهني حاد. أظهرت الفحوصات إصابة الطفل بالشحوب، وبعض الشذوذ في الوجه، بالإضافة إلى إصابته بالكساح. كما وأظهرت تحاليل المختبر إصابته بنقص في مستويات كلاً من: الهيموغلوبين (3.7 غرام/ديسيلتر)، والألبومين (28 غرام/لتر)، ونقص الكولسترول والدهون الثلاثية في الدم. كشفت لطخة الدم عن وجود كريات دم حمراء شائكة، فيما أظهرت الخزعة المأخوذة من أنسجة الأمعاء الدقيقة تباعد الخلايا المعوية عن بعضها مع وجود قطرات دهنية. استجاب المريض لعلاجه المكون من الفيتامينات القابلة للذوبان في الدهون (ADEK)، والحليب الصناعي المصنوع من البروتين المُهدرج والذي يحتوي على دهون ثلاثية متوسطة السلسلة. ولقد أصبح برازه طبيعياً بعد ثلاثة أشهر، بالإضافة إلى عودة نسبة الفيتامينات القابلة للذوبان في الدهون إلى معدلها الطبيعي وكذلك زيادة وزن الطفل من 4.1 كجم إلى 5.9 كجم.

Abetalipoproteinemia (ABL) is characterized by acanthocytosis, hypocholesterolemia, and steatorrhea. Here, we describe a case of ABL associated with rickets and dysmorphic findings and the subsequent therapeutic course in an 18-month-old male referred for evaluation for failure to thrive and chronic fatty diarrhea. Examination revealed a pale child, dysmorphic face, and signs of rickets. Laboratory examination revealed low hemoglobin (3.7 gm/dl), low albumin (28 gm/L), low cholesterol and triglyceride levels. The blood smear showed acanthocytes while the small bowel histology showed the enterocytes were distended with lipid droplets. He was diagnosed with ABL and treated with fat-soluble vitamins (ADEK), and hydrolyzed protein formula containing medium chain triglycerides. Three months later, his fatty diarrhea becomes normal stool, his serum fat-soluble vitamins normalized, and his weight increased from 4.1 kg to 5.9 kg.


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Abetalipoproteinemia (ABL) is a rare autosomal recessive disorder of lipid metabolism characterized by the absence of very low-density lipoproteins (VLDLs) and low-density lipoproteins (LDLs) from plasma, acanthocytosis, and steatorrhea.[1] We present this case to report both rickets and dysmorphic findings together as an initial presentation of ABL, with the subsequent therapeutic course.

**Case Report.** An 18-month-old Saudi male was referred for evaluation for failure to thrive and chronic diarrhea. He was the product of a full-term, uncomplicated pregnancy, and birth weight of 2.9 Kg. His stools were described as being "oily" since birth, not bloody, and consisted 4 times/day. There was a poor appetite and poor weight gain associated with abdominal distension. There was no history of vomiting, pulmonary complaints, feeding difficulties, or recurrent infections. There was no travelling history or contact with animals. His diet consisted of breast feeding and baby food. Other systemic review was unremarkable. Examination revealed weight of 4.1 Kg (below 5th

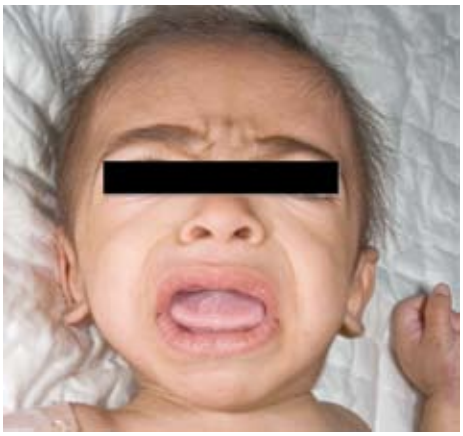

**Figure 1 -** Dysmorphic findings in abetalipoproteinemia.

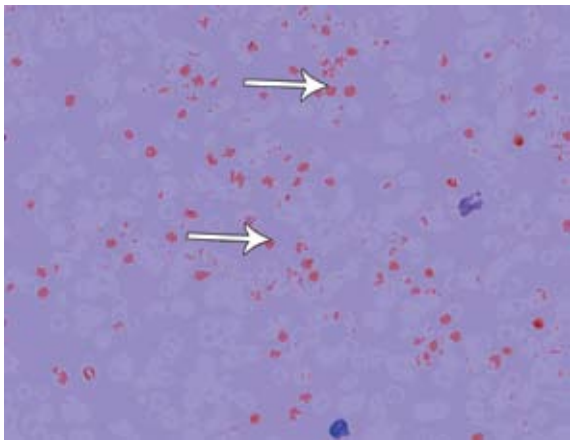

**Figure 2 -** The peripheral blood smear showed acanthocytosis (crenated erythrocytes with spiny excrescences) (arrows).

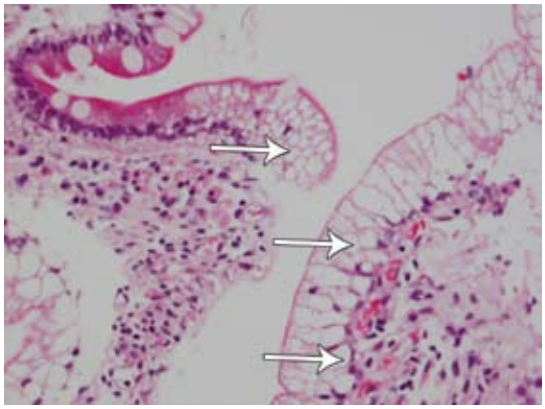

**Figure 3 -** The small bowel histology showed normal villi with marked lipid vacuolization of glandular epithelial cell (arrows).

percentile), length of 60.5 cm (below 5th percentile), and head circumference of 39 cm (below 5th percentile). He was pale looking with decreased subcutaneous fat tissue. He had signs of rickets including box-shape head, rickety rosary, and wide wrist joints. He had dysmorphic features including hypertelorism, short nose, long philtrum, thin upper lip, and large mouth (**Figure 1**). The abdomen was slightly distended and there was no organomegaly. There were no cutaneous lesions. Other systemic examinations were unremarkable except decreased reflexes in lower limbs. Laboratory examination revealed serum calcium 1.84 mmol/L (2.1-2.5); phosphate 0.60 mmol/L (0.74-1.5); magnesium 0.67 mmol/L (0.70-0.95), and alkaline phosphatase 724 IU/L (0-500). He had normal serum electrolytes, blood urea, nitrogen, creatinine, and aminotransferase concentrations. A complete blood count revealed normal platelet and white blood cell counts, but the hemoglobin (3.7 gm/dl), mean corpuscular volume (MCV), and mean corpuscular hemoglobin (MCH), were low. The blood smear showed a significant number of acanthocytes (**Figure 2**). The serum albumin was low (28 gm/L). International normalized ratio (INR) was 1.5. Stool analysis revealed significant fat droplets, but 72-hour stool collection was not carried out. A fasting lipid profile showed a cholesterol level of 0.75 mmol/L (<4.40), triglyceride 0.08 mmol/L (<2.25) and high-density lipoprotein (HDL) 0.48 mmol/L (>1.55). The upper endoscopy showed pale duodenal mucosa. The small bowel histology revealed normal villi with enterocytes that were distended with lipid droplets (**Figure 3**). He was diagnosed with ABL based on the presence of acanthocytes on peripheral blood smear, low lipid profile (cholesterol and triglycerides) and characteristic lipid droplets on duodenal biopsy. He was treated with fat-soluble vitamins (ADEK) supplements 2 ml once daily and special hydrolyzed protein formula (Monogen), which contains 90% of fat as medium chain triglycerides (MCT). He was also received oral high dose of vitamin E 800 I.U/day. Three months later, his fatty diarrhea became normal stool, his serum fat-soluble vitamins were normalized, his hemoglobin of 3.7 gm/dl was improved to 8.7 gm/dl, and his weight increased from 4.1 kg to 5.9 kg.

**Discussion.** Abetalipoproteinemia (Bassen-Kornzweig syndrome) was first described in 1950 as a condition characterized by acanthocytosis, hypocholesterolemia, progressive combined posterior column degeneration, peripheral neuritis, mental retardation, retinitis pigmentosa, and steatorrhea.[1] This autosomal recessive disorder results from mutations of the microsomal triglyceride transfer protein (MTP), the gene of which maps to 4q22–q24.[2] Patients manifest defective assembly and secretion of apoprotein B (apoB)-containing lipoproteins, leading to the absence of chylomicrons, VLDL, and LDL in the plasma.[3]

Apo(B) is the main apolipoprotein of chylomicrons and LDLs. It occurs in the plasma in 2 main forms: apoB48 and apoB100. The ApoB48 is synthesized exclusively by the gut and apoB100 by the liver.[3] The low plasma cholesterol concentrations are due to the low levels of apoB-containing lipoproteins (VLDL and particularly LDL) that transport most of the cholesterol. In turn, low levels of apoB are due to low production rates of both mutant and wild-type forms of apoB in heterozygotes.[4] Affected children usually present within the first year of life with failure to thrive. Fat malabsorption results in foul-smelling, bulky stools. Other gastrointestinal symptoms include abdominal distention, diarrhea, and vomiting.[5] These symptoms are similar to our patient in addition to signs of rickets, which is an unusual initial presentation of ABL as rickets is due to vitamin D deficiency. Narchi et al[6] described an unexpected initial manifestation of rickets in 2 children with ABL and hypobetalipoproteinemia. The dysmorphic features in our patient, which includes hirsutism, hypertelorism, short nose, long and slightly smooth philtrum, thin upper lip, large mouth, decreased subcutaneous fat and distended abdomen are unusual initial presentations of ABL. Solomon et al[7] described dysmorphic findings in 2 cases of ABL/hypobetalipoproteinemia. Our patient was diagnosed with ABL based on the presence of acanthocytes on peripheral blood smear, low lipid profile (low VLDLs, cholesterol and triglyceride) and characteristic epithelial vacuolization on duodenal biopsy in the context of normal parental cholesterol profiles. Genetic testing to rule out other causes for the dysmorphic features included chromosome analysis on peripheral blood, testing for fragile X syndrome, and fluorescence in-situ hybridization testing around the MTP locus to assess for a small microdeletion, all of which were not carried out. Hematological manifestations of ABL are usually mild. Hemolytic anemia is due to vitamin E deficiency. Decreased cholesterol levels result in deformation of red blood cell membranes, which cause the acanthocytosis apparent on the peripheral smear.[8] The ABL is associated with a number of visual disturbances, including night blindness, nystagmus, ophthalmoplegia, and retinitis pigmentosa.[5] Neuromuscular signs of ABL appear in the first or second decade of life, beginning with the loss of deep tendon reflexes. Untreated patients eventually manifest diminished proprioception, cutaneous sensory loss, and movement disorders, such as ataxia, intention tremors, and chorea. Mental retardation occurs in nearly one-third of affected patients.[5] Treatment of ABL consists of restriction of long-chain fatty acids, supplementation with medium chain fatty acids, and megadoses of vitamins A, D, E, and K to prevent long-term complications.[3] Long-term complications are those associated with malabsorption of fat-soluble vitamins. If left untreated, ABL results in progressive neurological manifestations due to decreased vitamin E levels. Low vitamin E levels lead to peroxidation of unsaturated myelin phospholipids.[5]

In summary, we report a rare lipid disorders (ABL), characterized by acanthocytosis, low lipid profile, and characteristic fat droplets on duodenal biopsy. In addition, our case reports the presence of both rickets and dysmorphic finding in ABL. Early diagnosis and initiation of treatment of ABL offers the best chance for improved outcome.

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