CASE REPORT

Abetalipoproteinemia: A novel mutation of microsomal triglyceride transfer protein (MTP) gene in a young Tunisian patient

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Received 28 October 2015; accepted 7 December 2015
Available online 25 January 2016

KEYWORDS
Abetalipoproteinemia; apoB-containing lipoproteins; Hypcholesterolemia; MTP gene mutations

Abstract Abetalipoproteinemia (ABL), or Bassen–Kornzweig syndrome, is a rare autosomal recessive disorder of lipoprotein metabolism, characterized by fat malabsorption, hypocholesterolemia, retinitis pigmentosa, progressive neuropathy and acanthocytosis.

We report the case of a Tunisian male child born from consanguineous marriage. He presented at the age of 4 months with failure to thrive, greasy stool and vomiting. His clinical phenotype and serum lipid profile suggested the diagnosis of ABL. The MTP gene analysis revealed a novel homozygous mutation [c.2313-2314delinsAA (p.771Tyr>x)]. The parents were heterozygous for the same mutation.

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1. Introduction

Abetalipoproteinemia (ABL), also known as Bassen–Kornzweig syndrome (OMIM#200100), is a rare autosomal recessive disorder characterized by extremely low levels of apoB-containing lipoproteins, fat malabsorption, fat-soluble vitamins deficiency and acanthocytosis in infancy [1,2]. Deficiency of fat-soluble vitamins could lead to a number of variable manifestations, including spinocerebellar degeneration, coagulopathy, and pigmented retinopathy [2]. Plasma total cholesterol and triglyceride levels are extremely low and apoB-containing lipoproteins are nearly absent in plasma.

Mutations in the gene encoding the large subunit of microsomal triglyceride transfer protein (MTP) gene (OMIM*157147) are responsible for the phenotype [3].

MTP gene encodes a protein required for the assembly and secretion of apoB-containing lipoproteins in the liver and intestine [4,5]. In presence of MTP deficiency, apoB cannot be properly lipidated and undergoes rapid intracellular degradation; for this reason apoB-containing lipoproteins are almost undetectable in plasma. It seems that there is no race preference for abetalipoproteinemia or familial hypobetalipoproteinemia [6]. However, a conserved haplotype and a common MTP mutation p.G865X0 with a carrier frequency of 1:131 in Ashkenazi Jewish population has been reported [7].
We describe in this paper the clinical phenotype and the molecular genetics in a Tunisian child having a novel mutation of MTP gene.

2. Case report

A Tunisian male child, first in the order of birth of healthy first degree consanguineous parents, was admitted to hospital at the age of 4 months. He presented with failure to thrive, greasy stool and vomiting. On examination, weight was 3650 g (< 5th percentile), height was 56 cm (< 5th percentile), and head circumference was 38.5 cm (3rd–15th percentile). His birth weight, height and head circumference were respectively, 3050 g, 49 cm and 32.5 cm. The rest of the examination was unremarkable.

Patient laboratory data are summarized in Table 1.

Screening for celiac disease, cow’s milk protein allergy, sweat test and thyroid function was normal. The upper gastrointestinal endoscopy was normal too (particularly no yellow discoloration of the small intestinal mucosal surface). The abdominal sonography showed homogenous hyperechogenic pattern of the liver. No diagnosis was made.

At the age of 20 months, he developed frequent, loose, semi-solid and light colored stools. He was managed as exocrine pancreatic insufficiency and improved slightly under a restricted fat diet and pancreatic extracts. At the age of 28 months, he became pale and dehydrated and was hospitalized. Physical examination was unremarkable expect failure to thrive, signs of dehydration and pale skin. The cell blood count showed normochromic normocytic non regenerative anemia and the bone marrow examination was normal. Low fat diet and pancreatic extracts were maintained.

During the following years, the patient continued to have frequent episodes of diarrhea with steatorrhea, the stools became large, soft and sometimes even watery and oily. His neurological development was normal.

At the age of 13 years, the diarrhea became again profuse. The physical examination showed no significant abnormal findings and especially no neurological, muscular or ophthalmic impairment.

Plasma total cholesterol, HDL-cholesterol, triglyceride and concentrations were measured by a standard method after an overnight fast. Apo lipoproteins were measured by immunonephelometry. Low levels of total cholesterol, triglycerides, Apolipoprotein B were detected (Table 2).

![Table 1](image-url)
ABL is a rare disease of lipoprotein metabolism that has drawn attention to the importance of the MTP gene in the assembly and secretion of apoB-containing lipoproteins. Without treatment, ABL symptoms can be debilitating in most of the patients and life expectancy is reduced. Current evidence suggests that early treatment with high oral doses of combined vitamin A and E, if introduced early enough, can reduce the potential severity of neuropathy and retinopathy. However, there is still a need for novel therapeutic approaches to ABL, since vitamin therapy alone is not sufficient to completely control or cure this disease.

Role of funding source

No benefits or funds were received in support of this study.

Conflict of interest

Authors of manuscript declare no conflict of interest.

References


