

## Family Abetalipoproteinemia: About an Observation

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| Received: 09.06.2019 | Accepted: 18.06.2019 | Published: 30.06.2019

DOI: [10.36347/sjams.2019.v07i06.027](https://doi.org/10.36347/sjams.2019.v07i06.027)

### Abstract

### Original Research Article

Abetalipoproteinemia (ABL) is a very rare autosomal recessive disorder caused by mutations in the microsomal triglyceride transfer protein gene (MTTP). ABL is characterized by lack of lipids and apolipoprotein B (apoB), in plasma, fat malabsorption, acanthocytosis and hypocholesterolemia in infancy. Later in life, deficiency of fat-soluble vitamins is associated with development of atypical retinitis pigmentosa, neuropathy and myopathy. We describe a 13-years -old infant boy, born from consanguineous parents and presented with growth retardation and reduced visual acuity. The patient was diagnosed to have ABL. A family investigation including the mother, the siblings, and the first cousins, was also realized to consolidate this diagnosis.

**Keywords:** Abetalipoproteinemia; Microsomal triglycerid transfer protein; Apolipoprotein B.

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## INTRODUCTION

Abetalipoproteinemia (ABL) is an inherited autosomal recessive disease of lipid metabolism characterized by the absence of Apolipoprotein B (Apo B) in plasma. This absence leads to a lack of assembly of chylomicrons in the intestine and VLDL in the liver resulting in very low plasma concentrations of triglycerides and cholesterol and deficiencies in fat-soluble vitamins. This pathology is initially in the form of a lipid malabsorption syndrome. Secondarily neurological (ataxia, peripheral neuropathy) and ophthalmological (retinitis pigmentosa) manifestations appear [1].

We present the observation of a young child consultant in the pediatric department for a stunted weight loss and a decrease in visual acuity. The completion of a diagnostic report revealed the existence of abetalipoproteinemia. A family survey including the mother, the fraters, and the first cousins, was also carried out in order to confirm this diagnosis.

## OBSERVATION

This is a young child aged 13 from a consanguineous marriage, admitted to the pediatric department for management of a weight-loss delay associated with a decrease in visual acuity.

The clinical examination of our patient showed a failure to thrive, a peripheral neuropathy and a characteristic pigmentary retinopathy. The same clinical manifestations were found in one of his 11-year-old cousins. Her younger sister, meanwhile, had a beginner weight-loss delay, and early-stage pigment retinopathy. The rest of the family members did not present any significant clinical manifestations.

A complete assessment was carried out in our patients, parents, siblings and first cousins also from a consanguineous marriage (Table 1). This assessment included: total cholesterol, low density lipoprotein (LDL) cholesterol, high density lipoprotein (HDL) cholesterol, Apolipoprotein B (Apo B), Apolipoprotein A (Apo A), transaminases (AST, ALT) and a formula blood (NFS) associated with a blood smear.

The patient, his younger sister and their cousin had levels of triglycerides and total cholesterol collapsed or even absent with plasma levels of 0.06g/ and 0.29g/l, 0.0g/l and 0.19g/l, 0.03g/l and 0.15g/l (Tab 1) respectively. LDL cholesterol was absent, and Apo B almost undetectable  $<< 0.2g / l$ .

The patient's hemogram showed moderate anemia and the blood smear showed acanthocytosis. The same anomalies were met with his sister and cousin.

**Table-1: Results of biological assessments**

biology report	Patient	Mother	Father	Sister 1	Brother 1	Sister 2	Oncle	Uante	Cousin 1	Cousin 2	Normal values
Triglycerid	0.06g/l	0.84g/l	0.95g/l	0.0g/l	0.51g/l	0.5g/l	0.37g/l	0.5g/l	0.03g/l	0.52g/l	0.4à1.5g/l
Cholesterol	0.29g/l	1.36g/l	1.45g/l	0.19g/l	1.35g/l	1.27g/l	1.37g/l	1.18g/l	0.15g/l	1.40g/l	1.4à2.5g/l
HDL CHOL	0.35g/l	0.51g/l	0.6g/l	0.21g/l	0.41g/l	0.41g/l	0.41g/l	0.45g/l	0.25g/l	0.55g/l	0.35à0.8g/l
LDL CHOL	0.0g/l	0.78g/l	0.9g/l	0.0g/l	0.83g/l	0.86g/l	0.65g/l	0.68g/l	0.0g/l	0.7g/l	0.9à1.6g/l
ApoA	1.58g/l	2.23g/l	1.86g/l	0.92g/l	1.52g/l	1.97g/l	2.2g/l	1.64g/l	0.99g/l	2.1g/l	1.2à2.2g/l
ApoB	<0.2g/l	1.33g/l	1.26g/l	<0.2g/l	1.29g/l	1.42g/l	1.2g/l	1.13g/l	<0.2g/l	1.4g/l	0.55à1.3g/l
AST	38UI/l	40UI/l	35UI/l	51UI/l	26UI/l	37UI/l	14UI/l	35UI/l	25UI/L	27UI/l	10à35UI/l
ALT	49UI/l	44UI/l	40UI/l	35UI/l	13UI/l	37UI/l	14UI/l	26UI/l	35UI/L	45UI/L	10à45UI/l

## DISCUSSION

Abetalipoproteinemia (ABL) is a rare disorder in lipid metabolism, first described in 1950 by Bassen and Kornzweig [2] who noted a particular association between acanthocytosis with atypical retinitis pigmentosa and ataxia. In 1958, Jampel shows the presence of a significant drop in cholesterol levels in patients affected by this pathology [3]. The name of ABL was attributed by Salt in 1960 who noticed a total absence of beta-lipoproteins in the serum of patients with this syndrome [4].

Abetalipoproteinemia (ABL) is an extremely rare autosomal recessive disorder characterized by the complete absence of Apolipoprotein (ApoB) in plasma. It is due to a mutation in the Microsomal Triglycerid Transfer MTP gene that codes for the microsomal triglyceride transfer protein (MTTP) [5]. This protein, which catalyzes the transfer of lipids to ApoB, is essential for the first stage of lipoprotein formation containing ApoB.

The molecular basis of this disorder is the succession of two mutations in the ; MTTP gene that is located on chromosome 4q23 and encodes the large MTTP subunit (a 97-KDa protein containing 894 amino acids) that forms a heterodimer with an enzyme of endoplasmic reticulum: protein Disulfide Isomerase (PDI) [6] and accelerates the transfer of lipids to Apolipoprotein B, resulting in the assembly and secretion of ApoB and the formation of VLDL, and chylomicrons in the liver and intestine respectively [5,7].

Apolipoproteins are substances necessary for the constitution of solubilized lipid particles which make them usable for metabolic purposes. The lipids absorbed in the intestine are integrated in the chylomicrons for the constitution of which the ApoB 48

is necessary. ApoB 100 is necessary for the constitution of VLDL of hepatic origin [8, 9].

In ABL, ApoB 100 and Apo B 48 are absent from plasma, as are chylomicrons, VLDL and low density lipoprotein (LDL). Cholesterol and triglycerides, in low levels, are not found only in high density lipoproteins (HDL). In addition, liposoluble vitamins A, D, E and K are usually incorporated into these lipoproteins; vitamins A and K, on the other hand, have an autonomous transport system. It is therefore for vitamin E (or tocopherol), the absorption and transport of which is dependent on the existence of ApoB, that deficiency will be most marked in ABL [10].

However, vitamin E, as an antioxidant, has a protective role for lipid tissues and especially neurological tissues [11]. Clinically, our patient, his sister, and the first cousin had a weight-loss delay, probably related to fat malabsorption; indeed, the clinical picture is most often marked by digestive signs related to malabsorption (vomiting, diarrhea, steatorrhea, and insufficient weight gain) [1]. Endoscopic examination of the fasting small intestine shows an almost pathognomonic white jelly appearance of genetic hypocholesterolemia. The histopathological examination of the duodenal biopsies shows, for its part, a normal villous relief [1].

An advanced pigmentary retinopathy was found in our patient, as well as in one of these cousins, it was less in his younger sister. Retinopathy is one of the most common ophthalmic manifestations associated with ABL. Retinal pigment degeneration is progressive. Patients may have reduced night vision and color vision disorder early in the course of the disease [12, 13].

The first neurological signs begin gradually at the age of 6-12 years, and often result in a decrease, then a loss of osteotendinous reflexe (ROT), followed

by cerebellar syndrome and muscle weakness. In our case, peripheral neuropathy was found. Evolution is variable. It results in the absence of treatment, the progressive installation of a major handicap to walking, or even a bedridden state [14]. The association of an abetalipoproteinemia on the neurological table raises the differential diagnosis with Friedrich ataxia [15].

Biologically, many anomalies were found in our patient, as well as in different members of his family; including hypocholesterolemia, collapsed triglyceride levels and absent LDL. These data join those of the literature. Indeed, several biological abnormalities make it possible to direct towards this diagnosis among others hypocholesterolemia, the absence of LDL and VLDL, the presence of acanthocytes and the collapse of triglycerides.

Hematological involvement is characterized by the presence of acanthocytosis which represents 50% to 70% of the erythrocyte population associated with anemia most often moderate [1]; it was the case of our patient, his sister as well as his cousin.

The diagnosis can be discussed with familial hypobetalipoproteinemia, which is also characterized by hypocholesterolemia. This is an autosomal dominant disease: heterozygous subjects have lower LDL and ApoB levels, and codominant proponents have collapsed ApoB levels. In the latter, the clinical pictures are less marked than in the ABL. In this disease, it is the gene coding for ApoB which is altered and the investigation makes it possible to highlight decreased LDL and ApoB levels in the ascending heterozygotes, unlike the ABL where the ascendants have a normal lipid profile [16].

The presence of biological abnormalities such as: hypocholesterolemia, absence of LDL, collapsed triglycerides, presence of acanthocytes, ApoB plasma level almost undetectable by conventional techniques, in addition to the clinical signs noted in our patient; in addition to its hereditary nature (clinical manifestations and biological disturbances in other members of the family), it made it possible to orient our diagnosis towards an ABL.

The diagnosis of certainty is based on the demonstration of the mutation in the MTP gene which encodes the large subunit of the microsomal triglyceride transfer protein. The diagnosis must be made early, because of the irreversible nature of the neurological lesions which condition the functional and then vital prognosis and the ophthalmologic prognosis which evolves towards the blindness.

Treatment is based on a diet low in dietary fat and high-dose vitamin E supplementation due to absorption disorders [13, 18].

## CONCLUSION

Abetalipoproteinemia (ABL) is a rare disease of lipoprotein metabolism that has drawn attention to the importance of MTP. The latter catalyzes the transfer of lipids to ApoB, and is essential for the first stage of lipoprotein formation containing ApoB.

In the absence of treatment, the symptoms of ABL can be debilitating, or even put into play the functional and vital prognosis of the patients. The diagnosis of ABL should be made in the presence of malabsorption and stunting in children and management should be early with the introduction of a low-fat diet and supplementation with vitamins A and E. However, the therapeutic management of patients remains disappointing, due to an often late diagnosis of irreversible and advanced lesions.

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