Familial hypobetalipoproteinemia in an adult with low cholesterol level and malabsorption

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Abstract

Familial hypobetalipoproteinemia (FHBL) is a hereditary disorder of apolipoprotein metabolism. It has heterozygous and homozygous forms. Heterozygous forms are frequently asymptomatic, plasma cholesterol level is low, LDL cholesterol level is usually equal to 80 mg/dl, or below. Absorption of lipids and vitamins that dissolve in lipids is impaired, chronic diarrhea, growth retardation and neurological disorders are mostly present in homozygous patients.

Herewith we present a 33-year old woman who was admitted to our clinic in Sakarya University Hospital, Turkey, with complaints of abdominal pain, diarrhoea, paresthesia at hands, feet and peroral region, and diagnosed as heterozygous FHBL and having symptoms of lipid intolerance and malabsorption which are rarely observed in these heterozygous patients.

Keywords: cholesterol, familial hypobetalipoproteinemia, malabsorption.

Introduction

Mutation of Apo B is involved in the pathogenesis of FHBL, which is a rare hereditary disorder of apolipoprotein metabolism. As a result of this mutation, lipoprotein synthesis decreases, clearance of LDL and VLDL decreases, fatty liver occurs due to accumulation of lipids at liver, and steatorrhea occurs due to the impaired absorption of lipids and fat-soluble vitamins. Heterozygous form is observed at a 1/5,000 frequency, and homozygous form at 1/1,000,000. Although heterozygous forms are usually asymptomatic and only incidentally observed, homozygous forms are presented with lipid malabsorption due to impairment of chylomicron synthesis in bowels, acanthosis, retinitis pigmentosa and progressive neurological symptoms due to vitamin E deficiency during childhood (1). Abnormal physical examination findings are not usually present in heterozygous forms, but hepatomegaly rarely occurs due to lipid accumulation at liver. Total serum cholesterol, triglyceride, LDL cholesterol and VLDL cholesterol levels are low; HDL cholesterol level is normal, or slightly increased. In heterozygous forms, LDL cholesterol and total cholesterol levels are usually under half of normal levels, in homozygous total cholesterol level falls under 50 mg/dl limits. Vitamin support and lipid free diet are recommended to these patients (2).

Case report

A 33-year old woman was admitted to our clinic in Sakarya University Hospital, Turkey, with complaints of abdominal pain, diarrhoea, paresthesia at hands, feet and peroral region. We learned from patient's anamnesis that she had foul-smelling, fizzy, and mild defecation on average 7-8 times a day in the last two years. However, after a few days, her defecation restored. Patient's weight was 58 kg, height 172 cm, and body mass index 19.6. In her physical examination, we found out chvostek sign, a slight abdominal distension, increase in bowel sounds, and hepatomegaly. Her neurological and eye examination were normal. In her biochemical analysis we detected ALT: 9.4 (0-35) IU, Calcium: 8 (8,5-10) mg/dl; Phosfate: 2.3 mg/dl (2.5-4.8) 25-OH-D_3: 5 (30-74) ng/ml, total cholesterol: 110 mg/dl (0-200), triglycerides: 108 mg/dl (0-150), LDL cholesterol: 46 mg/dl (0-160), HDL cholesterol: 42 mg/dl (35-75), Apo B: 40 mg/dl (40-115). In her mother's lipid profile, total cholesterol was 106 mg/dl (0-200), triglycerides: 41 mg/dl (0-150), LDL cholesterol: 37 mg/dl (0-160), HDL cholesterol: 61 mg/dl (35-75). In her fathers' lipid profile total cholesterol was 200 mg/dl, triglycerides: 150 mg/dl, LDL cholesterol: 100 mg/dl, HDL cholesterol: 85 mg/dl. Her complete blood count was normal. We found lipid particles in her gaita specimen but no erythrocyte, leucocyte, parasitic egg or cysts. There was no reproduction in her gaita samples. In abdominal ultrasonography, an increase of liver echogenicity and grade 1-2 fat accumulation were detected. Tests about coeliac disease were normal. Mucosa of stomach and small intestine were normal in gastroscopy. In her small intestine biopsy, we found out that intestinal villi were in normal appearance, and there was a non-specific inflammation in mucosa. Acanthosis existed in peripheral smear. According to these findings the patient was diagnosed with familial hypobetalipoproteinemia. Heterozygous familial hypobetalipoproteinemia is clinically asymptomathic, laboratory findings are total cholesterol: < 120 mg/dl, LDL-cholesterol: < 80 mg/dl, Triglycerides: < 150 mg/dl, usually normal (4). In the treatment of this disease, adding medium chain fatty acids to the diet and supplementation of high dose vitamin E are recommended. With this treatment, diarrhea frequency can be reduced and neurological complications can be delayed. Hence, we gave to our patient a high dose vitamin E, calcium and vitamin D in the treatment and added medium chain fatty acids to her diet. Patient's complaints about abdominal pain and diarrhea regressed and her calcium, phosphate and 25-OH-D_3 levels came to normal limits.

Discussion

FHBL is an autosomal dominant disorder, characterized by decreased Apo B levels, and which should be thought in the differential diagnosis of hypocholesterolemia and malabsorption status. Because our patient's mother lipid profile was appropriate with hypobetalipoproteinemia and father's lipid profile was normal, we accepted our patient as heterozygous FHBL patient. In heterozygous FBHL, total cholesterol is <120 mg/dl. Apo B level is usually less than normal (3,4). Our patient's LDL cholesterol level was 46 mg/dl and Apo B: 40 mg/dl, which was compatible with heterozygous FHBL.

Some patients can apply to our clinic with symptoms like homozygous patients although they are heterozygous. In homozygous FHBL patients, there are symptoms related to lipid malabsorption and deficiency of fat-soluble vitamins (5). In our case, calcium was 8 mg/dl (8.5-10), phosphate: 2.3 mg/dl (2.5-4.8), 25-OH-D_3: 5 ng/ml (30-74) and lipid particles were seen in gaita specimens. Our patient had also some clinical and laboratory findings similar to homozygous patients. Malabsorption, acanthosis, retinitis pigmentosa, neuromuscular degeneration and hepatosteatosis can be seen in homozygous FHBL patients. Most of FHBL patients are heterozygous, usually asymptomatic and are detected in family or population scans (6). In our patient, malabsorption and acanthosis were detected, but retinitis pigmentosa and neuromuscular degeneration were not detected. Our patient was asymptomatic until the age of 31 years and she was symptomatic for the last two years.

In FBHL, the production of VLDL, which is a normal export system for triglycerides, is impaired due to the decrease in synthesis of Apo B100, a normal lipid transporter from the liver. By this mode of transmission, triglycerides and probably other lipid components of VLDL accumulate in liver. Also, because triglyceride transport capacity of shortened Apo B proteins, which are formed by mutations in Apo B, is less than normal Apo B100, fatty liver may be present. This condition cannot be differentiated upon histological examination from other causes of macrovesicular hepatosteatosis. The amount of fat accumulated in liver shows differences between FHBL patients. This condition is probably modulated by some kind of genes and related to patient's genetic background (7,8). In our case, we detected in abdominal ultrasonography an increase in liver echogenicity and grade 1-2 fat accumulation although the patient was heterozygous.

Familial heterozygous hypobetalipoproteinemia should be kept in mind about causes of steatorrhea in childhood when there is no growth and development retardation. Restriction of fat in diet and supplementation of high dose vitamin E can reduce diarrhea frequency and delay or prevent neurological complications. Although diagnosed as heterozygous, having lipid intolerance and malabsorption, which are rarely observed in these patients, it is accepted as remarkable for our case. It is very important to diagnose correctly the disease causing malabsorption, in order to manage promptly its treatment. When total cholesterol and LDL-cholesterol are found low in certain patients, malabsorption due to FBHL should be considered as a potential diagnosis and other individuals of the family should be examined for the presence of this disease.

Conflicts of interest: None declared.

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