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CASE REPORT

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Treatment and follow-up of coronary artery disease in a child with homozygous familial hypercholesterolemia

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Abstract

Familial hypercholesterolemia is a metabolic disease caused by a mutation in the low-density lipoprotein receptor gene. It carries early atherosclerosis and coronary artery disease risks. Coronary artery disease has been reported 20 times in the pediatric population with familial hypercholesterolemia compared to the normal population. Early diagnosis and treatment may reduce morbidity and mortality. In this article, we present a 16-year-old patient, who followed up for 12 years due to hypercholesterolemia and applied to our hospital due to chest pain, shortness of breath, and palpitation. After a detailed evaluation, we detected critical left and right main coronary artery stenosis, and bypass surgery was performed by cardiovascular surgeons. Early diagnosis of children with familial hypercholesterolemia or patients who have a family history of hypercholesterolemia will allow treatment of the disease and prevention of the complications.

Keywords: Familial hypercholesterolemia, atherosclerosis, cardiovascular disease, coronary artery stenosis, children

Introduction

Familial hypercholesterolemia (FH) is an autosomal dominant inherited metabolic disease caused by mutation in the low-density lipoprotein (LDL) receptor gene [1]. Although the homozygous form is rare (1/1000000), the heterozygous form is common (1/500). Patients with familial hypercholesterolemia have high plasma cholesterol levels with xanthomas on the skin, especially on the extensor surfaces of tendons and joints, and hypercholesterolemia leads to early atherosclerotic coronary artery disease. The risk of early-onset coronary artery disease in patients with FH is 20 times higher than in the normal population but coronary artery disease may overlook in early childhood and their treatment may delay due to mild symptoms. Only 20% of the patients with coronary artery disease can be diagnosed in childhood [2]. Therefore, early diagnosis and treatment is an important issue and early diagnosis of children with familial hypercholesterolemia will allow treatment of the disease and prevent the complications it will reduce the morbidity and mortality associated with coronary artery disease. In this article, we present a 16-year-old patient, who followed up for 12 years due to hypercholesterolemia and applied to our hospital due to chest pain, shortness of breath, and palpitation. After a detailed evaluation, we detected critical left and right main coronary artery stenosis, and bypass surgery was performed by cardiovascular surgeons.

Case

16-year-old patient, who followed up for 12 years due to hypercholesterolemia and applied to our hospital due to chest pain, shortness of breath, and palpitation. We learned from the history of patients that was the complaint of the patient was started one month ago and complaints aggravated with exercise.

We also learned from the medical history of patients that he applied to our hospital due to the development of yellow-colored swelling (xanthomas) on his elbows and knees. After physical examination evaluation of high cholesterol levels biochemical analysis. After the patient was diagnosed with familial hypercholesterolemia, simvastatin treatment was started. However, rosuvastatin and ezetimibe treatment was started during follow-up due to after the patient had high cholesterol levels and lipid apheresis was started

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every 3 months when the patient was 13 years old.

On physical examination vital findings were normal. Height was 167 cm (10-25 P), weight was 53 kg (3-10 P). Physical examination revealed xanthomas in both knees and elbows (figure 1), there were no other abnormalities in other system examinations.

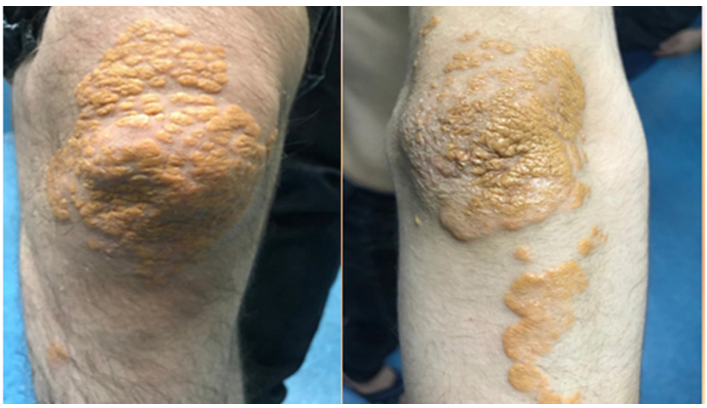

Figure 1. Pictures shows xhantoms on knee and elbow

Electrocardiography (ECG) was normal. 1st-degree aortic valve regurgitation and trace mitral valve regurgitation were detected with normal Left ventricular systolic functions were detected on echocardiographic. On laboratory examinations, serum total cholesterol level was> 705 mg / dl, LDL cholesterol level was > 646 mg / dl. Triglyceride level was determined as 127 mg / dl. Abdominal ultrasonography (USG) was evaluated as normal.

An exercise test was performed due to the patient having chest pain, shortness of breath, and palpitations. At the third minute of the exercise test, chest pain, shortness of breath, and pain that travel the left arm was developed and ST depression was detected on the simultaneous ECG, especially in V4-V6 (figure 2). Coronary angiography was performed due to the ischemia findings on the exercise test. Selective coronary angiography revealed 90% narrowing in the left main coronary artery and 60-70% narrowing in the right main coronary artery and its branches (figure 3). The patient underwent coronary bypass surgery by thoracic and cardiovascular surgery. There were no postoperative complications. However, the presence of hypercholesterolemia and having undergone coronary bypass surgery were evaluated in terms of liver transplantation as this would increase the risk factor. He was added to the list of liver transplantation by liver transplant Surgeons.

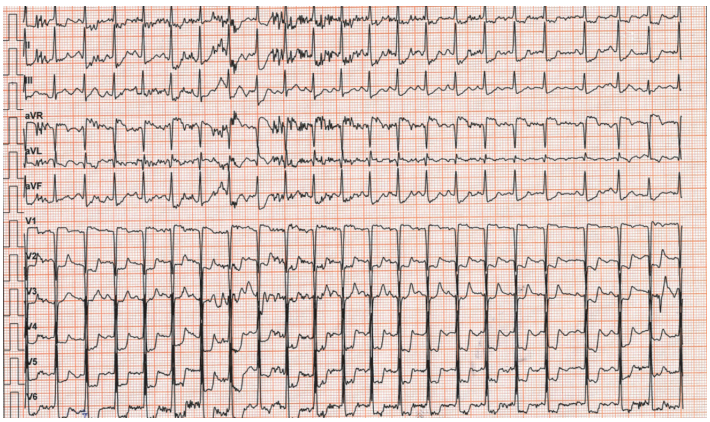

Figure 2. ST depression on the ECG in exercise test

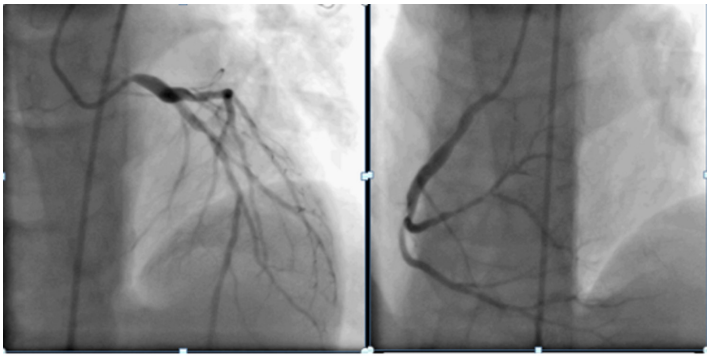

Figure 3. Angiographic picture shows critical stenosis of left main coronary artery and right main coronary artery and its branches

Discussion

Familial hypercholesterolemia is an autosomal dominant genetic disease caused by LDL receptor deficiency or absence in liver cells and peripheral tissues. Four important gene mutations that determine LDL cholesterol levels have been identified in familial hypercholesterolemia. Familial hypercholesterolemia develops as a result of mutations in genes encoding LDL-R, Apolipoprotein B (Apo B), pro-protein convertase subtilisin / kexin 9 (PCSK9), and LDL-R adapter protein 1 (LDLRAP1) proteins [3].

Cholesterol binds to Apoprotein B-100 on the surface of the LDL particle and forms a receptor-ligand complex, and this complex is taken into the cell by endocytosis [4]. Familial hypercholesterolemia develops as a result of mutations in the LDL receptor gene located on the short arm of the 19th chromosome. There is a mutation in this gene in 85-90% of FH cases. In our case, homozygous LDL receptor mutation was detected.

There are two variants of this disease, homozygous and heterozygous. The frequency of homozygous FH in the general population is around 0.2%. However homozygous FH is seen rarely as 1/1000000, heterozygous FH is seen more frequently like 1/500 [5]. In familial hypercholesterolemia, the plasma cholesterol levels and the clinical situation resulting from it differ depending on whether the person is homozygous or heterozygous. In homozygous FH total cholesterol level is between 650-1000 mg/dl and LDL cholesterol is> 650 mg/dl. In heterozygous patients, the total cholesterol level is about 350-550 mg/dl and LDL cholesterol levels are between 200-400 mg/dl [2].

Atherosclerosis that starts in childhood causes valve pathologies by affecting the aortic root and this sclerotic plaque extends to the coronary arteries. Serious coronary artery disease begins to occur in the second decade of untreated patients. These patients are affected by the atherosclerotic vascular disease in the age of 30s at the latest.

High serum cholesterol levels caused by LDL receptor gene mutation are the main factors in the formation of endothelial damage in the vessels, transformation of monocytes into macrophages and foam cells, development of atherosclerotic plaques, early-onset coronary artery disease, peripheral artery disease, and aortic valve diseases [6].

In heterozygous FH, they are usually asymptomatic in the first and second decades of childhood, or xanthomas are rarely seen (10-

15%). Coronary artery disease usually begins to be seen earlier than the normal population, but it may see after the 30-40s. It is thought that the risk of coronary artery disease may be reduced by early diagnosis and treatment. Recommended with a cholesterol-low diet in the treatment of heterozygous cases of FH. In cases with homozygous FH is required that combined drug therapy with diet. Cholestyramine, colestipol, nicotinic acid, and hydroxymethyl glutaryl CoA reductase (HMG-CoA) enzyme inhibitors and ezetimibe are used in these patients. Plasma exchange or lipid apheresis should apply in patients who do not respond to diet and drug treatments [7]. Coronary artery bypass treatment option is available in patients who show cardiac ischemic symptoms due to atherosclerosis during follow-up [8,9]. Our patient, who showed symptoms of chest pain, had ischemic findings in the exercise test and whose selective angiography showed severe narrowing of the coronary arteries, was performed bypass surgery on both the left coronary artery and the right coronary artery by cardiovascular surgery. Liver transplantation, partial ileal resection, and portocaval shunt treatment can also be performed [10].

The homozygous mutation was detected in the LDL-R gene in our patient. He was also included in a liver transplant program.

In conclusion, early screening of patients who detected hypercholesterolemia in their family and screening for triglyceride and cholesterol should recommend for every child at the age of 9-10 years. Patients with familial hypercholesterolemia should be examined more frequently due to early atherosclerotic heart disease, especially about lipid levels, exercise tests and angiographic imaging should be performed. Early diagnosis of children with familial hypercholesterolemia or patients who have a family history of hypercholesterolemia will allow treatment of the disease and prevention of the complications. Exercise testing and angiography should perform in case of clinical suspicion.

Conflict of interests
The authors declare that they have no competing interests.

Financial Disclosure
All authors declare no financial support.

Patient Informed Consent
Consent form was abtained from the patients before the article.

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