Familial Hypercholesterolaemia and Early Coronary Artery Disease: A Case Report and Review of the Literature

AİLESEL HİPERKOLESTEROLEMİ VE ERKEN KORONER ARTER HASTALİĞİ: BİR OLGU SUNUMU VE LİTERATÜRÜN GÖZDEN GEÇİRİLMESİ

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Abstract

Familial hypercholesterolaemia (FH) is an important public health problem due to the high incidence of premature coronary artery disease leading to a reduction in life expectancy, observed in many families with FH. It is an autosomal dominant disorder caused by mutations of the LDL receptor gene. FH heterozygotes have approximately twice the normal LDL-cholesterol concentration in early childhood, and have increased risk of early myocardial infarction.

In this report, a 21-year-old male patient with FH type IIa who was referred to our hospital with a diagnosis of non-Q myocardial infarction, and who underwent subsequent coronary bypass grafting after coronary angiography, was presented.

Key Words: Hypercholesterolemia, familial, coronary arteriosclerosis

Özet

Ailesel hiperkolesterolemi, yüksek erken koroner arter hastalığı riski ve hayat beklenisini azalmış nedeniyle tüm dünyada önemli bir halk sağlık problemidir. Ailesel hiperkolesterolemi, LDL rezepör geni mutasyonundan kaynaklanan otosomal dominant geçişli bir hastalıktır. Heterozigot ailesel hiperkolesterolemi erken çocukğun döneminde normal kolesterol düzeyinin yaklaşık 2 kat artışa neden olur ve erken koroner hastalığı riskinde artış ile birliktedir.

Bu yazida, klinigimize non-Q miyokard infarktusunu tansıya sevk edilen ve koroner anjiyografi sonrası koroner bypass operasyonu önerilen 21 yaşındaki, ailesel hiperkolesterolemi Tip 2a’lı 1 olgu sunuldu.

Anahtar Kelimeler: Ailesel hiperkolesterolemi, koroner arteroskleroz

It is well established that high serum cholesterol level is one of the most important risk factors for coronary artery disease (CAD) in young patients. FH is one of the most common genetic disorders characterized by hypercholesterolaemia throughout childhood leading to premature atherosclerosis, CAD, and tendon and cutaneous xanthomas.

FH is believed to be responsible for 10% to 20% of all early coronary heart diseases (CHDs). Long-term follow-up studies show that the main cause of death in FH patients is CHD and that about 200,000 persons die globally each year of preventable early heart attacks due to FH. With adequate long-term pharmacological treatment, many FH patients may achieve substantial reductions in LDL-cholesterol levels, and probably increase their life expectancy by 10-30 years.
initiation of treatment are major issues in the prevention of premature cardiovascular disease and death among this population.

**Case Report**

A 21-year-old male patient with FH was referred to our hospital from a state hospital with the symptoms of typical chest pain lasting for 2 days. He had 2 years history of intermittent left sided chest pain on exertion radiating to the left shoulder, smoking history of 1 pack/day/3 years and FH history in his father.

Physical examination revealed arterial blood pressure of 120/80 mmHg and the heart rate was 71 beats per minute on admission. Xanthomas on the extensor surfaces of the joints and on the eyelids were present. Corneal arcus was also present on eye examination (Figure 1).

His ECG displayed normal sinus rhythm and ST depression in the V4-V6, DII–DIII and aVF derivations suggesting of ischemia (Figure 2). Chest X-ray was normal. On echocardiographic study, left ventricular ejection fraction was 60% and anterolateral and apical wall hypokinesia was present. There was also a slight mitral regurgitation.

His triglyceride, total cholesterol, high-density lipoprotein, low density lipoprotein, very low-density lipoprotein levels were 67 mg/dL, 509 mg/dL, 35 mg/dL, 461 mg/dL, 13 mg/dL, respectively.

Acute non-Q wave myocardial infarction was diagnosed after serial enzymatic evaluations and in the setting of ongoing chest pain. After initial stabilization of patient with tirofiban, clopidogrel, acetyl salicylic acid, heparin, nitrates, beta-blockers and atorvastatin, he underwent coronary angiography. Cardiac catheterization with angiography revealed 80% stenosis of the proximal left anterior descending artery (LAD), 100% occlusion of the mid-LAD, two 80 and 70% stenoses of the first diagonal branch of LAD, 99% stenosis of the distal circumflex and a 20% lesion in the right coronary artery (Figure 3a, 3b). Left ventriculography demonstrated hypokinesia of anterolateral and apical walls. The patient was referred for coronary artery bypass grafting surgery. He was discharged with metoprolol 25 mg/day, acetylsalicylic acid 300 mg/day, perindopril 2 mg/day, atorvastatin 40 mg/day, and ezetimibe 10 mg/day. After 2 weeks, 3-vessel coronary bypass grafting (left internal mammarian artery to LAD, saphenous vein graft to D1, and radial artery to OM1) was performed.

**Discussion**

FH is one of the most common genetic disorders with a prevalence of heterozygotes of about

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Figure 1. Corneal arcus appearance in our patient with FH.

Figure 2. Electrocardiography of the patient showing ST depressions in V4-V6 and D2, D3, aVF leads on admission.
In the heterozygous form, one of the two LDL-receptor genes has a mutation and is non-functioning. This is due to a decrease in the number of active LDL receptors on the surface of liver cells and the resultant inefficient uptake of LDL by the liver. Serum cholesterol in most heterozygous familial hypercholesterolemic children exceeds 280 mg/dL and ranges between 360 and 560 mg/dL in affected adults and triglyceride levels are usually normal (Type 2a) as in our case, or may be elevated (Type 2b). In FH heterozygotes the child is asymptomatic in the first decade. Characteristic cholesterol deposits called tendon xanthomas are seen deep in the tendons of the dorsum of the hand or knuckles, and the Achilles tendon, often by age 20. Some affected individuals may exhibit cholesterol deposits around the cornea (corneal arcus) and eyelids (xanthelasma). In our case, xanthomas on the extensor surfaces of the joints and on the eyelids were present. Corneal arcus was also present on eye examination.

Untreated heterozygous FH patients have a 100-fold increased risk of death from CAD before the age of 40 years, while a 5-fold increased risk is still observed in patients over 40. Mabuchi et al reported that in the male FH population, coronary artery stenoses detectable by angiography occur as early as age 17, and MI can develop near the age of 30. The rate of MI in patients diagnosed with FH was 37% in another series. Our male patient was 21 years old and acute non-Q wave myocardial infarction was diagnosed after serial enzymatic evaluations. Furthermore, he was referred for coronary artery bypass graft surgery after coronary angiography.

In contrast to most genetic diseases, efficient therapy is available for FH in the form of lifestyle changes and lipid-lowering drugs. However, very few patients are treated and very few reach the targeted levels of serum cholesterol. A study from 14 western countries indicated that approximately 20% of the patients were diagnosed, 16% were on lipid-lowering drugs, and only 7% were being adequately treated. Unfortunately although our patient had a history of FH in his father, he had not undergone any lipid profile evaluation and did not receive medical therapy.
In most familial hypercholesterolemic adult heterozygotes, dietary management is usually ineffective and the maximum dose of the potent statin drugs is often required to lower the high cholesterol levels. The combination of a bile-acid-sequestrating drug or ezetimibe can also be prescribed when the potent statin drug is not effective. Therapeutic lifestyle changes including healthy diets, exercise, weight control, and avoidance of smoking are also concurrently recommended in all familial hypercholesterolemic cases.

**Conclusion**

It is mandatory to search for FH subjects for early diagnosis. The best approach in most populations at present is to determine LDLc in all first-degree family members of a heterozygous FH proband and screening of all second-degree family members is also recommended. Every heterozygous FH subject should be seen at least twice a year by a trained physician who will actively search for symptoms of CAD. Effective lipid-lowering therapy should be given particularly to young patients. High risk subjects over 20 years, all subjects with non-coronary atherosclerotic disease and all males over 30 years and females over 45 years are recommended to undergo a test for myocardial ischemia every 3-5 years. Other screening tests may also be considered.

**REFERENCES**