

Surgical correction in a patient with homozygous familial hypercholesterolemia

Homozigot ailesel hiperkolesterolemili bir hastada cerrahi tedavi

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Familial hypercholesterolemia is characterized by rapidly progressing coronary atherosclerosis and aortic stenosis. A 21-year-old man presented with anginal pain. He was diagnosed as having homozygous familial hypercholesterolemia and treated with coronary artery bypass grafting, aortic root enlargement, and aortic valve replacement. The postoperative course was uneventful and no recurrence was observed within a follow-up of two years.

Key words: Aortic valve stenosis/etiology; arteriosclerosis/etiology/surgery; coronary artery bypass; homozygote; hypercholesterolemia, familial/complications/surgery.

Ailesel hiperkolesterolemi koroner arterlerde hızlı gelişen ateroskleroz ve aort stenozu ile karakterize bir hastalıktır. Göğüs ağrısı şikayetiyle başvuran 21 yaşındaki bir erkek hasta, homozigot ailesel hiperkolesterolemi tanısıyla aortokoroner bypass, aortik kök genişletme ve aort kapak replasmanı ile tedavi edildi. Ameliyat sonrası dönemi sorunsuz geçen hastanın iki yıllık takibi süresince nüks saptanmadı.

Anahtar sözcükler: Aort kapağı stenozu/etyoloji; arterioskleroz/etyoloji/genetik; koroner arter bypass; homozigot; hiperkolesterolemi, ailesel/komplikasyon/cerrahi.

Familial hypercholesterolemia (FH) is an autosomal dominant disorder caused by a mutation of the gene for low-density lipoprotein (LDL) receptor. It is clinically characterized by high serum cholesterol concentrations, xanthomas, premature atherosclerosis of the coronary arteries and the aortic root. Although the heterozygous form occurs in approximately 1 in 500 individuals, the homozygous form occurs in 1 in a million. Clinical features of the disease are much more severe in homozygous than those in heterozygous patients.^[1] Patients with heterozygous FH commonly have two-fold higher plasma LDL cholesterol (LDL-C) levels than normal, while homozygotes have four- to five-fold elevations.^[2] Premature coronary artery disease and aortic root stenosis (consequences of cholesterol deposition in the aortic root) develop in early life in the homozygous form. Conversely, aortic root and valve involvement are rare in heterozygotes and occur only with severe, prolonged hypercholesterolemia, possibly due to accelerating age-related degenerative effects.^[3] Xanthomas developing in the buttocks, tongue, eyelid, buccal mucosa, or on the extensor surfaces of joints strongly suggest a diagnosis of FH.^[1]

CASE REPORT

A 21-year-old man was admitted to our hospital with chest discomfort (Canadian class III). There was a second degree consanguinity between his parents. On physical examination, a grade 3/6 systolic ejection murmur was elicited along the left sternal border. Xanthomas on the extensor surfaces of joints and on the eyelids were also present. Other findings were normal. Resting ECG revealed ST-segment depression in the precordial derivations, D I and D II, and signs of left ventricular hypertrophy. There was mild cardiomegaly on telecardiography. Serum lipid concentrations were as follows: triglyceride 230 mg/dl, total cholesterol 720 mg/dl, HDL-C 23 mg/dl, LDL-C 650 mg/dl, and VLDL-C 46 mg/dl. On echocardiography, the left ventricle end-systolic diameter was 41 mm, left ventricle end-diastolic diameter was 55 mm, interventricular septum thickness was 14 mm, left ventricle parietal wall thickness was 12 mm, ejection fraction was 55%, and aortic valve area was 0.7 cm². There was a 80-mmHg systolic gradient at the aortic valve level and the aortic annulus was small in proportion to the patient's body surface area (BSA=1.6 m²). Other parameters were nor-

Received: March 18, 2004 Accepted: June 6, 2004

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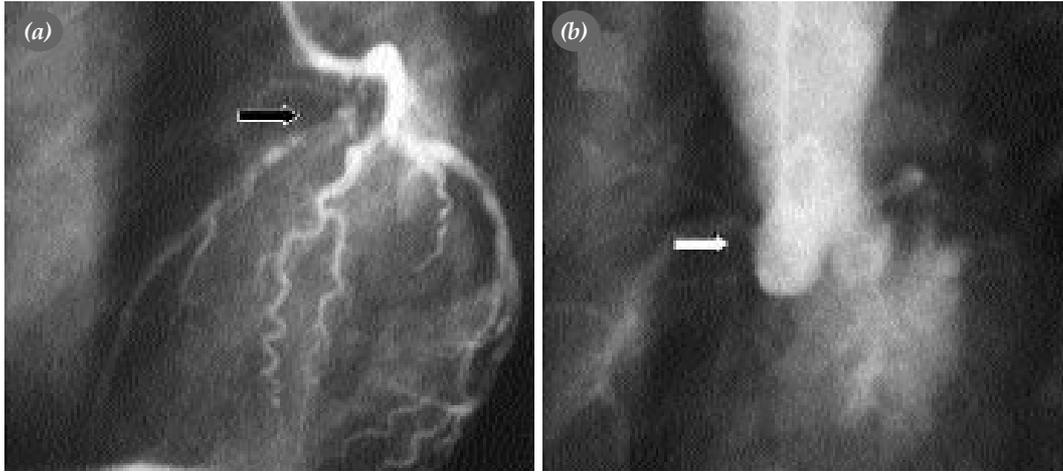


Fig. 1. (a) The left anterior descending coronary artery in a left lateral projection. Black arrow indicates total occlusion of the proximal coronary artery. (b) An aortogram in a left anterior oblique projection showing a small aortic annulus and ostial stenosis of the right coronary artery (white arrow).

mal. Cardiac catheterization revealed severe ostial stenosis of the right coronary artery and total occlusion of the proximal left coronary artery (Fig. 1). There was a 90-mmHg systolic gradient between the aorta and the left ventricle. A low-lipid regimen and atorvastatin in a dose of 40 mg/day were started.

The patient underwent coronary artery bypass grafting under hypothermic (28 °C) cardiopulmonary bypass (CPB) and aortic valve replacement. For myocardial protection, antegrade multidose crystalloid cardioplegia, topical hypothermia, and antegrade warm blood reperfusion were used. Following aortotomy, severe stenosis and a small annulus (through which a 19-no sizer could not be passed) were observed (Fig. 2). The aortic valve cusps were significantly thickened by foam cell infiltration. The posterior aortic root was enlarged using a bovine pericardial patch (Tutopatch, Tutogen Medical GmbH,

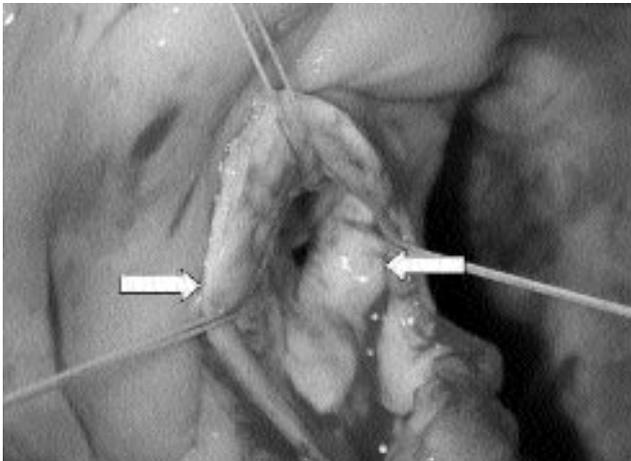


Fig. 2. Appearance of the aortic valve before resection. Critical stenosis and cholesterol depositions (arrows) are easily identified.

Neunkirchen-Germany) and a 21-mm St. Jude mechanical bileaflet prosthetic valve was implanted in the supraannular position. The right coronary artery and the left anterior descending coronary artery were revascularized by the right and left internal thoracic arteries, respectively. Aortic cross-clamping time was 95 minutes and CPB duration was 130 minutes.

The postoperative course was uneventful. Echocardiographic examination in the second postoperative month revealed a 15-mmHg systolic gradient between the aorta and the left ventricle. In the second postoperative year, there were no clinical manifestations of coronary artery disease and aortic stenosis. Lipid levels were close to normal range with a low-lipid diet and statin treatment (atorvastatin 40 mg/day).

DISCUSSION

Although a clinical diagnosis of FH is commonly made, a definitive diagnosis can only be made by genetic screening, whereby mutations are detected only in 30% to 50% of patients with a clinical diagnosis. Moreover, genetic screening is costly.^[4] Early detection of FH is critical to prolong survival. Once identified, patients with FH can be placed on a diet and drug management. Being the most efficacious and well-tolerated agents, statins are the drugs of choice, which may be supplemented by bile acid sequestrants, niacin, and occasionally fibrates.^[2] Patients who are resistant to drug therapy are treated with plasma low-density lipoprotein apheresis.^[5]

Coronary artery bypass grafting alleviates angina and improves the quality of life in patients with FH. Kawasuji et al.^[5,6] reported that aggressive use of arterial grafts may be helpful in patients with FH and may improve long-term freedom from reoperation.

Aortic valve dysfunction in FH suggests that hypercholesterolemia affects not only the coronary arteries but also the aortic valve. Aortic stenosis is common in the homozygous form and aortic root involvement is always present.^[3] Patients with a small aortic annulus and a critical valvular aortic stenosis can be treated by aortic valve replacement, combined with an appropriate technique of aortic root enlargement that will relieve left ventricular outflow tract obstruction.

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