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Case Report / Olgu Sunumu

Coronary revascularization in a 13 year old patient with homozygous familial hypercholesterolemia

On üç yaşında bir homozigot ailevi hiperkolesterolemi hastasında koroner revaskülarizasyon

Eylem Tunçer, Murat Başaran, Nihat Çine, Behzat Tüzün, Hakan Ceyran

Department of Cardiovascular Surgery, Kartal Koşuyolu Yüksek İhtisas Training and Research Hospital, İstanbul, Turkey

Homozygous familial hypercholesterolemia is an autosomal dominant disorder caused by mutations in the low density lipoprotein receptor gene. The disease is associated with an increased risk of coronary artery disease early in life. In this article, we present a 13-year-old boy with familial homozygous hypercholesterolemia who had an extensive coronary artery disease and underwent successful coronary artery bypass graft surgery.

Key words: Coronary artery disease; coronary bypass artery grafting; familial hypercholesterolemia; surgery.

Ailesel homozigot hiperkolesterolemi düşük yoğunluklu lipoprotein reseptör gen mutasyonlarından kaynaklanan otozomal dominant bir hastalıktır. Hastalık erken yaşta koroner arter hastalığı gelişme riskinde artış ile ilişkilidir. Bu yazıda, yaygın koroner arter hastalığı ve ailesel homozigot hiperkolesterolemisi olan ve başarılı koroner arter baypas greft cerrahisi yapılan 13 yaşında bir erkek olgu sunuldu.

Anahtar sözcükler: Koroner arter hastalığı; koroner baypas arter greftleme; ailesel hiperkolesterolemi; cerrahi.

Homozygous familial hypercholesterolemia (HFH) is an autosomal dominant disease caused by a mutation in the low-density lipoprotein (LDL) receptor. This mutation leads to increased serum LDL and is characterized by cutaneous, tendinous xanthomas, premature corneal arcing, and an increased risk of coronary artery disease (CAD). In addition, it may necessitate coronary artery bypass graft (CABG) surgery in children and young adults. In this article, we present a patient with HFH and severe obstructive CAD who underwent successful total revascularization.

CASE REPORT

A 13-year-old boy was admitted to our cardiac clinic with a history of exertional angina [Canadian Cardiovascular Society (CCS) angina class II]. He had a diagnosis of HFH before admission and been on anti-lipidemic therapy with plasmapheresis for more than six months concomitantly. He also had a family history of hypercholesterolemia, premature CAD, and sudden cardiac death without no other major risk factors. On physical examination, the patient showed the characteristic findings of the disease, including tendinous xanthomas over his fingers, elbow and knee joints, and Achilles tendons. In spite of intensive therapy, he had an LDL level of 512 mg/dl and a total cholesterol level of 576 mg/dl, a high-density lipoprotein (HDL) level of 30 mg/dl, and a triglyceride level of 137 mg/dl.

Electrocardiography showed no changes that were specifically related to CAD, and echocardiographic Doppler scanning revealed mild aortic regurgitation and stenosis (maximum gradient 28 mmHg) along with mild mitral regurgitation. The patient's ejection fraction (EF) was normal. Coronary angiography identified severe proximal left system and right coronary artery (RCA) disease (Figure 1).

Myocardial revascularization was indicated. Surgery was performed via median sternotomy under general anestesia. The bilateral internal thoracic artery (BITA) along with the saphenous vein graft (SVG) were harvested. Both ITA grafts were confirmed to be of good quality, based on our careful observation

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Correspondence: Eylem Tunçer, M.D. Kartal Koşuyolu Yüksek İhtisas Eğitim ve Araştırma Hastanesi, Kalp ve Damar Cerrahisi Kliniği, 34890 Cevizli, Kartal, İstanbul, Turkey.
Tel: +90 216 - 500 15 00 e-mail: eylemkvc@yahoo.com

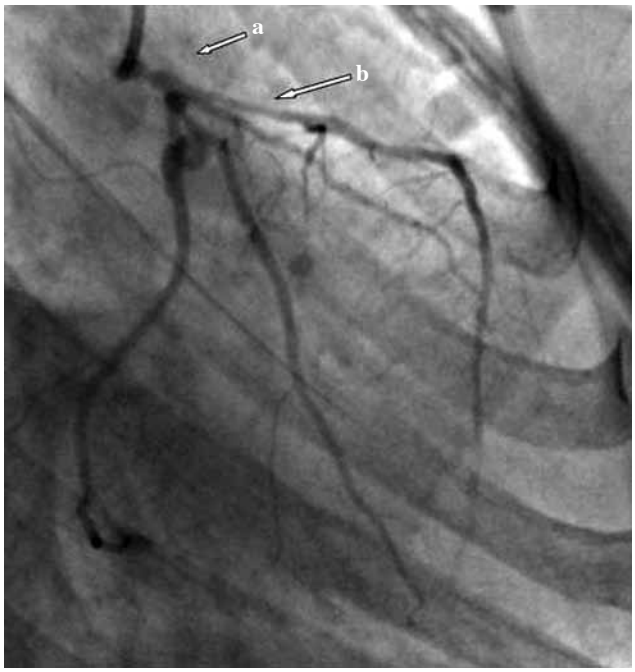

Figure 1. (a) Left main coronary artery stenosis and **(b)** diffuse proximal left anterior descending lesion.

suggesting that they were free of atheromatous plaques with an adequate blood flow. Cardiopulmonary bypass (CPB) commenced in a standard way. Myocardial protection was achieved by antegrade cardioplegic arrest and the RCA was revascularized with the SVG, while the obtuse margin and the left anterior descending (LAD) artery both received ITA grafts. The right ITA graft was anostomosed to the obtuse margin after being routed through the transverse sinus. The LAD artery was diffusely affected by HFH as indicated by the formation of severe atheromatous plaques. A long arteriotomy (6 cm) was then carried out in order to reach a clear intima region. After SVG patch plasty, the left ITA was anastomosed to that graft. Patient was successfully weaned from the CPB. The postoperative course was uneventful, and the patient was extubated seven hours after the surgery was completed. He then stayed in the intensive care unit (ICU) for one day and spent a total of six days in the hospital. The postoperative echocardiographic findings and enzyme levels were normal, and the patient was prescribed atorvastatin as well as acetylsalicylic acid on discharge. The postoperative follow-up continues today. He is still under follow-up to ensure strict control of his cholesterol levels, whether with antilipidemic agents or plasmapheresis and he also undergoes periodic physical examinations including echocardiography. Currently, the patient is free of angina.

DISCUSSION

Homozygous familial hypercholesterolemia is an autosomally dominant, inherited disorder which is associated with accelerated atherosclerosis and the development of multiple tendon xanthomas. Patients with HFH are prone to develop CAD usually in the second or third decades of life; however, very early onset of CAD in childhood has also been reported.[1,2] In those cases, coronary revascularization may inevitably be indicated. The type of graft to be used for this procedure is a matter of concern, with some articles advocating arterial revascularization as the best approach.[3,4] Since hypercholesterolemia may accelerate atherosclerotic changes in veins, ITA grafts are usually preferred because of their enhanced long-term patency. Takahashi et al.[3] reported that the gastroepiploic artery has also been used. Although arterial grafting provides many benefits, acceptable results have also been reported with from venous grafts.[2] Since there is a high risk of stenosis in these patients, visualization of the possible arterial grafts during angiography is of the utmost importance.

Another concern regarding the grafts to be used for revascularization in the pediatric population is the growth potential. Internal thoracic artery grafts expand in proportion to somatic growth, whereas SVGs do not increase in length or diameter.[5] However, isolated reports have showed excellent growth and patency with venous grafts up to 13 years after CABG surgery.[4] We used both ITA grafts and SVGs for revascularization in this patient. We preferred to use the SVG rather than radial artery because of the non-dominant nature of the native RCA. Moreover, we aimed to preserve the radial artery as an arterial graft for possible future reoperations.

The need to screen the first-degree relatives and extended family members of patients with HFH must be emphasized. In our case, the patient was diagnosed after his sister had an acute coronary event at the age of 15 and died following CABG. This indicates the crucial role of the screening process for early diagnosis and treatment. Despite recent advances in lipid-lowering treatment of HFH cases, the disease remains a significant challenge. Patients can benefit from the lipid-lowering therapy and plasma apheresis to some degree, however, liver transplantation is the best option for normalization of the lipid profile and prevention complications in the long-term.[2]

Homozygous familial hypercholesterolemia may also lead to valvular and supravalvular aortic stenosis.[6] Our patient had mild aortic stenosis that did not require any further intervention. However, Tsuchida et al.[6]

presented a patient with familial hypercholesterolemia who developed severe aortic stenosis years after CABG in spite of aggressive lipid-lowering therapy. In the same article, they also discussed two recent, prospective, placebo-controlled studies that used high-dose statin therapy to prevent the progression of aortic valve stenosis, but the effectiveness of such therapy is still controversial.[6]

Even if serum LDL levels are strictly controlled, aortic valve stenosis may still develop, which is consistent with both our findings and those of Tsuchida et al. Caution, hence, must be paid to the progression of aortic valve stenosis under optimal cholesterol-lowering therapy, even.

In conclusion, patients with HFH must be followed up closely for the development of coronary atherosclerosis. The surgical results have been satisfactory, however, long-term survival of the patients depends on strictly controlling lipid levels, due to the ongoing nature of the disease. In addition, periodic postoperative follow-up must take place to watch for the progression of CAD and aortic valve stenosis.

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