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Case Report
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# Hemoperfusion during Coronary Artery Bypass Grafting Promotes Lipid-Lowering in Familial Hypercholesterolemia

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## Abstract

Patients with Familial Hypercholesterolemia (FH) presented with early-onset Coronary Heart Disease (CAD) usually require Coronary Artery Transplantation (CABG) treatment. However, the effect of lipid-lowering therapy plays a critical role in long-term survival. In this case, a young woman was clinically diagnosed as homozygous FH and received CABG under Cardiopulmonary Bypass (CPB). During CPB, we used hemoperfusion to lower blood lipids and found that its effect was much better than other lipid-lowering therapies. This case enables us to further realize the importance of hemoperfusion for lipid-lowering therapy in patients with homozygous FH.

**Keywords: Familial hypercholesterolemia; Xanthomas; Coronary artery disease; Hemoperfusion**

## Introduction

Familial Hypercholesterolemia (FH) is a genetic disorder characterized by high levels of Low-Density Lipoprotein (LDL) and the presence of xanthomas. FH often leads to early Coronary Artery Disease (CAD). Homozygous FH (HoFH) usually presents as xanthoma tuberosum in childhood and is associated with CAD-related death at a young age [1]. Effectively reducing blood lipid levels and controlling blood lipid growth are the keys to the improvement of prognosis. The management of HoFH patients requires lifestyle modifications and therapeutic interventions. Furthermore, Coronary Artery Bypass Grafting (CABG) becomes necessary when severe coronary artery stenosis develops.

Here, we present the case of a young female HoFH patient presented with CAD, effort angina, multiple xanthomas, and markedly elevated levels of serum LDL. We describe the combined modality therapy used during the surgical management of HoFH.

## Case Presentation

A 23-year-old female patient was admitted to our hospital with complaints of effort angina and two episodes of syncope reported during the previous six months. Physical examination revealed multiple extensive cutaneous xanthomas over her buttocks, eyelids, elbows, knees, and metacarpophalangeal joints (Figure 1A, 1B). The xanthomas were first noticed at ten years of age and since then gradually expanded in size. At admission, her fasting lipid profile was high, with total cholesterol of 227.7 mg/dL, LDL 216.36 mg/dL, HDL 19.08 mg/dL, and Triglycerides (TGs) 14.04 mg/dL. Serum high-sensitivity cardiac Troponin T (h-cTnT ) was 3.07 pg/mL (normal range 0 pg/mL to 14.00 pg/mL), ECG was normal with non-specific ST-T changes. 2D echocardiography documented a normal left Ventricular Ejection Fraction (LVEF) of 64% and absence of aortic valve lesions. However, the dual-source 64-slice Computed Tomography (CT) revealed a non-calcified plaque at the distal end of the left main coronary artery and multiple plaques on the right coronary artery, with moderate to severe stenosis (Figure 1C). These changes were combined with the calcification of the aortic root (Figure 1D, 1E) and the formation of calcified plaque in bilateral carotid arteries (Figure 1F). Subsequent coronary angiography demonstrated that the end of the left main coronary artery had 90% stenosis (Figure 2A), the middle segment of the anterior descending artery had 70% stenosis, the middle and distal segments of the diagonal artery had 85% stenosis (Figure 2A), the first obtuse marginal branch of the circumflex artery had 70% stenosis, and the right coronary artery had 90% stenosis (Figure 2B).

During the first ten years after the onset of xanthomas, the patient remained asymptomatic and was only intermittently treated with alginic sodium diester, statins, and some unknown traditional

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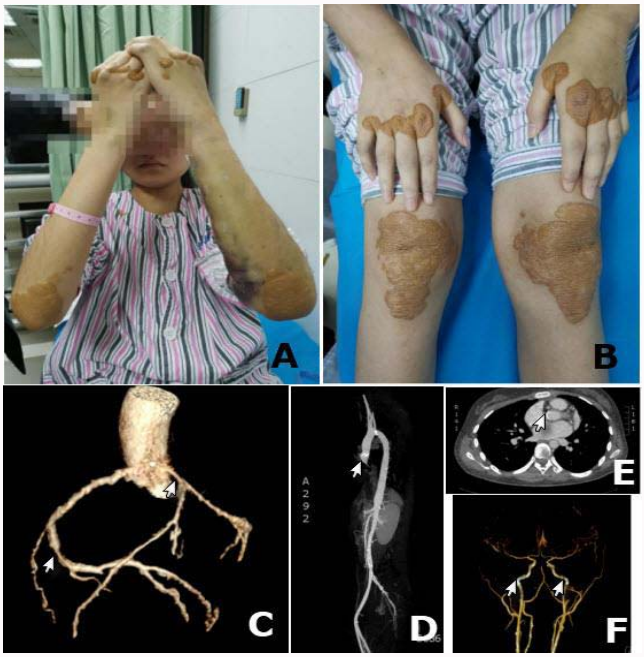


**Figure 1:** Clinical presentation of the patient.
A, B: Cutaneous xanthomas on elbows (A), knees, and metacarpophalangeal joint (B).
C: Dual-source 64-slice computed tomography showing plaques and stenosis (arrow) in the left main coronary artery and right coronary artery.
D, E: Calcification of the arterial wall at the right aortic root (arrow) and its cross-section image.
F: Calcification of arterial walls in both carotid arteries.

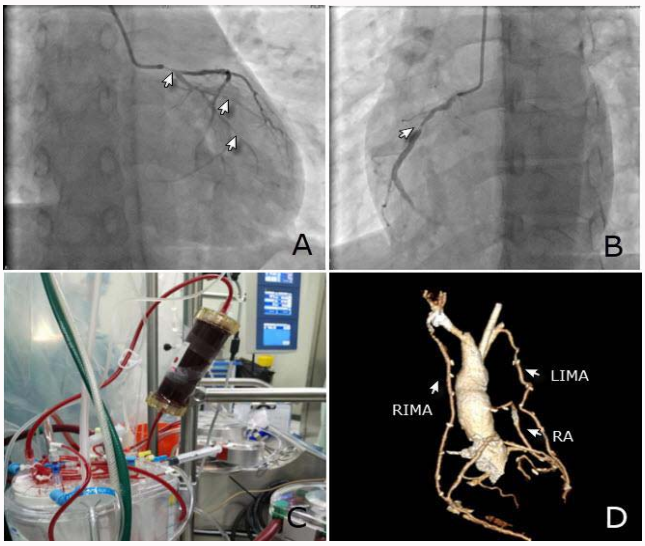


**Figure 2:** Coronary angiography showing the degree of stenosis in arteries.
A. 90% stenosis at the end of the left main coronary artery, 70% stenosis in the middle segment of the anterior descending artery, and 85% stenosis in the middle and distal segments of the diagonal artery.
B. 90% stenosis in the right coronary artery.
C. The hemoperfusion device used during CPB.
D. 64-slice CT of the coronary artery demonstrating that all anastomoses of the grafts were patent.
LIMA: Left Internal Mammary Artery; RIMA: Right Internal Mammary Artery; RA: Radial Artery

Chinese medicines. Combination therapy consisting of atorvastatin 40 mg QD and ezetimibe 10 mg QD was initiated only three years ago and resulted in a partial reduction in the level of cholesterolemia.

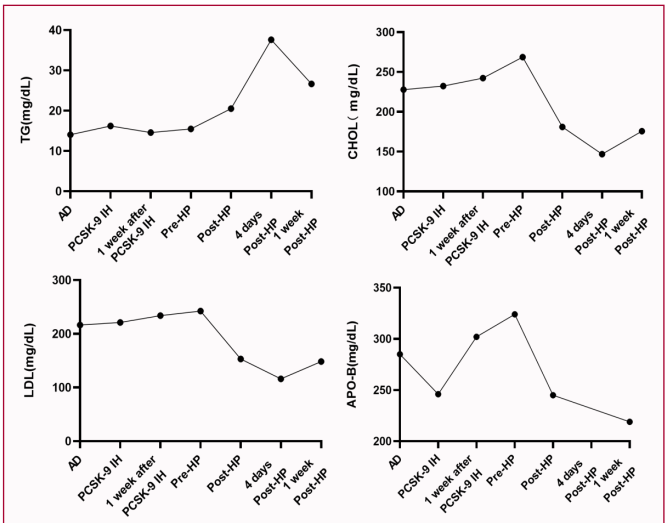


**Figure 3:** LDL levels at different time points.
On admission, CHOL (normal range 52.2 mg/dL to 93.6 mg/dL), LDL (normal range <56.16 mg/dL), and Apo B (normal range 60 mg/dL to 120 mg/dL), but not TG (normal range <30.78 mg/dL), were significantly higher than the normal range. After two doses of the PCSK9 inhibitor, the level of lipids did not change. However, after hemoperfusion during CPB, the concentrations of CHOL, LDL, and Apo-B decreased significantly. The level of TG was transiently increased, likely reflecting the recovery of diet post-operation.
TG: Triglycerides; CHOL: Total Cholesterol; LDL: Low-Density Lipoprotein; Apo-B: Apolipoprotein B; Time points: AD, On Admission; PCSK-9 IH: After the Administration of the Second Dose of PCSK-9 Inhibitor; 1 week after PCSK-9 IH: One week after the Second Dose of PCSK-9 Inhibitor; Pre-HP: Pre-Hemoperfusion; Post HP: Post-Hemoperfusion; 4 days Post-HP: Four days Post-Hemoperfusion; 1 week Post-HP: One week Post-Hemoperfusion

At the present admission, higher-intensity lipid-lowering treatment was initiated. It included probucol 500 mg bid and evolocumab, a Proprotein Convertase Subtilisin Kexin-9 (PCSK9) inhibitor (Amgen Inc., Thousand Lakes, CA, USA), twice a month.

CABG using bilateral Internal Thoracic Artery (ITA) and radial artery was performed under Cardiopulmonary Bypass (CPB) with aortic cross-clamp. A total arterial grafting bypass was performed using the left ITA to LAD and the right ITA to the main right coronary artery. The first obtuse marginal branch and diagonal artery bypass were sequenced with radial artery bypass. During the CPB, a hemoperfusion instrument (Jafron Biomedical Co, Zhuhai, Guangdong, China) was connected with the membrane oxygenator (Figure 2C), and blood lipid components were continuously absorbed and removed perioperatively. The recorded total CPB time was 150 min. Postoperative care went smoothly with no complications. Postoperative CT of the coronary artery demonstrated that all anastomoses of grafts were patent (Figure 2D). The comparison of lipid levels before and after the operation on the day of surgery revealed a decrease in major blood lipid indicators, including total cholesterol (from 268.56 mg/dL to 180.9 mg/dL), LDL (from 242.3 mg/dL to 153 mg/dL), and Apolipoprotein B (Apo B, from 324 mg/dL to 245 mg/dL). (Figure 3, compare time points 3 and 4).

All procedures performed adhered to the ethical standards of the Second Xiangya Hospital Ethics Committee, and the patient's parents provided consent for publication of her data.

## Discussion

HoFH is an autosomal dominant inherited genetic disorder causing premature CAD [2]. Clinical diagnosis of Homozygous

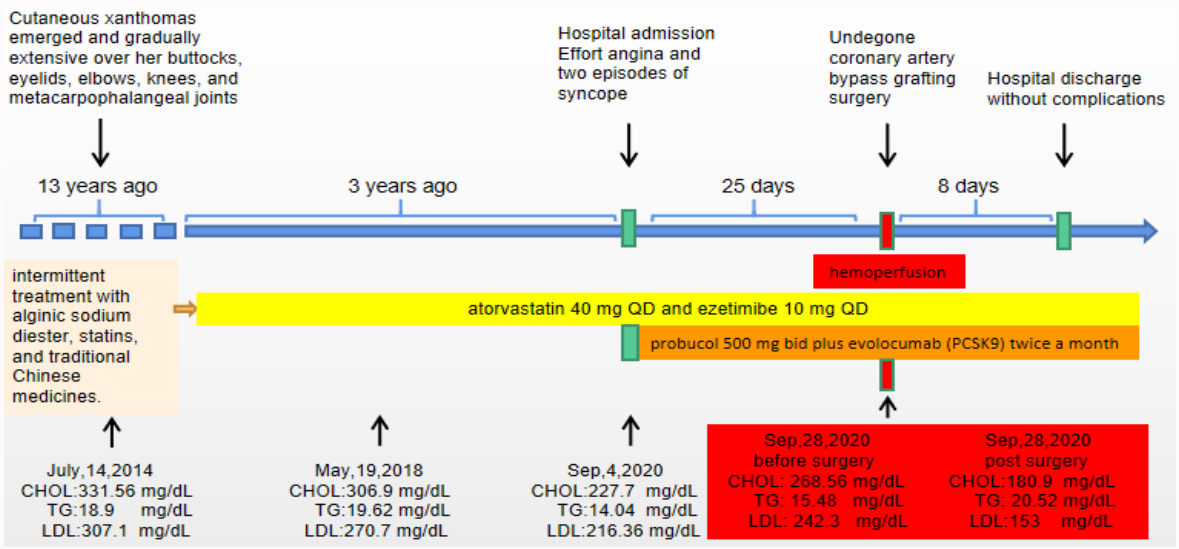


**Figure 4:** Timeline of diagnosis and treatment.

HF patients is usually straight forward because persistent hypercholesterolemia produces atherosclerosis and xanthoma in childhood. However, untreated HoFH typically leads to death before the third decade of life [3]. According to the consensus statement on Familial Hypercholesterolemia released by the European Atherosclerosis Society [1], the case reported here can be clinically diagnosed as HoFH because of the high level of LDL and extensive cutaneous xanthoma around the age of ten years.

Unfortunately, only during the past three years, the patient received intensive lipid-lowering treatment, consisting of a combination of statins and ezetimibe. However, blood lipid levels could not be appreciably reduced, leading to the rapid progression of plaques in both the coronary and carotid arteries and the development of symptoms of angina and syncope. After hospitalization, although probucol and two doses of the PCSK9 inhibitor were given, the lipid-lowering effect of the treatment could not be fully demonstrated due to the short course of treatment (Figure 3, compare time points 0 and 3).

Coronary atherosclerosis in FH patient's progresses faster than in the general population. Blood lipid levels must be strictly controlled in addition to complete arterial graft [4]. The maintenance of normal lipid concentrations is essential to reduce the possibility of restenosis caused by atherosclerotic plaque formation at the distal segments of grafts and ensure the long-term patency of the graft. Lipoprotein apheresis is an extracorporeal therapy in which Apo B-containing lipoproteins are selectively removed from the plasma of a patient; it effectively limits or reverses atherosclerotic complications of high cholesterol [5]. The hemoperfusion device used in lipoprotein apheresis achieves lipid filtration of the whole blood and can be directly connected to the extracorporeal circulation. Therefore, we did not use an off-pump to perform CABG but chose to perform bypass surgery under CPB with aortic cross-clamping. The main components of blood lipids were significantly reduced (Figure 3).

We report a case of a young female HoFH patient complaining of coronary heart disease, presenting with effort angina and syncopes. The patient was treated by performing total arterial grafts under CPB combined with hemoperfusion to reduce lipid levels. The timeline of diagnosis and treatment of this case was summarized in Figure 4. This case may provide a reference for the comprehensive lipid-lowering treatment of such patients. We hope that this report will stimulate the medical and research community to search for improved timely interventions and use appropriate bypass surgery to reduce morbidity and mortality.

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