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Case Report

Familial hypercholesterolemia with extensive coronary artery disease and tuberous and tendinous xanthomas: A case report and mutation analysis

Deniz Agirbasli, MD, PhD, Tommy Hyatt, Mehmet Agirbasli, MD*

Acıbadem Mehmet Ali Aydınlar University School of Medicine, Department of Medical Biology, İstanbul, Turkey Dr Agirbasli; Howard Hughes Medical Institute, University of Texas Southwestern Medical Center, Dallas, TX, USA Dr Hyatt; and Medeniyet University Medical Center, Department of Cardiology, İstanbul, Turkey Dr Agirbasli

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LDL;
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Abstract: This is a case report of a 38-year-old Syrian refugee male with early-onset extensive atherosclerosis. The physical and laboratory examination were remarkable with severe xanthomas in the upper and lower extremities and with low-density lipoprotein cholesterol (LDL-C) 417 mg/dL, total cholesterol 495 mg/dL, high-density lipoprotein cholesterol 30 mg/dL, and triglycerides 242 mg/dL. LDL-C level responded poorly to the high-dose statin treatment. The genetic analysis indicated that the patient had a large homozygous deletion in LDL receptor gene including the exons 7–14. A 12-kb deletion had occurred between the 2 Alu repetitive sequences that were oriented in opposite directions, one in intron 6 and the other in intron 14. This deletion eliminated exons 7–14, which exactly corresponded to the entire exon sequence coding the epidermal growth factor precursor homology domain. This deletion in LDL receptor was previously reported. This rare case of homozygous familial hypercholesterolemia presenting with multiple large and widely distributed xanthomas implicates the need for novel treatment options in familial hypercholesterolemia patients. The case is a Syrian refugee and emphasizes the urgent need to address orphan disease in refugee populations throughout the world.

Introduction

Familial hypercholesterolemia (FH) is a metabolic disorder that is inherited as an autosomal dominant trait. It exhibits significantly increased levels of low-density lipoprotein cholesterol (LDL-C), cutaneous or tendon xanthomas, corneal arcus, and premature coronary heart disease.[1] FH is a common genetic disorder (1/250),[2] yet homozygous FH (HoFH) remains rare (1:1,000,000). The management of patients with FH presents a challenge.

Case report

The patient is a 38-year-old Syrian male with early-onset extensive atherosclerosis. The patient underwent coronary artery bypass surgery at the age of 27 years. His father passed away from myocardial infarction at the age of 52 years. His mother (52 years) is healthy and lives with him. Lipid levels of the mother and the pedigree are displayed in Figure 1. His mother has no history of smoking, body mass index = 24.4 kg/m^2, and blood pressure was 120/78 mm

* Corresponding author. Medeniyet University Medical Center, Department of Cardiology, Yesilbahar sok. Palmiye Apt 68/14 Goztepe 34730 Kadikoy, Istanbul Turkiye.
E-mail address: magirbasli@gmail.com
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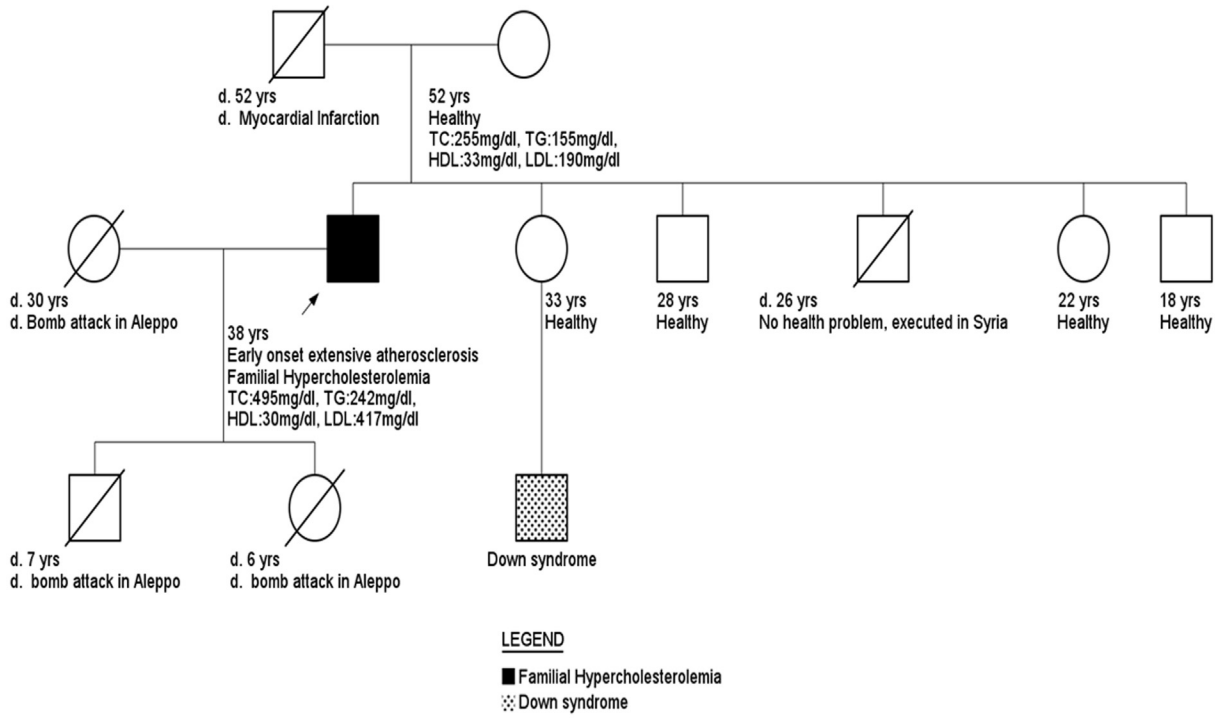

Figure 1 Family pedigree; the arrow indicates the presented index case. LDL, low-density lipoprotein; TC, total cholesterol; TG, triglyceride.

Hg. The patient has 3 brothers and 2 sisters. One brother was killed in the Syrian war. One of his sisters has a child with Down syndrome (Fig. 1). The physical examination was remarkable with severe xanthomas in the upper and lower extremities (Fig. 2).

Laboratory examination displayed significant hypercholesterolemia with LDL-C: 417 mg/dL, total cholesterol: 495 mg/dL, high-density lipoprotein cholesterol: 30 mg/dL, and triglycerides: 242 mg/dL. Other laboratory assessment revealed anemia hemoglobin: 8.2 g/dL, hematocrit: 27%, and mean corpuscular volume: 52.4 fL.

At the time of initial visit, the patient was not on any treatment. The continuity of his care was disrupted, and he received no medical treatment during the time of displacement. After initial visit, he was started on Rosuvastatin 40 mg per day, along with aspirin and beta blockers. Repeat lipid levels were checked within after 8 weeks, which displayed LDL-C level of 395 mg/dL. We analyzed LDL receptor (LDLR) gene for mutations. Informed consent was obtained from the patient for genetic analysis. Genetic studies were approved by the Institutional Review Board. Peripheric blood was collected for genetic analysis. Genomic DNA was isolated from peripheric blood. Multiplex ligation-dependent probe amplification (MLPA) analysis was performed according to manufacturer's instructions. MLPA is a widely used method for screening of samples for the presence of deletions and copy number variations. Probe set (SALSA MLPA probemix P062-C2 *LDLR*) was purchased from MRC-Holland. The MLPA reaction was run on Applied Biosystems ABI 3730XL. The patient had a large homozygous deletion in *LDLR* gene including the exons 7–14 (Fig. 3.). A 12-kb deletion had occurred between the 2 Alu repetitive sequences that were oriented in opposite directions, one in intron 6 and the other in intron 14. This deletion eliminated exons

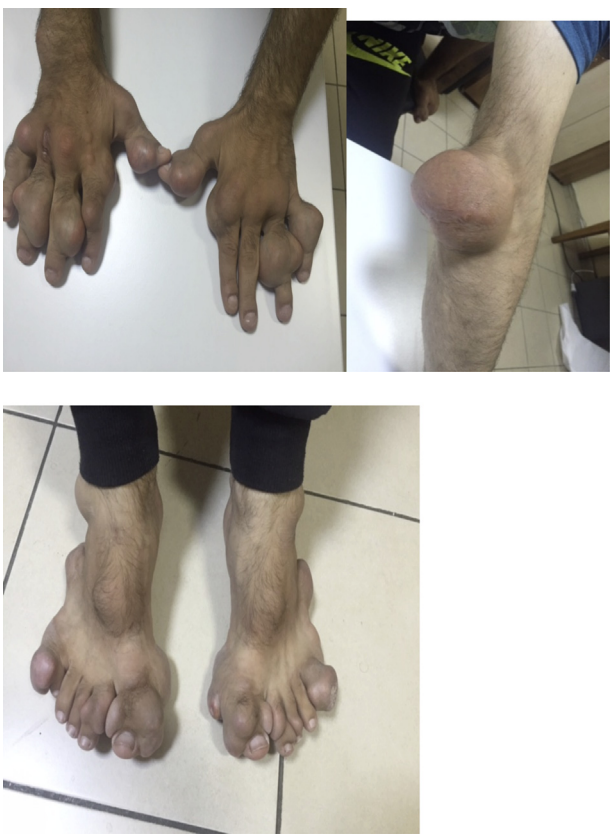

Figure 2 Severe tuberous xanthomas in the upper and lower extremities.