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Case Report

Young Fatal Case of Familial Hypercholesterolemia: A Case Report

Introduction

Familial hypercholesterolemia (FH) is a genetic disease presented by high levels of serum low density lipoprotein (LDL), xanthomas and early coronary artery disease (CAD). The main cause of FH is LDL receptor abnormalities that decrease the uptake of LDL into cells, particularly into the liver cells, from the blood, resulting in the increase of serum LDL-cholesterol levels [1]. The incidence of homozygous FH (HoFH) is very low (1 in million people). However, heterozygous FH occurs in 1 of 500 people, and is frequently detected by routine medical health check-up [2]. Since xanthomas may precede the diagnosis of hyperlipidemia, early identification can lead to preventive treatment that reduces the risk and morbidity of cardiovascular disease, including myocardial infarction. This case report presents a 24 year-old Indian female with multiple xanthomas involving the Achilles tendon, soles, hands, knees, elbows, and was associated with the premature severe coronary artery disease.

Case

A 24 year young married lady presented to our emergency with history of chest pain for 3-4 days duration which was retrosternal, moderate intensity, mostly on exertion associated with sweating. She had a significant family history of her younger sisiter who died at a young age of 13 years with sudden death. On evaluation her examination showed xanthomas on elbows, Achilles tendon, knee joints and xanthelasmas were present. She had hepatomegaly and Cardiac examination showed a systolic murmur of grade 4/6 at aortic area. Investigations showed anemia with hemoglobin of 9.7gm% and dyslipidemia (T.Cholesterol 882 mg/dl, LDL 434 mg/dl, Triglycerides 235

mg/dl & HDL 29 mg/dl). 2d Echo showed supralvalvular aortic stenosis in tubular part of aorta with mild narrowing in proximal descending aorta, Mitral valve was thickened and mild calcified, LV systolic ejection fraction of 65% with no regional wall motion abnormality. Coronary angiography showed triple vessel disease with left main ostial disease (Figure 1a,b). She was advised early myocardial revascularization but attendants and patient refused any intervention in present admission and wanted it to be done at later date and she was discharged in stable condition on high dose statins, fibrates, antiplatelets but after 2 weeks she got admitted in emergency with cardiogenic shock and succumbed to her illness with VT/VF before any definite procedure could be done.

Discussion

Hyperlipidemia is caused by increased concentrations of plasma lipoproteins. Alterations resulting from genetic defects are classified as primary disorders of lipoprotein metabolism. Alternatively, other factors that alter lipoprotein metabolism, such as diabetes mellitus or hypothyroidism, lead to increased plasma lipoprotein concentrations; these are classified as secondary disorders of lipid metabolism. The heritable hyperlipidemia is of six types: I, IIa, IIb, III, IV and V. Subcutaneous xanthomas typically occur in patient with heritable hyperlipidemia [3].

FH is an autosomal dominant genetic disorder due to mutations in the LDL receptor gene located on chromosome 19 [3]. According to the Frederickson's classification, this

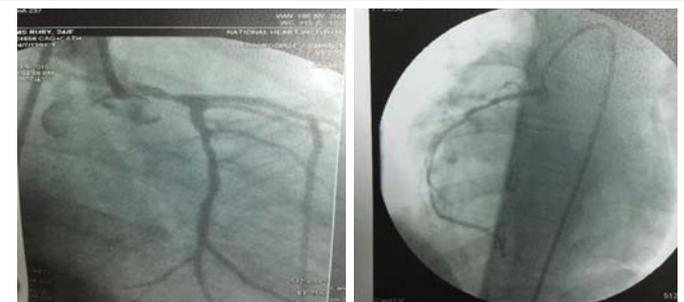


Figure 1a,b: Coronary angiography showing triple vessel disease with left main disease.

condition is categorized as a type II hyperlipoproteinemia [4]. There are two types of familial hypercholesterolemia: the heterozygous form in which the patient has one normal allele and one mutated allele is the most common form with an incidence of 1 out of 500, whereas the homozygous form in which the patient has two mutated alleles, considered an autosomal codominant disorder, is rare with an incidence of approximately one in a million. Patients with heterozygous FH are usually diagnosed during adulthood and often respond well to medical therapy. On the other hand, patients with homozygous FH are often diagnosed early in childhood, do not respond well to medical therapy, and can progress rapidly to premature coronary artery disease [4].

Simon Broome formed criteria for definite and possible diagnosis of FH.

A definite diagnosis of FH is established if the case has:

Cholesterol concentrations (LDL cholesterol > 13 mmol/L (234mg/dl) in adults and > 11mmol/L (198mg/dl) in children)

Tendon xanthomas, or evidence of these signs in first or second-degree relative or DNA-based evidence of an LDL-receptor mutation, familial defective apo B- 100, or a PCSK9 mutation.

A clinical diagnosis of HoFH is possible where LDL cholesterol > 13 mmol/L (234mg/dl) in adults and > 11mmol/L (198mg/dl) in children. Where potential cases of FH are identified, an extensive family history must be obtained (ideally a three-generation pedigree) with particular attention given to relatives with significant vascular incidents, the age of onset of events, cardiovascular risk factors and any formal FH diagnoses [5,6].

Several types of cutaneous xanthomas are recognized and associated with FH including xanthelasma, xanthoma tendineum, and xanthoma tuberosum. Other types of xanthomas, such as eruptive xanthomas, xanthoma planum, palmar xanthomas, and tuberous xanthomas, are not usually associated with FH [7].

Our patient had tendon xanthomas and also her LDL levels were 434 mg/dl (>72mg/dl), with positive family history of likely a cardiac event, conforming to the definite diagnosing of FH criteria's.

Treatment is focused on decreasing LDL levels through the

use of statin medications, or ezetimibe, combined with dietary modification and counseling regarding the risks of alcohol, smoking, and sedentary lifestyle [9]. For more severe cases, combination therapy with a bile acid sequestrant [10], nicotinic acid, fibrates, low-density lipoprotein apheresis [8,11], or orthotopic liver transplantation [8] may be required. The workup should almost always include a cardiology evaluation to rule out early coronary artery disease.

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