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Case Report

FAMILIAL HYPERCHOLESTEROLEMIA

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ABSTRACT

Abstract
Familial hypercholesterolemia is an autosomal dominant disorder due to mutations in the low-density lipoprotein receptor gene, characterized by skin and tendon xanthomas, xanthelasma and premature arcus corneae. It is associated with an increased risk of premature coronary heart disease.
Here we report a case of 40 year old male who presented with xanthomas and an elevated serum low density lipoprotein cholesterol. His elder sibling had similar complaints.
This report is to emphasise the need to clinically recognize xanthomas and its association with elevated LDL-C, premature atherosclerosis and familial inheritance. Screening of first-degree relatives and extended family members plays an important role in early detection and treatment. Early diagnosis and early initiation of treatment will save the affected individual and the other family members from catastrophic cardiac events.

Key words: familial hypercholesterolemia, low density lipoprotein cholesterol, xanthomas.

INTRODUCTION:

Familial hypercholesterolemia (FH) is an autosomal codominant disorder characterized by high serum low density lipoprotein cholesterol (LDL-C), tendon xanthomas, and premature coronary atherosclerosis. The prognosis is reserved with progression to atherosclerosis, coronary arterial disease and early death.

FH patients require lipid lowering drug therapy. If medical treatment is inefficient then LDL-C apheresis and liver transplantation are needed.[1] Due to the rarity of this condition and the severity of its complications, the present article aims to report a case of a 40 year old male patient who developed xanthomas since the age of 15years and elevated serum LDL-C. The significance, characteristic features, diagnosis and treatment of familial hypercholesterolemia are discussed.

CASE REPORT:

A 40- year- old male, presented with history of multiple swellings over elbow and ankle since the age of 15 years. His elder sibling had similar complaints. There was no history of diabetes mellitus, hypothyroidism, hepatic disease, or renal disease. On physical examination, multiple nodules of varying size (1mm- 40mm) were observed on extensor surface of hands

(Figure 1), elbow (Figure 2), buttocks, knee, ankle (Figure 3) and feet, suggestive of xanthomas. In addition, there was corneal arcing (Figure 4). Systemic examination was unremarkable.

Investigations revealed total cholesterol of 660 mg/dl, low density lipoprotein cholesterol of 551mg/dl, high density lipoprotein cholesterol of 40 mg/dl and triglyceride of 281 mg/dl. Complete hemogram, blood sugar, renal function test, liver function test and thyroid function test were within normal limits. Chest X-ray and electrocardiogram were normal. Echocardiogram showed calcification of aortic valve. There was no gradient across the aortic valve. Stress test was negative for inducible ischemia. Fine needle aspiration cytology from one of the nodule revealed foamy histiocytosis (Figure 5). Based on the above findings, a diagnosis of familial hypercholesterolemia was considered. He was started on atorvastatin 40 mg, with ezetimibe 10 mg daily.

Figure 1: Photograph of right hand showing xanthomas on extensor surface.

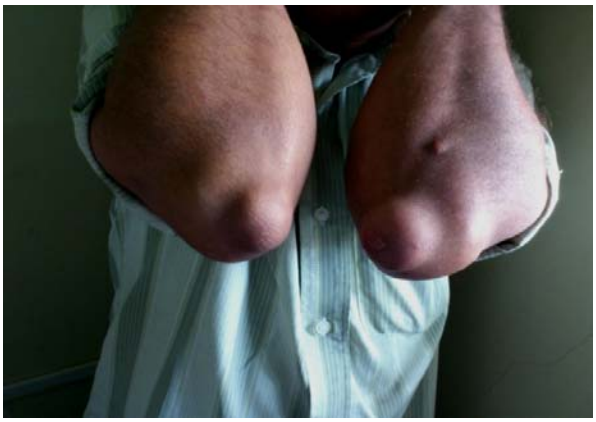

Figure 2: Photograph of left elbow showing xanthomas.

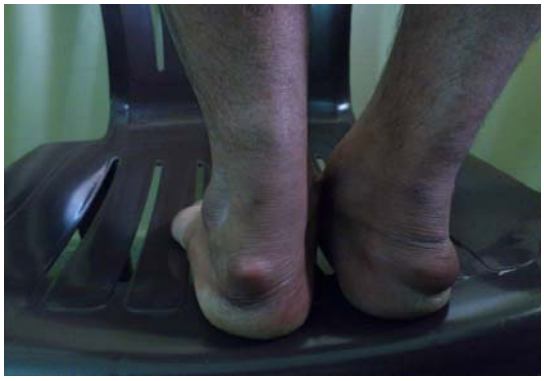

Figure 3: Photograph of both ankles showing xanthomas at Achilles tendon.

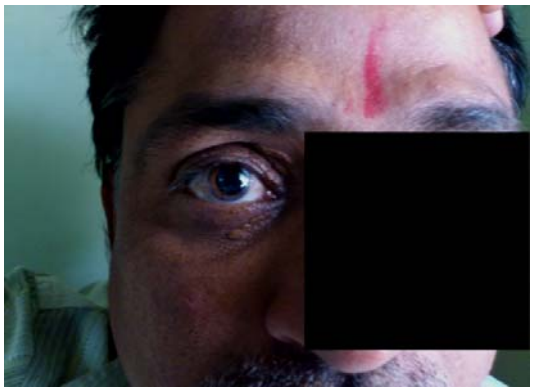

Figure 4: Photograph of right eye showing corneal arcus (white rim coating the limbus in eye) and xanthelasmas around medial side of eye.

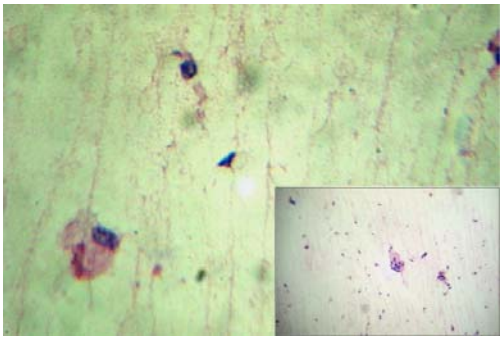

Figure 5: Photomicrograph of FNAC smears showing foamy histiocytes (xanthoma cells) along with lymphocytes. (H & E, X 400). Inset shows multinucleate giant cells (H & E, 400).

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. [2] The heritable hyperlipidemia is of six types: I, IIa, IIb, III, IV and V. Subcutaneous xanthomas typically occur in patient with heritable hyperlipidemia.[1]

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 condition is categorized as a type II hyperlipoproteinemia.[1] 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.[1]

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. [4] Other clinical manifestations of FH include xanthomas located in the tongue and buccal mucosa, and arcus senilis corneae.[5]

Our patient had eruptive and tuberous cutaneous xanthomas, as well as Achilles tendon, lower leg extensor, hand extensor tendon xanthomas and arcus senilis corneae, which are all classical, signs of FH. Although xanthomas started appearing at the age of 15, he was investigated and diagnosed with hypercholesterolemia only at the age of 40. Another important manifestation of cholesterol deposition includes cardiovascular complications. Fortunately our patient did not have any cardiac involvement.

Simon Broome's diagnostic criteria for familial hypercholesterolemia says a definite diagnosis of familial hypercholesterolemia can be made if either the total cholesterol concentration is above 7.5 mmol/liter in adults or the LDL cholesterol concentration is above 4.9mmol/liter in adults and if tendinous xanthomas were present in the patient or a first-degree relative.[6-7]

Our patient had total cholesterol of 17.06mmol/liter and a LDL-C of 14.24mmol/liter. He and his elder sister had xanthomas. Hence this confirms the diagnosis of familial hypercholesterolemia in our patient.

Treatment options available for FH are lipid lowering drugs like statins, bile acid sequestrants, apheresis and liver transplantation[1]. Our patient was put on atorvastatin 40 mg, with ezetimibe 10 mg daily. After one month fallow up there was significant regression of xanthomas, even though biochemical parameter remained same.

CONCLUSION:

The major complication of familial hypercholesterolemia is accelerated atherosclerosis, resulting in significant morbidity and mortality due to coronary artery disases. Hence, early recognition is important. Clinical identification of xanthomas and knowledge of its

association with coronary artery disease is essential for every physician as early diagnosis and treatment can prevent premature deaths. All the relatives in the family should be screened for dyslipidemia. In this report, we highlight the typical clinical manifestation of familial hypercholesterolemia

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