CASE REPORT

TUBEROUS XANTHOMA :A RARE PRESENTATION OF FAMILIAL HYPERCHOLESTEROLEMIA

BereketFantahun[1], Tesfaye Deme[2]

ABSTRACT

Familial hypercholesterolemia (FH) is an autosomal dominant genetic disorder characterized by elevated plasma levels of low-density lipoprotein-cholesterol (LDL-C).FH often leads to accumulation of holesterol in the skin, where xanthomas can occur. We report a case of FH in an 11 year old female child which is alerted by multiple nodular lesions over the buttock, knee and elbow. Lipid profile showed elevated serum levels of LDL-C in the child and her mother. Biopsy taken from the lesion showed focal aggregates of foamy macrophages with a conclusion of Tuberous Xanthoma.

Key Words: Xanthomas, Familial hypercholesterolemia, LDL-C

INTRODUCTION

There are both 'heterozygous' (heFH) and 'homozygous' (hoFH) forms of Familial hypercholesterolemia (FH). In the general population, the prevalence of the heFH phenotype has been reported as 1 in 500 and the prevalence of the hoFH form is estimated to be 1 in 1 million.[1]The highest prevalence of FH is seen in the Afrikaner population-estimated as 1 in 70 in the heFH form. Xanthomas are well circumscribed lesions in the connective tissue of the skin, tendons or fascia that predominantly consist of foam cells.These specific cells are formed from macrophages as a result of an excessive uptake of LDL particles and their oxidative modification.

Xanthomas particularly affect the tendons: elbows, Achilles tendons, and hands.[2]There is no single internationally accepted set of criteria for the clinical diagnosis of FH. The most commonly used are the US-MEDPED[3],the UK (Simon Broome)[4] and the Dutch Lipid Clinic[5] sets of criteria that have been statistically and genetically validated. Genetic testing may give a definitive diagnosis of FH by detection of pathological mutation.[6]

CASE PRESENTATION

An 11 year old female child was presented with a 5 year history of skin lesion. The lesion began from the knee and buttock area

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and gradually involved her elbow and flexor area of forearm. She was born from a non-consanguineous marriage and her prenatal, natal and postnatalhistory was uneventful. She had no past history of illness. The parents denied any family history of chronic illness. Her parents were divorced when she was 2 years old and she was raised by her mother. Physical examination revealed normal vital signs and anthropometry. On dermatologic examination there were multiple nodular yellowish colored lesions over the knee (figure 1), buttock (figure 2), forearm (figure 3), and elbow (figure 4), the maximum measuring 4cm by 5cm.

Laboratory examination showed elevated lipid profile with Total Cholesterol of 698 mg/dl, LDL-Cof 646.2 mg/dl, HDL-C was low(27 mg/dl). Triglyceride value was in the normal range. Biopsy taken from the lesion showed focal aggregates of foamy macrophages with a conclusion of Tuberous Xanthoma. The mother's lipid profile was also done and showed elevated LDL– C value with 261.4 mg/dl.Total Cholesterol was also slightly elevated with 322 mg/dl.HDL-C was 43 mg/dl andTriglyceride value was in the normal rang.

All investigations for secondary causes of hypercholesterolemia were non- revealing. The patient fulfilled the 'definitive' criteria for FH according to both the UK[4] and Dutch Lipid Clinic[5] criteria for clinical diagnosis of FH. The patient was started on low dose of statin and appointed for 6 weeks to follow up clinic.

Figure 1

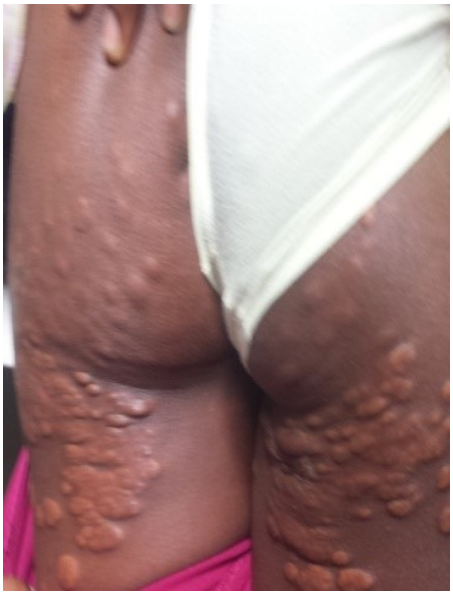


Figure 2

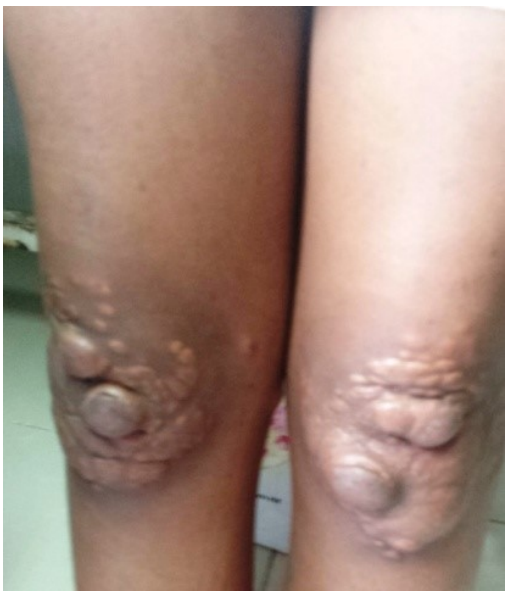


Figure 3

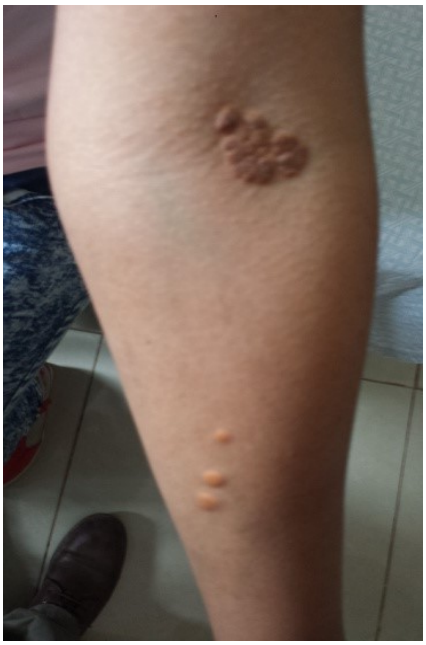
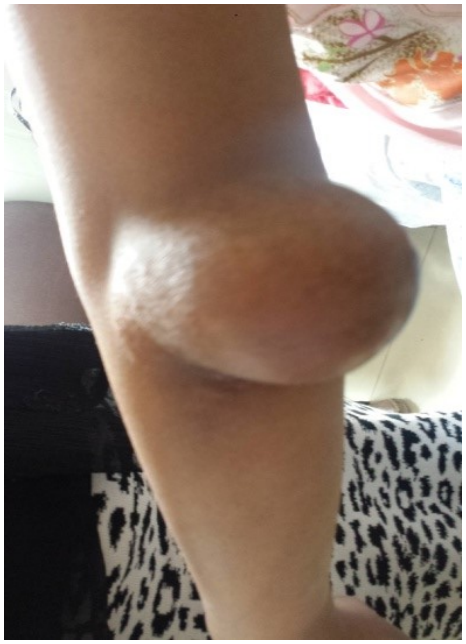


Figure 4



DISCUSSION

Familial hypercholesterolemiacomprises a minimum of three separate genetic conditions due to mutations in the genes for(i) LDLR, (ii)ApoB, and (¡¡¡)PCSK9.[1]The consequences of LDLR gene mutations are high total cholesterol and high serum LDL-C.[2]Plasma levels of key lipoprotein particles, including LDL-C levels, are major determinants of the initiation of changes in vascular endothelial damage, of monocyte differentiation into macrophages and foam cell formation, leading to the development of atherosclerotic lesions[7] premature coronary artery disease (CAD), peripheral arterial disease[8] and valvular disease (predominantly aortic stenosis).

Concerning the targets of treatment in FH guidelines from the US NLA and NICE in the UK recommend a reduction in LDL-C concentration of >50% from levels before treatment in patients with FH [9,10] First-line treatment for patients with heFH is with statins.[9,11,12] Ezetimibe, a cholesterol absorption inhibitor, use results in compensatory increase in hepatic LDLRs and anabout20% reduction in LDL-C.[13] Bile acid sequestrants also have a strong LDL-C lowering effect and are frequently used at high doses in monotherapy when statins alone are not well tolerated or in combination with statins when statins alone are not able to achieve the LDL-C target. Statins may be effective in some hoFH patients.[9] Ezetimibe combined with a statin resulted in clinically important reductions in LDL-C concentrations in patients with hoFH.[14] The current treatment offered to patients with hoFH is weekly or biweekly apheresis.[9,11]

Historically, left untreated clinical symptoms of premature cardiovascular disease (CVD) typically manifest in men in their fourth decade and in women in their fifth decade of life in heterozygous FH (heFH). In contrast homozygous FH (hoFH) patients can experience serious cardiovascular events as early as childhood and, on average, in their twenties.[11,13]

CONCLUSION

Xanthomas are manifestations of an underlying lipid disorder. Therefore patients as well as their family members should be screened for lipid profiles so that appropriate medications can be started earlier to delay the development of premature CGHAD. In our patient, we couldn't trace the father and hence we considered heFH because of epidemiologic reason.[1]

Conflict of Interests : None

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