Case Report: Familial Hypercholesterolaemia and Multiple Xanthomas in a 14-Year-Old Girl

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ABSTRACT

Familial hypercholesterolaemia is a genetic disorder of low-density lipoprotein cholesterol (LDL-C) metabolism which is characterized by elevated serum levels of LDL-C. This results in an increased risk of coronary heart disease and early death in affected individuals. Familial hypercholesterolaemia manifests on the skin as plaques, nodules and tendinous xanthomas on the elbows, hands, knees, Achilles tendon and gluteal region. The goal of treatment is to reduce serum LDL-C levels and the associated coronary heart disease risk. We present a case of familial hypercholesterolaemia in a 14-year-old girl highlighting the cutaneous manifestations of a systemic disease which could be fatal.

Key words: Familial Hypercholesterolaemia, Xanthomas, hyperlipidaemia, APO B100

Rapport De Cas: Hypercolesterolemie Familiale et Xanthomes Multiples chez une Fille de 14 Ans

ABSTRAIT

L'hypercholestérolémie familiale est une maladie génétique du métabolisme du cholestérol à lipoprotéines de basse densité (LDL-C) qui se caractérise par des taux sériques élevés de LDL-C. Il en résulte un risque accru de maladie coronarienne et de décès prématuré chez les personnes touchées. L'hypercholestérolémie familiale se manifeste sur la peau sous forme de plaques, de nodules et de xanthomes tendineux sur les coudes, les mains, les genoux, le tendon d'Achille et la région fessière. L'objectif du traitement est de réduire le LDL-C et le risque de maladie coronarienne associé. Nous présentons un cas d'hypercholestérolémie familiale chez une jeune fille de 14 ans mettant en évidence la manifestation cutanée d'une maladie systémique peut-être fatale.

Mots clés: Hypercholestérolémie familiale, Xanthomes, hyperlipidémie, APO B100

Introduction

Familial hypercholesterolaemia (FH) is a genetic disorder of low density lipoprotein cholesterol (LDL-C) metabolism and it is classified as type II under Fredrickson's classification of hyperlipidaemias[1,2] It is characterized by elevated serum levels of LDL-C and affected individuals have an increased risk of coronary heart disease and early death.[3-5] Familial hypercholesterolaemia occurs in 404/100,000 (1/250) of the population and is commoner in females.[6] There are scarce reports on the prevalence of FH in Africa. Mutations in (LDL-R) alleles which is responsible for cellular cholesterol uptake is responsible for FH.[1,2] This mutation can be either in the apolipoprotein B (APO B100) gene or in the proprotein convertase subtilisin/kexin type 9 (PCSK 9) gene or in both.[1] Cutaneous manifestations include plaques, nodules and tendinous xanthomas on the elbows, hands, knees, Achilles tendon and gluteal region.[4,7,8] We present a case of FH in a 14 year old black African girl.

Case Report

A 14-year-old girl was seen in the clinic with a history of multiple, asymptomatic growths on the inter-gluteal cleft from birth. At the age of 9 years, she developed similar growths of various sizes on the elbows, knees, gluteal and periorbital areas (figures 1a & b). She is the fourth of four siblings, and there was a history of similar lesions and chest pain in her older brother. Her father was also being treated for hypercholesterolemia. She was initially attended to by a general practitioner who assessed her to have keloids and injected the lesions with triamcinolone.

Clinical examination revealed multiple soft yellowish-brown papules, plaques and nodules on the eyelids, interdigital spaces, elbows, gluteal cleft and gluteal region. Additionally, she had large hard nodular protuberances (tuberous xanthomata) on both knees. Anthropometric measurements revealed a body mass index of 14.2 kg/m^2 (weight; 35.5kg, height; 1.58m^2). A diagnosis of familial hypercholesterolaemia with multiple xanthomas was made. Laboratory investigations done included liver function tests, thyroid function tests, complete blood count and fasting blood sugar and they were normal. However, her fasting lipid profile (FLP) was consistent with hypercholesterolaemia; the total cholesterol was four times the normal and her LDL-C was seven times the normal (Table 1). Histopathology from a skin biopsy done was consistent with xanthoma (lipidized histiocytes dissecting through the dermal collagen, Figure 2). Familial hypercholesterolaemia was confirmed. She was placed on Atorvastatin 20mg daily and referred to the lipid and metabolic clinic with whom she was co-managed. Serial monitoring of her FLP is as shown in table 1.

Table 1. Serial fasting lipid levels with dates

	29/11/16 mg/dl	**11/2/17** mg/dl	**09/3/17** mg/dl	**15/3/17** mg/dl	**05/6/17** mg/dl	**10/8/17** mg/dl
TCHOL	826 (<200)	424	389	378	456	440mg/dl
HDL	42	42	40	44	53	64
LDL	763 (<100)	366	340	325	393	364
TGC	103	79	45	44	52	58
VLDL	21	9.9	09	09	10	10

DISCUSSION

Familial hypercholesterolaemia (FH) is a genetic disorder of low-density lipoprotein cholesterol (LDL-C) metabolism characterized by elevated serum levels of LDL-C and it is associated with a 3-fold increased risk of coronary heart disease and early death.[1,3] Familial hypercholesterolaemia has a prevalence of 3.2%.[9] Early recognition and treatment to lower cholesterol levels prevents the progression of systemic atherosclerosis and the associated morbidity and mortality.[1,3]

The criteria for the diagnosis of FH include; LDL-C >180mg/dl, xanthomas on tendons/skin, a history of hypercholesterolaemia in a family member or premature coronary heart disease in a second degree blood relative.[10] At least 2 of these criteria are required to make a diagnosis of FH.[10] Our patient met all three criteria. All individuals who have FH have a mutation in the LDL-R allele and like our patient usually have a parent who has hypercholesterolaemia.[3,11-13]

In FH, there is a deficiency of normal LDL receptors on cell membranes, which leads to the poor hepatic clearance of circulating LDLs and thus elevated serum LDL cholesterol levels.[11-13] There is less efflux of cholesterol from plasma and macrophages leading to the formation of atherosclerotic plaques in the vessels.[11] Familial hypercholesterolaemia occurs in both adults and children.[7,14,15]

The cutaneous manifestations of FH include plaques, nodules and tendinous xanthomas on the elbows, hands, knees, Achilles' tendon and gluteal region.[4,7,8,16,17] These were the involved sites in our patient. Xanthomas are characterised by infiltrates of lipid-laden macrophages in various areas of the skin or visceral organs due to increased efflux of lipids through vascular walls into connective tissue spaces.[16,18]

There is no spontaneous resolution of cholesterol levels in individuals who have FH. In children older than 10 years, treatment is advocated once serum LDL-C is greater than 180mg/dl.[10,19] Treatment involves the use of statins, probucol and ezetimibe which reduce serum LDL-C levels thus reducing coronary disease risk.[8,15,20,21] Our patient was older than 10 years and her LDL-C was greater than 180mg/dl. She was commenced on a statin and probucol to lower cholesterol levels. Treatment, however, has variable effects on the resolution of xanthomas. Resolution with treatment is reported in some studies[22] while others report no resolution.[17]

In conclusion, this report is made to remind

dermatologists that some cutaneous diseases are manifestations of internal diseases which have the potential of being fatal.

The authors declare no conflict of interest

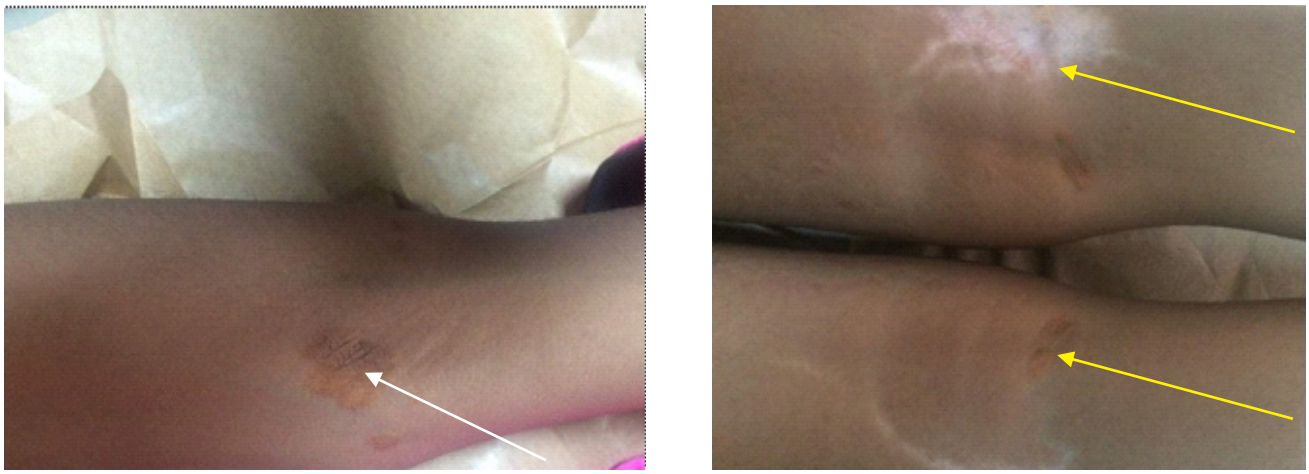

Figure 1A. Xanthoma: Brown patches and plaques on antecubital and popliteal fossae (yellow arrows), hypopigmented patch following intralesional triamcinolone injection (white arrow).

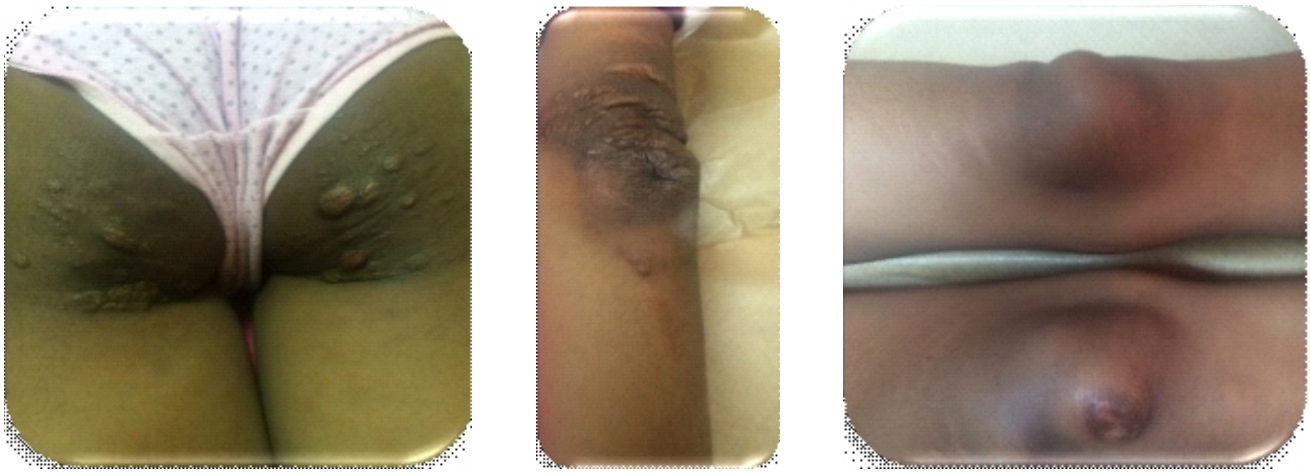

Figure 1B. Xanthoma: Plaques and nodules (gluteal, elbows and knees).

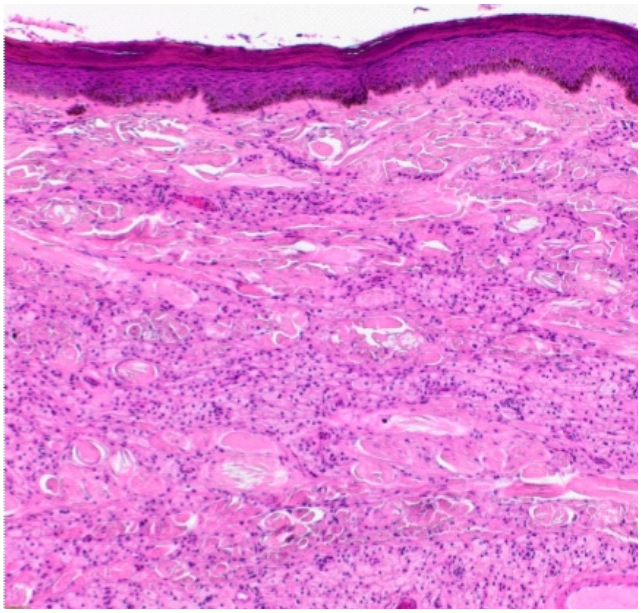

Figure 2. Histopathology of Xanthoma: Lipidized histiocytes

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