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Case Report

Tuberous xanthoma in an amputated stump

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Abstract Xanthomas are focal infiltrates of lipid-containing histiocytic foam cells that are usually found within the dermis or tendons. It is a clinical manifestation of lipoprotein metabolic disorders. We report a case of tuberous xanthoma in a 45-year-old woman who presented with multiple firm papules and nodules involving multiple sites of the body including the amputated right forearm with elevated serum cholesterol, triglycerides, LDL and VLDL.

Key words
Xanthoma, tuberous xanthoma, amputated stump.

Introduction

Xanthoma is a deposition of yellowish cholesterol rich material that can appear anywhere in the body in various disease states. They are cutaneous manifestations of lipidosis in which lipids accumulate in large foam cells within the skin. Xanthomas are plaques or nodules consisting of abnormal lipid deposition and foam cells in skin or in tendons. They do not represent a disease but rather are signs of a variety of lipoprotein disorder. Clinically, xanthomas can be classified as eruptive, tuboeruptive or tuberous, tendinous or planar **(Table 1)**. Tuboeruptive xanthomas are nodules that are frequently localized to the extensor surface of the elbow, knees, knuckles and buttocks.

Case Report

A 45-year-old female patient presented to us with asymptomatic multiple nodules over left elbow, left hand and knuckles, amputated stump of right forearm, both the legs on knees, soles and buttocks since 5 years. There was no complain of fever, itching. There was no history of similar lesions in family. Similarly, there was no history of diabetes mellitus, hypertension, tuberculosis and asthma. She gave history of snake bite 20 years back on right hand which became gangrenous and eventually amputated.

On examination, multiple yellowish shiny, smooth nodules are present over left elbow **(Figure 1)**, l. Multiple small papules were also present around it which coalesced forming a nodule. Similar lesions were present over palmar aspect of left hand, dorsum of the fingers and over knuckles of left hand **(Figure 2)**, over right elbow joint and stump of amputated right hand **(Figure 3)**, over both knees, around ankle joint, over medial and lateral aspect, over both sole and buttocks.

On investigation complete blood count, renal function tests, liver function tests, thyroid function tests were within normal limits. Only her alkaline phosphates enzyme level was slightly raised (146 U/L). Routine urine examination was within normal limits. Her blood sugar levels, fasting (98 mg%), and postprandial (153 mg%) were within normal limits. Her lipid profile revealed, serum cholesterol - 686 mg%, serum triglycerides - 743 mg%, HDL cholesterol - 37 mg%, LDL cholesterol - 342 mg% and VLDL cholesterol - 149 mg%.

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Table 1 Clinical presentations of xanthomas [1].

Type of xanthoma	*Genetic disorders*	*Secondary disorders*
Eruptive	Familial lipoprotein lipase deficiency (Type I) ApoC-II deficiency (Type I) Familial hypertriglyceridemia (Type IV) Familial hypertriglyceridemia with chylomicronemia (Type V)	Obesity Cholestasis Diabetes mellitus Medications: retinoids, estrogen therapy, protease inhibitors
Tuberous	Familial hypercholesterolemia (Type II) Familial dysbetalipoproteinemia (Type III) Phytosterolemia	Monoclonal gammopathies Multiple myeloma Leukemia
Tendinous	Familial hypercholesterolemia (Type II) Familia defective apoB Familial dysbetalipoproteinemia (Type III) Phytosterolemia Cerebrotendinous xanthomatosis	
Planar		
Palmar	Familial dysbetalipoproteinemia (Type III) Homozygous apoA-I deficiency	Cholestatis
Intertriginous	Familial homozygous hypercholesterolemia (Type II)	Monoclonal gammopathies, cholestasis
Diffuse	Familial hypercholesterolemia (Type II)	Monoclonal gammopathies
Xanthelasma	Familial dysbetalipoproteinemia (Type III)	
Other		
Corneal arcus	Familial hypercholesterolemia	
Tonsillar	Tangier disease	

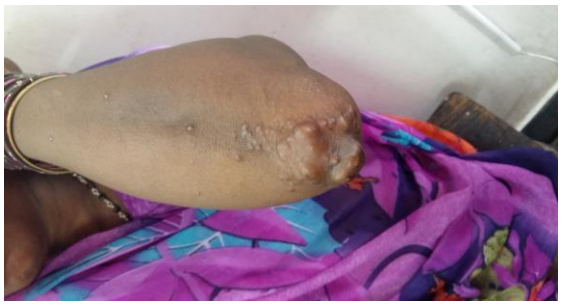

Figure 1 Multiple yellowish shiny nodules on left elbow. A few papules also noted.

Figure 3 Similar lesions on amputated right hand.

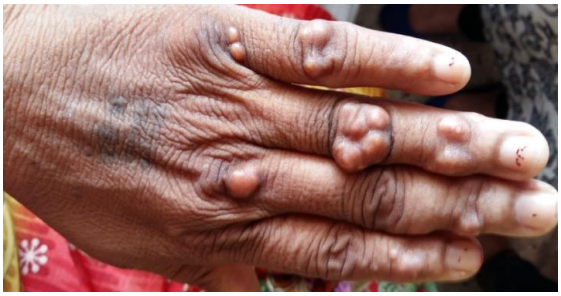

Figure 2 Diffuse dense infiltrate of foamy histiocytes involving whole of dermis. H & E 40x (Biopsy from nodule over thigh).

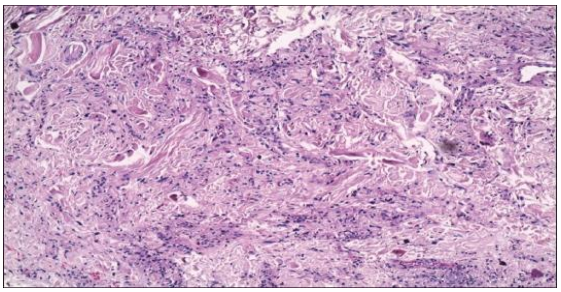

Figure 4 Multiple shiny nodules on dorsum of fingers of left hand.

Histopathological examination showed a diffuse, dense, nodular infiltrate of foamy histiocytes involving whole of the dermis. The overlying epidermis was flattened and surrounding dermis showed mild fibroplasias (**Figure 4**). The foamy histiocytes showed

abundant pale foamy cytoplasm and a small centrally located nucleus. Biopsy thus confirmed diagnosis of tuberous xanthoma. Electrophoresis was not done as this facility is not available at our institute.

Discussion

The term 'xanthoma' derived from the Greek word 'Xanthos' meaning yellow and is used to describe a variety of subcutaneous lipid deposits, even those that do not appear yellow.[1] Xanthomas are common presentation of a focal or generalized disorder of lipid metabolism. They are often linked with high risk of arteriosclerotic vascular diseases, pancreatitis, etc. During childhood, type I and type IIa are seen and are hereditary.[2] They are characterized by accumulation of lipid laden macrophages. Pathogenesis involves a complex process by means of dysregulation of macrophage sterol flux. Xanthomas are predisposed by increased levels of cholesterol, rich LDL and VLDL remnants. Under normal circumstances, around 80% of LDL cholesterol is taken up by LDL receptor-mediated endocytosis. The residual LDL is cleared by scavenger receptor pathways of macrophages. In familial hypercholesterolemia, the accumulation LDL and VLDL remnants are primarily scavenged by macrophages without feedback regulation, resulting in continuous cellular lipid accumulation and foamy cells. Clinically tuberous xanthomas are characterized by yellow to skin-coloured nodules that are firm, painless, indurated with an erythematous halo and are generally localized to extensor surfaces of buttocks, knees, elbows and knuckles. The lesions can be seen in inguinal and axillary folds and in the sites of trauma and they may be fissured, pedunculated and suppurative.

Frequently associated with primary hypercholesterolemia which includes familial hypercholesterolemia (Frederickson type II) and dyslipoproteinemia (Frederickson type III, an autosomal dominant genetic disorder of lipid metabolism) and in secondary hypercholesterolemia with biliary disease, monoclonal gammopathy and hypothyroidism. In familial hypercholesterolemia, raised LDL levels are due to increased production and decreased resorption of LDL secondary to dysfunctional LDL receptors. As a result of altered endothelial function, elevated serum total cholesterol and LDL with normal triglycerides are found and manifests as atherosclerosis and coronary artery disease.[3] Histopathological examination reveals large and small aggregates of foamy cells, which are macrophages engulfing lipid droplets. Xanthoma cells are mononuclear and may also show Touton giant cells with a wreath of nuclei. Early lesions show a mixture of nonfoamy cells, neutrophils, lymphocytes and macrophages and well-developed lesions show infiltrates consisting mainly of foamy cells which are later replaced by collagen bundles. Cholesterol clefts are also seen.[4]

Treatment options include lifestyle modification with dietary changes and pharmacotherapy including statins, fibrates, nicotinic acid and bile acid sequestrants like cholestyramine. This condition responds well to a combined therapy involving statins, cholesterol absorption inhibitors and a bile acid sequestrant, if needed.[5] Invasive procedures namely lifelong lipid apheresis and liver transplantation can also be considered.[6] Tuberous xanthoma shows slower rate of regression after appropriate therapy.

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