Unilateral Multiple Tuberous Xanthomas Mimicking Multiple Lipomatosis in Type IIa Hypercholesterolemia- A Case Report with Review

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INTRODUCTION

The term Xanthoma was derived from a Greek word "Xanthos" meaning yellow and was generally used to describe lipid deposits in the subcutaneous plane.[1] They do not represent a particular disease, but are cutaneous markers for dyslipidaemia or may even arise without any underlying metabolic defect.[2] Tuberous xanthomas present as yellow or reddish nodules located mainly over the extensor surface of the extremities and buttocks.[1] They may be confused with lipomas. Early diagnosis and treatment may help to prevent complications such as coronary artery disease, myocardial infarction and pancreatitis.[3] We here report a case of unilateral multiple tuberous xanthomas in a young lady with elevated Low density lipoprotein levels consistent with familial hypercholesterolemia Type IIa.

PRESENTATION OF CASE

A 27-year-old female presented to the surgery outpatient department with a history of multiple firm and non-tender nodular unilateral lesions on the left gluteal region, left little toe and left elbow joint for the past ten years. The initial lesions started over the left gluteal region followed by similar nodules over the bony prominences of left little toe and left elbow joint. Otherwise the patient was healthy with no family history of similar lesions in parents or siblings. There was family history of diabetes, hypertension and deranged lipid metabolism. On physical examination, multiple yellowish, firm, non-tender cutaneous lesions were identified over the left gluteal region, left little toe and left elbow joint, largest measuring 11 cms in size over the left gluteal region. There was no involvement of palmar creases, lymphadenopathy or organomegaly. No clinical evidence of systemic involvement was observed. She had a normal haemogram. A 12 lead ECG was found to have no apparent cardiac abnormalities. Her biochemical investigations showed normal blood glucose levels, liver function tests, renal function tests and electrolytes levels, however the lipid profile was deranged and showed elevated Cholesterol (468 mg%) and Low density lipoprotein (LDL) (361 mg%) levels. Very low density lipoprotein (VLDL) and high density lipoprotein (HDL) levels were within normal reference range. Fine needle aspiration cytology was performed from multiple sites. One of the attempts yielded oily aspirate while rest were blood mixed. Smears were sparsely cellular and showed predominantly few benign mesenchymal cells with mature adipocytes and occasional inflammatory cells in a haemorrhagic background. A possibility of Lipoma was considered on cytology. On ultrasonography, a diagnosis of lipoma was made and an excision for histopathological correlation was advised. Macroscopy showed a

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skin covered nodular mass measuring 10.5 x 9.5 cms (Figure 1) and cut section showed a poorly circumscribed solid yellow areas (Figure 2) below the skin. Histopathological examination from one of the lesions revealed infiltration of dermis by foamy histiocytes along with few giant cells, fibrosis and cholesterol clefts, thus confirming the diagnosis (Figures 3, 4, 5 & 6). Based on clinical, biochemical and pathological findings; a final diagnosis of Unilateral Multiple Tuberous Xanthomas - Type IIa Hypercholesterolemia was considered.

DISCUSSION OF MANAGEMENT

Xanthomas are rare, non-neoplastic lesions which are characterized by yellowish plaques or nodules consisting of abnormal lipid deposition and foam cells. They were earlier considered as a benign neoplasm, but their association with hyperlipidaemic states confirms that these are non-neoplastic reactive lesions. It is also a known fact that they usually do not represent a disease process but rather represent symptoms of dyslipidaemia.[4] The possible hypothesis suggested for xanthoma is the accumulated lipids in these lesions are derived from blood. The serum lipoproteins might leave the vascular compartment and traverse through the small vessels. Later they enter the tissues and are ingested by macrophages which degrade the lipoproteins into lipid that is released into the extracellular compartment. Hence, increased uptake of lipids transported through the capillaries or increased lipid synthesis in the dermal macrophages resulting in production of foam cells. It is believed that fibrogenic properties of the extracellular cholesterol in the longstanding xanthoma could be related to fibrosis. Ultrastructurally, it has been confirmed by the finding of lipoprotein between endothelium and basement membrane and finally in the pericytes. The extravasated lipoproteins can also recruit more macrophages in association with stress factors like heat, movement and friction. This might increase the capillary leakage of lipoproteins which explains the location of tuberous xanthomas, tendinous xanthomas, and xanthelasmata. Local trauma, inflammation which can affect epithelium turnover in conditions like viral infections, candida infections, carcinoma in situ and any other local immunological disorders have also been considered as possible etiologic agents in xanthoma.[5] Hyperlipidaemias are either familial (also called primary) or acquired (also called secondary) when resulting from another underlying disorder that leads to deranged lipid and lipoprotein metabolism. Familial hyperlipidaemias are classified according to Fredrickson classification,[6] which is based on the pattern of elevated lipoproteins; Type I familial hyperchylomicronaemia has increased chylomicron levels while in Type II A Familial hypercholesterolemia, LDL levels are raised. Both LDL and VLDL levels are elevated in Type II B Familial combined hyperlipidaemia whereas Type III Familial dysbetalipoproteinaemia has increased intermediate-density lipoprotein (IDL) levels. The predominant raised lipoprotein level is VLDL in Type IV Familial hypertriglyceridemia and both VLDL and chylomicrons are elevated in Type V Endogenous hypertriglyceridemia.

Various cutaneous xanthomas are observed in different types of familial hyperlipidemia and are termed as per their appearance and clinical presentation.[7] Eruptive xanthomas are small, yellow papules observed in Type I, III, and V hyperlipidemias. Tuberous xanthomas are nodular or large plaque lesions of the subcutis usually seen with type IIa or III hyperlipidemia which was seen in our patient. Plane palmar xanthomas occur in skinfolds, such as the palmar creases, and are characteristic of type III hyperlipidemia. Type II B and Type IV hyperlipidemia do not have a particular type of xanthoma. Xanthoma disseminatum and verruciform xanthoma occur in normolipemic patients. Xanthomas can be a part of general metabolic disease. Clinically xanthomas can be classified into several categories:[1,2] Tendinous xanthoma, tuberoeruptive or tuberous xanthoma, eruptive xanthoma, xanthoma planum, and palmar xanthoma. The most common xanthomas with familial hypercholesterolemia are tendinous xanthomas located within the tendons either unilateral or bilateral. They usually present over pressure areas such as extensor aspect of elbows, knees and buttocks. In our patient there were discrete, multiple, painless, nodular masses located in the buttock region, over the little toe and elbow joint. In our case, despite several attempts from different lesions, FNAC yielded scant aspirate. Biochemical investigations revealed deranged lipid metabolism and helped in clinching a diagnosis of xanthoma. Histopathological examination of one of the excised lesions showed infiltration of dermis by foamy macrophages along with cholesterol clefts, fibrosis and few giant cells thus confirming our diagnosis of xanthoma. Diagnostic difficulty can occur due to fibrohistiocytic tumors, such as dermatofibroma and atypical fibroxanthoma, which show prominent "lipidization". But xanthoma shows foam cells and dense collagenization, without the prominent cellular component of dermatofibroma. In atypical fibroxanthomas, the spindle cell component shows pleomorphism and is usually seen in head and neck region of elderly people.[7] We conclude that tuberous xanthomas can be considered as a marker for the underlying deranged lipid metabolism which should be diagnosed and managed as early as possible to decrease the risk of complications like coronary artery disease, myocardial infarction and pancreatitis.

Macroscopy

A skin covered nodular mass (Figure 1) measuring 10.5 x 9.5 cms was received. Cut section revealed a poorly circumscribed solid yellow areas (Figure 2) below the skin.

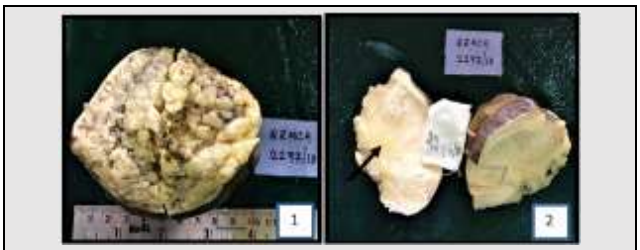

Figure 1 and 2

Microscopy

Skin composed of intact epidermis with underlying dermis containing the lesional area with fibrosis (Figure 3]. The lesion is composed of sheets of foam cells with lipid and moderate lymphocytic infiltration in the dermis (Figure 4 & 5]. Furthermore, cholesterol clefts (Figure 6] with few giant cells were also observed.

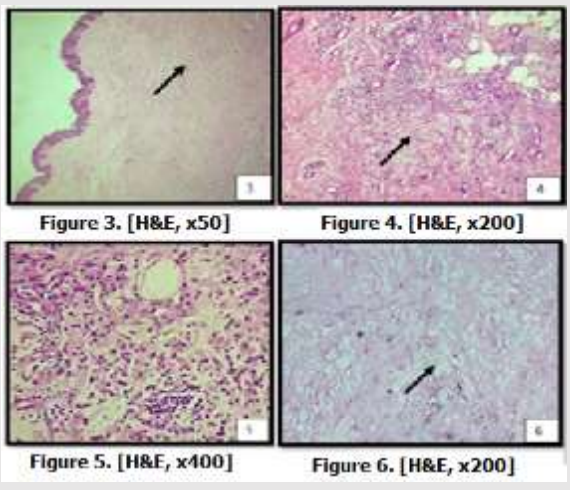

Figure 3, 4, 5, 6

REFERENCES

[1] Sarkany RPE, Breathnach SM, Morris AAM, et al. Metabolic and nutritional disorders. In: Burns T, Breathnach S, Griffiths C, et al, eds. Rook's text book of dermatology. 8th edn. West Sussex (UK): Blackwell Publishing Ltd 2010:81-92.

[2] White LE. Xanthomatoses and lipoprotein disorders. In: Wolff K, Goldsmith LA, Katz SI, et al, eds. Fitzpatrick's dermatology in general medicine. 7th edn. United States of America: McGraw-Hill Companies Inc 2008:1272-1281.

[3] Nair PA, Kota RS, Sheth NK. Tuberous xanthoma with xanthelesma palpebrarum in a normolipemic patient. Austin Intern Med 2016;1(3):1012.

[4] Marcoval J, Moreno A, Bordas X, et al. Diffuse plane xanthoma: clinicopathologic study of 8 cases. J Am Acad Dermatol 1998;39(3):439-442.

[5] Wallton KW, Thomas C, Dunkerley DJ. The pathogenesis of xanthomata. J Pathol 1973;109(4):271-289.

[6] Fredrickson DS, Lees RS. A system for phenotyping hyperlipoproteinemia. Circulation 1965;31:321-327.

[7] Bhartiya R, Agarwal P, Kumar R, et al. Multiple tuberous xanthomas: a diagnostic dilemma on cytology. Ann Pathol Lab Med 2017;4(6):169-172.