Case Report

Multiple tuberous xanthomas diagnosed on fine-needle aspiration cytology – Report of a rare case

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ABSTRACT

Xanthomas are papulonodular skin lesions present in lipoprotein metabolism disorders, which result in cholesterol deposits in subcutaneous tissue, tendons, ligaments, periosteum, etc. A 28-year-old male presented with multiple soft-tissue swellings, prominently over joints. Fine-needle aspiration (FNA) from multiple sites had similar appearance with foamy histiocytes and giant cells. We describe an unusual case of tendinous and tuberous xanthoma diagnosed by cytology. Acquaintance with FNA cytology findings in xanthomas can help to avoid the need of surgical biopsy, as xanthomas can regress on medical therapy alone.

Keywords: Cytology, Subcutaneous nodules, Tendinous xanthoma

INTRODUCTION

Xanthomas are benign plaques, papules, or nodules characterized by accumulation of lipid laden macrophages that develop in the cutis and subcutaneous tissue.1 It is not a true neoplasm but, rather, a reactive histiocyte proliferation that occurs in response to alterations in serum lipids and is usually of great cosmetic concerns to the patient.2 It mostly develops in primary and secondary hyperlipoproteinemias. Tuberous xanthomas are firm, painless, yellow-red nodules most commonly seen over extensor aspects of limbs and buttocks.2 We hereby report a case of a 28-year-old male presenting with multiple tuberous xanthomas diagnosed on fine-needle aspiration cytology (FNAC). This case is being reported to emphasize the challenge faced while diagnosing such lesions on FNAC.

CASE REPORT

A 28-year-old male presented to the medicine outpatient department with a history of multiple, yellowish plaques, papules, and nodules over the body for the past 1 year with a gradual increase in size. These lesions involved the knuckle, foot, lateral malleolus, gluteal region, and right and left upper eyelid and were associated with itching [Figure 1a-c]. On examination, the swellings were firm, non-tender, mobile, non-adherent to skin, or to underlying structures. The largest swelling...
was in the gluteal region and measured 4 × 3 cm the nodules over the knuckles were cystic in consistency. There was absence of similar lesions and cardiovascular disease in other family members.

MRI pelvis revealed multiple variable sized protruding well circumscribed soft-tissue lesions arising from skin and subcutaneous of sacroccygeal, posterolateral, and inferomedial aspect of bilateral gluteal region. Complete blood count, liver, renal, and thyroid function tests were normal. Serum lipid profile showed markedly elevated levels of total cholesterol and low-density lipoprotein cholesterol level (LDL-C), namely, 515 mg/dl and 434 mg/dl, respectively. However, high-density lipoprotein cholesterol, very LDL cholesterol, and triglycerides levels were normal. Chest X-ray, electrocardiogram, two-dimensional echocardiography, and fundus examination of both eyes were normal.

FNAC from nodular cystic swellings over the interphalangeal joint (knuckle) and bilateral gluteal swelling revealed similar findings comprising of predominantly foamy macrophages in clusters as well as scattered singly, multinucleated giant cells, few benign mesenchymal cells, and occasional inflammatory cells in a hemorrhagic background [Figure 2a and b]. Skin biopsy from lateral ankle lesion showed pan dermal infiltration by foamy macrophages [Figure 2c].

The diagnosis was thus established as a case of tuberous xanthoma. The patient was advised strict dietary control regarding the intake of fats and started on tablet atorvastatin 40 mg daily at bed time. Complete lipid profile along with other relevant investigations was advised for the remaining family members as the condition is usually familial and may not clinically present with xanthoma. Other tests such as computed tomography angiography, LDL receptor activity, and genetic mutational analysis were not done due to financial constraint.

**DISCUSSION**

Xanthomas are infiltrates of the skin that are yellow to brown-red in color and result from infiltration of the dermis by lipid containing cells. Xanthomas may be divided into several categories: Tendinous xanthoma, xanthoma tuberosum, eruptive xanthoma, xanthoma planum, and palmar xanthoma.\(^3\) The most common xanthoma among patients with FH is tendinous xanthoma (40–50% of patients). Studies have shown that the most frequent site for xanthomas in these patients is the Achilles tendon.\(^3\) Other sites can include the extensor tendons of the hands and feet, as the extensor tendon areas are subject to mechanical stress.\(^4,5\)

![Figure 1](image1.png)

Figure 1: (a) Single yellowish plaque over medial side of the left and right eye (arrow), (b) subcutaneous swelling on flank (c) multiple yellowish to skin colored firm, non-tender papules and nodules measuring approximately 1–2 cm in size over dorsum of hands; (d) MRI pelvis revealed protruding well circumscribed soft-tissue lesions (arrow).

![Figure 2](image2.png)

Figure 2: (a) Cytosmears show clusters of foamy histiocytes in a proteinaceous background (Giemsa, ×100), (b) lipid-rich background with many foamy histiocytes, upper right inset: Touton type giant cells (Giemsa, ×400), (b and c) skin biopsy shows pan dermal infiltration by foamy macrophages (H and E, ×100).
Courtice indicated that mechanical stress, similarly to the effect of mild heat injury to skin, also increases capillary permeability around the mechanical stress exposed areas, which may lead to the accumulation of LDL. This theory may explain why tuberous xanthomas are predominantly encountered in mechanical stress exposed regions.\textsuperscript{[6]}

Our patient presented with multiple xanthomas in the mechanical stress exposed parts of the body, including buttocks, extensor aspect of the knee, elbow, wrist, palm and ankle, and over tendons in hands and feet. The occurrence of multiple large xanthomas is rare. In most of the cases, xanthomas are asymptomatic unless they grow to be large and cause compression to adjacent structures, which may cause pain and mobility problems.\textsuperscript{[6]}

FH is an autosomal dominant genetic disorder caused by mutation in gene encoding the LDL receptor located on chromosome 19 resulting in increased LDL levels.\textsuperscript{[7]} Heterozygotes express half the number of LDL receptors whereas homozygotes have LDL receptors between 0% and 25%. The consequences of such defects in LDL receptor genes are changes in vascular endothelial function, high serum total cholesterol, and LDL cholesterol with normal triglycerides. These are also manifested as atherosclerosis and coronary artery disease.\textsuperscript{[8]} Thus, early diagnosis is necessary to prevent cardiovascular and cerebrovascular complications.

FNAC can be an easy, cost-effective method for diagnosis of such lesions as was seen in our case. Other conditions that could be considered in the differential diagnosis of xanthomas occurring at ankles and knees are as follows: Giant cell tumor of tendon sheath, diffuse villonodular synovitis, lipoma, neurofibroma, fibrohistiocytic tumors, such as dermatofibroma and atypical fibroxanthoma, and rarely sarcomas. Appropriate clinical setting and cytology would lead to the right diagnosis in such situations.\textsuperscript{[9]}

The treatment options in these patients include changes in lifestyle and diet, pharmacologic agents like statins, and in advanced cases invasive procedures like lipid apheresis and liver transplantation.\textsuperscript{[10]}

**SUMMARY**

Tuberous xanthomas may present as a diagnostic challenge on FNAC due to several reasons such as low yield, lack of specific cytological features, as well as features common with other lesions. However, in the right clinical setting and with the help of biochemical investigations, such a lesion should be kept in mind while making a diagnosis on cytology, thus emphasizing its role in diagnosing such lesions. Prompt diagnosis and treatment may help to prevent unnecessary surgical interventions and associated cardiovascular complications.

**COMPETING INTEREST STATEMENT BY ALL AUTHORS**

The authors declare that they have no competing interests.

**AUTHORSHIP STATEMENT BY ALL AUTHORS**

Each author has participated sufficiently in the work and takes public responsibility for appropriate portions of the content of this article.

**ETHICS STATEMENT BY ALL AUTHORS**

As this is a case report without identifiers, our institution does not require approval from institutional Review Board (IRB).

**LIST OF ABBREVIATIONS** (In alphabetic order)

- FH – Familial hypercholerolemia
- FNA – Fine needle aspiration
- LDL – Low density lipoprotein
- LDL-C – Low density lipoprotein
- MRI – Magnetic resonance imaging

**EDITORIAL/PEER-REVIEW STATEMENT**

To ensure the integrity and highest quality of CytoJournal publications, the review process of this manuscript was conducted under a *double-blind model* (authors are blinded for reviewers and vice versa) through automatic online system.

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