

Gouty Tophi-Diagnosis Clinched on Cytology with Review of Literature

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Abstract

Periarticular and articular nodules represent as one of the most common manifestations of a wide variety of non-neoplastic and neoplastic lesions. These nodules tend to create diagnostic dilemmas, as most of them present with variable signs/ symptoms and have nonspecific laboratory findings. Amongst these, gouty tophus is an important differential, the diagnosis of which can be difficult in cases of unusual presentations, i.e., in the absence of arthritis and/ or hyperuricemia. The authors hereby present a clinically unsuspected case of gouty tophi in a 37-year-old male with a soft tissue swelling at 1st metatarsophalangeal joint of the left foot. Fine needle aspiration cytology played a pivotal role in clinching the diagnosis, thus highlighting its substantial role in diagnosis of periarticular nodules.

Keywords: Gout, Tophus, FNAC, Crystals.

Introduction

Gout is a chronic hyperuricemic crystal-induced arthropathy, characterized clinically by relapsing and remitting attacks of joint pain and pathologically by deposition of monosodium urate (MSU) crystals in and around joints, skin and soft tissue leading to formation of nodules, commonly referred to as tophi.¹ The definitive diagnosis of gout is best established by demonstration of monosodium urate crystals in the synovial fluid or biopsy. However, fine needle aspiration cytology (FNAC) is becoming a popular valuable clinical tool in the diagnosis of such nodules; hence, it is important for the diagnosticians to be aware of its microscopic findings and differential diagnosis. The authors present clinico-cytological features of a case of gouty tophi without associated arthritis along with the review of literature.

Case Report

A 37-year-old male presented with swelling at 1st metatarsophalangeal joint of left foot since last 6 months. There was no history of any trauma or joint pains. History related to alcohol, diabetes, hypertension, drug intake was non-contributory. His other past, family and personal histories were insignificant. Local

examination revealed left foot swelling to be firm, non-tender, non-mobile and measured 3×3 cm in size (Fig. 1). The overlying skin was unremarkable. No abnormality was detected on systemic examination. X-ray left foot showed a soft tissue swelling at 1st metatarsophalangeal joint, with no evidence of arthritis in the adjacent bones (Fig. 2). A presumptive clinical diagnosis of a fibrous tumor was made and the patient was advised FNAC. On FNAC, chalky white material was aspirated. Simultaneously, Ziehl-Neelsen stain, Gram's stain, culture and KOH mount were done to rule out an etiological organism, if any. All of them were non-contributory. Unstained cytology smears revealed needle-shaped crystals. Giemsa-stained smears showed many uninucleate, binucleate and multinucleate histiocytes with feathery cytoplasm in the background of numerous slender, rod/ needle-shaped crystals, scattered singly as well as forming stacks (Figs. 3 and 4). Polarized microscopy showed negatively birefringent crystals, consistent with monosodium urate crystals. On the basis of these cytomorphological features, a diagnosis of gouty tophi was rendered. Following this report, patient was investigated for serum uric acid which was found to be raised to 16.4 mg/dL.

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Figure 1. Soft Tissue Swelling at 1st Metatarsophalangeal Joint



Figure 2. X-ray Left Foot (AP View)

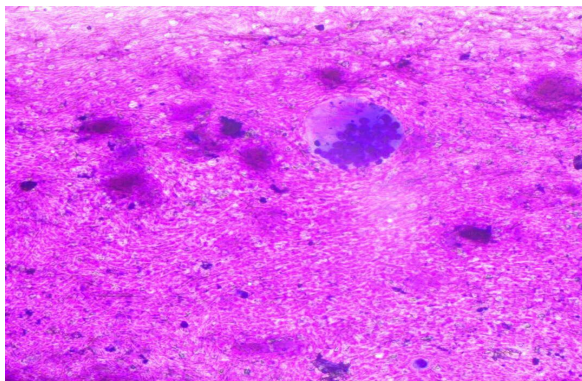


Figure 3. Needle-Shaped Crystals and Associated Inflammatory Reaction (Foreign Body Giant Cell and Lymphocytes) on FNAC Smears (Giemsa, 10x)

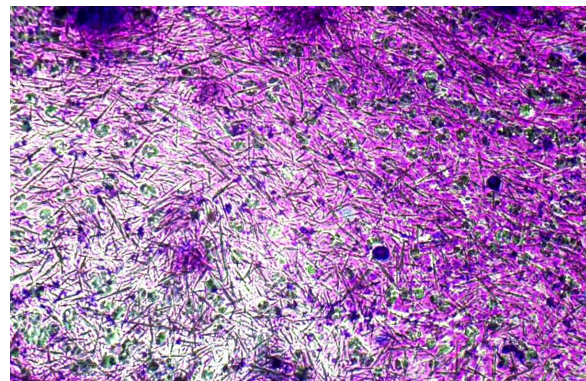


Figure 4. Monosodium Urate Needle-Shaped Crystals Arranged in Sheaves and Scattered Singly (Giemsa, 40x)

Discussion

Periarticular soft tissue lesions can be classified as cystic (bursitis), synovial proliferative (giant cell tumor of the tendon sheath), benign neoplastic (lipomas, neurogenic tumors, myxoid tumors), infectious (cat-scratch disease) and deposit diseases (chronic tophaceous gout).² Among these, gouty tophi presenting as periarticular masses is usually uncommon.

Gout is a uric acid metabolic disorder characterized by hyperuricemia caused by a disturbance in purine metabolism and deposition of monosodium urate crystals (MSU) in articular or periarticular tissues and in the urinary tract. Hyperuricemia can be primary or secondary. Primary hyperuricemia occurs due to inborn errors of purine metabolism or overproduction of uric acid, dietary factors, unknown enzyme defects (90% cases) and known enzyme defects. Secondary causes

include conditions with extensive cell turnover or acquired renal disease.³⁻⁵ Its prevalence is highest in industrialized countries, with major risk factors being alcohol, diuretic therapy, hypertension, diabetes, renal dysfunction and obesity. Other conditions include psoriasis, myeloproliferative diseases, post-operative state and hyperparathyroidism.⁶ None of these factors was present in this case.

Gout generally progresses from four clinical stages if it is left untreated: asymptomatic hyperuricemia, acute gout, intercritical or interval gout and chronic tophaceous gout. Although gouty tophi are seen in chronic disease, tophi may be the first sign of this disorder.⁵ Tophi are soft tissue masses usually periarticular, that develop after a long standing gouty arthritis. The term "gout nodulosis" used by Iglesias et al. described the subcutaneous deposits of MSU without gouty arthritis as initial manifestation.⁷ These tophi are usually seen around joints and subcutaneous tissues, mainly knee joint, olecranon process, Achilles tendon, helix of the ear and volar aspect of the forearm. Soft tissue tophi can be mistaken for neoplasm clinically and radiologically,⁸ as was suspected in our patient.

The diagnosis of gout is usually established when clinical features are classic, i.e., in the presence of arthritis and hyperuricemia. Gouty arthritis does not have any specific radiological feature. The radiological features seen are soft tissue masses (tophi), soft tissue swelling and bone erosion which can be seen in many other conditions.⁸ But, the most challenging state is when the presentation of the patient is atypical and serum uric acid is borderline value, because, occasionally, gout may present as a soft tissue tophus without antecedent painful arthritis or hyperuricemia. It can also develop in patients with normal serum uric acid levels, particularly in diabetic patients and alcoholics.⁹ Rao et al.¹⁰ reported a case of gouty tophus with normal serum uric acid level. Measurement of serum uric acid is of limited help in the diagnosis of chronic tophaceous gout. The uric acid level may be low or normal due to the uricosuric action of increased blood glucose levels.¹¹ There were no clinical or radiological evidence of gout in the present case but his uric acid levels were raised, which were only done after the FNAC had been performed.

FNAC has become an increasingly popular, minimally invasive tool for the diagnosis of gout. It not only helps in diagnosing the cause or the nature of periarticular nodules, but also excellently preserves the morphology of the crystals.¹²

The review of literature shows FNAC aspirates from tophi in most of the cases reported were chalky white as

with the present case. MSU crystals could be well demonstrated in wet mount preparations as well as in air-dried Giemsa/ Leishman-stained smears,¹³ as seen in the present case. Some authors have stated that the demonstration of these MSU crystals in FNAC smears from nodular masses establishes the diagnosis of gout unequivocally,¹⁴ though a definitive diagnosis of gout is based on the demonstration of crystals in the synovial fluid and biopsy.

Microscopy showed in most of the cases, amorphous or granular material with needle like MSU crystals and multinucleated giant cell along with chronic inflammatory infiltrate which also correlated with the microscopic findings of the present case.^{3,8}

The other advantage of crystal demonstration in FNAC smears is that it is superior to histopathology sections where crystals are more commonly lost during processing. In joint fluid analysis, coincident crystals like hydroxyapatite, steroid, etc., in the joint fluid may cause confusion.

Few drawbacks of cytology have been encountered by some authors, i.e., sometimes the crystal identification can be obscured by hemorrhagic background and inflammatory infiltrate.¹⁵ Paucity of crystalline material with an intense inflammatory reaction may also mask the true nature of the lesion. To overcome these obstacles, Sah et al.¹¹ has suggested that presence of amorphous or granular material should alert the cytopathologist to examine the smear under a polarizing microscope to avoid a diagnostic pitfall. Crystals can be very clearly seen on unstained smears. So, unstained smears can also be employed for polarized microscopy, as done by some researchers.¹⁶

The differential diagnosis of crystalline tophus, on cytology includes tumoral calcinosis (calcinosis cutis) and tophaceous pseudo-gout. Tophaceous pseudogout is one of the rare clinical forms of calcium pyrophosphate dihydrate crystal deposition (CPPD) disease. It involves massive CPPD crystal deposition in anatomical sites as temporo-mandibular joint, fingers, toes, cervical spine, wrist, hip, etc. Though tophaceous gout and pseudo gout may share some clinical features, radiological calcification is relatively uncommon in gout. Moreover, CPPD crystals are shorter, more often rhomboid than needle-shaped and show positive birefringence. Tumoral calcinosis is an idiopathic condition presenting as swelling around the large joints (hip, elbow, ankle and scapula). The calcified material in tumoral calcinosis is hydroxyapatite in nature and shows amorphous intensely basophilic granular appearance, but absence of crystalline structure on FNAC.¹⁷

Other differentials of periarticular swellings include rheumatoid nodules, ganglion cysts, pigmented villonodular synovitis, giant cell tumor, metastases, synovial chondromatosis and synovial sarcoma.⁴

Conclusion

Gouty tophi presenting as periarticular masses are uncommon. It can cause diagnostic dilemma as in most of the cases it remains clinically unrecognized on first instance as in the present case where it was clinically diagnosed as fibrous tumor. A high index of suspicion for gouty tophi must be kept in mind, while the cytopathologist looks at chalky white aspirate and amorphous granular material on smears. FNAC is a simple, rapid, reliable, cost-effective diagnostic tool, acting as an alternative to synovial biopsy and joint fluid analysis for diagnosing the cause of nature of these periarticular nodules.

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