

Case Report

Fine Needle Aspiration Cytology of Gouty Tophi with Review of Literature

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Abstract

Fine needle aspiration cytology (FNAC) is a valuable diagnostic tool and is replacing biopsy for the diagnosis of periarticular nodules. We present a case of fifty year old male with multiple soft tissue nodules in feet without any clinical and radiological features of arthritis. Fine needle aspiration revealed negatively birefringent needle shaped crystals consistent with monosodium urate crystals in amorphous granular debris. Diagnosis of gouty tophi was given. On follow up serum uric acid levels were found to be high and a diagnosis of gout was established. FNAC is a valuable diagnostic tool for the diagnosis of periarticular nodules and pathologists should be aware of cytological features of gouty tophi, particularly in cases of unusual presentation.

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Introduction

Periarticular nodules can prove to be a challenge to both clinicians and diagnosticians; various causes include rheumatoid nodules, ganglion cysts, pigmented villonodular synovitis, synovial chondromatosis and synovial sarcoma.¹ Gouty tophus is an important differential diagnosis and its diagnosis can be difficult in cases of atypical presentation in the absence of arthritis and /or hyperuricemia. As Fine needle aspiration cytology (FNAC) is becoming a popular clinical practice in diagnosis of soft tissue nodules, it is important for the pathologist to be aware of the microscopic findings and differential diagnosis of tophi. We present clinico-cytological profile of a case of gouty tophi without associated arthritis along with review of literature.

Case Report

A fifty years old male presented with multiple subcutaneous nodules on both the lateral malleoli and medial border of left great toe ranging in size from 0.5-1.5 cm diameter (Fig 1). These nodules were firm, mobile and non-tender. Patient had no systemic complaints. Radiographs of both the feet (anterior-posterior view) showed extensive soft tissue swellings overlying base of left great

toe and bilateral malleoli laterally. No evidence of any calcification or lucency was seen within the swellings. Underlying bones and articular surfaces appeared normal. No definite clinical diagnosis was given and patient was sent for FNAC.

FNAC was performed from all the three sites using a 21-gauge needle. It yielded white, chalky particulate material. Light microscopy of the Giemsa and Papanicolaou (Pap) stained smears demonstrated abundant granular amorphous material and scattered stacks and sheaves of slender needle shaped crystals, few foamy histiocytes, multinucleated foreign body type giant cells and chronic inflammatory infiltrate. Polarizing microscopy of the stained smears using first order red compensator demonstrated yellow negatively birefringent crystals, consistent with monosodium urate (MSU) crystals (Fig 2).

Based on the above findings, diagnosis of gouty tophi was given. On further investigations, patient's uric acid levels were found to be 8.5mg%.

Discussion

Gout is caused by persistent chronic hyperuricemia which can be either primary as a result of inborn errors of purine metabolism or diminished renal excretion of uric acid or can be secondary due to conditions with extensive cell turnover or acquired renal disease. Gout usually manifests as acute arthritis but can also present in the form of asymptomatic

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Fig. 1 : Clinical photograph demonstrating nodules on the great toe and lateral malleolus of the left foot.

hyperuricemia, chronic tophaceous gout or nephrolithiasis.²

Tophi are soft tissue masses usually periarticular, that develop after a long standing gouty arthritis. However, they can develop without the concomitant arthritis. Iglesias et al³ used the term "gout nodulosis" to describe the subcutaneous deposits of MSU without gouty arthritis as initial manifestation. Soft tissue tophi can be mistaken for neoplasm clinically and radiologically.²

Diagnosis of gout is easily made in typical cases with presence of arthritis and hyperuricemia. However, arthritis and hyperuricemia may not be present in all the cases. Uric acid levels can be normal especially in diabetics and alcoholics.^{2,4} Radiological features may also be atypical and misleading. The radiological features of gouty arthritis like soft tissue swelling,

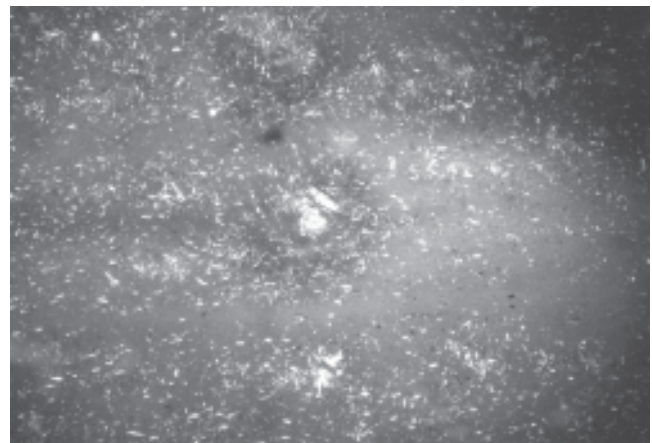


Fig. 2 : Polarizing microscopy showing negative birefringence of needle shaped MSU crystals (Giemsa, x 200).

bone erosion and solid soft tissue masses (tophi) are not specific and can be seen in various benign and malignant disorders.² In our case also, patient did not present with any clinical or radiological evidence of arthropathy. Serum uric acid levels were only marginally raised (8.5mg/dl).

FNAC has been under evaluation for the diagnosis of gout. On reviewing literature, we could find only six published reports of FNAC diagnosis of gouty tophi in indexed medical journals.^{2,5-9} Details of these are shown in Table 1.

Aspirate in most of the cases was chalky white, particulate with a tendency to get washed off the slides. Nasser et al⁶ mentioned the utility of Diff Quick stain in the evaluation of gouty tophi and recommended the use of air dried smears stained with Diff Quick Romanowsky stain.⁶ They did not find Papanicolaou stain to be useful for demonstration of MSU crystals and hypothesized that crystals were lost due to hydration steps involved in staining. This view was opposed by others who found crystals in Papanicolaou stained smears as well.^{2,7-9} We also found crystals and could demonstrate birefringence in Pap stained smears although birefringence was sharper and brighter in air dried Giemsa stained smears. Crystals can also be demonstrated in wet mount preparations from needle washings made by flushing the aspirating needle with absolute alcohol.⁶

Microscopy showed in most of the cases, amorphous or granular myxoid material with foamy histiocytes, multinucleated giant cell and chronic inflammatory infiltrate. Neutrophils^{8,9} and epithelioid cells can also be seen in some cases.⁹

Crystal identification can sometimes be obscured by background blood and inflammatory infiltrate.⁶ Paucity of crystalline material with an intense

Table 1 : Summary of published reports of FNAC diagnosis of gouty tophi

Name	Year	No. of cases	Sites	Clinical diagnosis	Uric acid Normal level: 2.5-8.0mg/dl(males); 1.5-6mg/dl (females)
1) Bhadani et al ⁹	2006	7	- Dorsum foot & arm (Rt) - Hand & foot - 2 nd toe, Rt foot - Hands & feet (multicentric) - Little finger (Lt) - Olecranon, middle finger(Rt) - 1 st toe (Rt)	GA GA GA Metastatic tumour GCT GCT GCT	High in three, normal in three and low in one case
2) Sah et al ⁸	2002	2	- Forearms, hands, dorsum feet, lateral malleoli. - Palmar aspect over base of little finger	Metastatic tumours GCT	Low High
3) Paik et al ⁷	2002	1	- Hands, feet, ear helix	Rheumatoid arthritis	High
4) Rege et al ⁶	2000	2	- Nodules on B\L malleoli - Nodules on dorsum foot, sole, lateral malleolus	Arthritis Gout suspicious	Normal Normal
5) Nicol et al ²	1997	3	- Dorsal ulnar, Rt distal forearm - I & III Metacarpal joints. - Rt foot & ankle	Sarcoma Gouty arthritis Sarcoma	Not given Normal range Normal range
6) Nasser et al ⁵	1994	2	- Vertebral level C3 L4 - Forearm nodule	Not given Not given	Not given Not given

GA= gouty arthritis, GCT = giant cell tumour, Rt = right, Lt = left, B/L = bilateral

Table 2 : Differential diagnosis of crystalline tophi

	Radiological calcification	Crystalline structure	Birefringent
Tumour calcinosis	Present	Absent	
Pseudotophi	Present	Smaller, rhomboid/ needle shaped	Weak positive
Gout	Absent	Needle shaped	Strong negative

inflammatory reaction may also mask the true nature of the lesion. Sah et al⁸ 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.

On cytology, differential diagnosis of crystalline tophus includes tumoural calcinosis and tophaceous pseudo-gout (Table 2). 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.¹⁰ 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. Tumoural calcinosis is an idiopathic

condition presenting as swellings around the large joints (hip, elbow, ankle and scapula). The calcified material in tumoural calcinosis is hydroxyapatite in nature and shows amorphous intensely basophilic granular appearance.¹⁰

To summarize, FNAC is proving to be a valuable tool in elucidating the nature of periarticular nodules. It serves as a good alternative to synovial biopsy and fluid analysis for crystal demonstration. It is less invasive, simpler and cost effective technique as compared to synovial biopsy, which causes more tissue trauma and requires sterile set up. Crystal demonstration has also been seen to be superior in FNAC smears versus histopathology sections in which crystals are more commonly lost during processing.⁶ FNAC also has the advantage over joint fluid analysis as coincident crystals like hydroxyapatite and steroid etc in the joint fluid may cause confusion.⁶

FNAC is a simple and effective technique for evaluation of gouty tophi and cytopathologist should be aware of their morphological features especially in cases of atypical presentation.

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