

# Fine Needle Aspiration Cytology in the Diagnosis of Gouty Tophi - Report of Two Cases

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## ABSTRACT

Gout is a chronic hyperuricaemic crystal induced arthropathy. Tophi are soft tissue nodules, usually periarticular, that develop after long standing gouty arthritis. Demonstration of monosodium urate crystals in synovial fluid or biopsy helps in confirming the diagnosis of gout. However, Fine Needle

Aspiration Cytology (FNAC) of nodules is becoming a popular and valuable tool in the diagnosis of gout. We report two patients admitted in our hospital and diagnosed to have gouty tophi. Both of them were elderly males who presented with multiple soft tissue nodules and FNAC along with polarizing microscopy was helpful in arriving at final diagnosis.

**Keywords:** Birefringence, Hyperuricaemia, Papanicolaou stain

## CASE REPORT

### Case 1

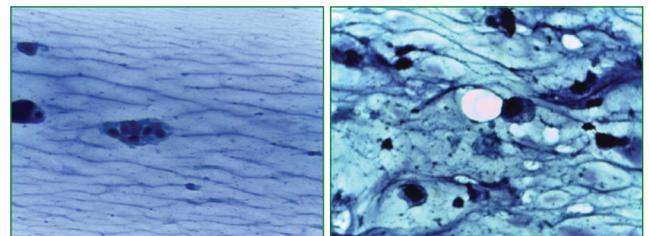
A 75-year-old male patient presented with multiple subcutaneous nodules for past one month. Local examination revealed nodules on dorsal aspect of both feet, extensor aspect of left forearm and right shin, their size ranging from 1x1 cm - 2x3 cm. They were firm, immobile, non-tender with tense overlying skin and some of them were ulcerated [Table/Fig-1,2]. The patient had pallor and also complained of loss of appetite and loss of weight. His haematological and biochemical examination revealed anaemia (haemoglobin 9.5 g/dL), raised serum uric acid (12 mg/dL), leucocyte count (TC-4300/cumm), thrombocytopenia (platelet-79,000/ $\mu$ L), elevated blood urea (58 mg/dL) and raised serum creatinine (1.7 mg/dL). Liver function tests, urinalysis and serum electrolytes were within normal limits. Rheumatoid factor was



**[Table/Fig-1]:** Nodular swelling 1x1 cm in size, firm, immobile, non-tender.



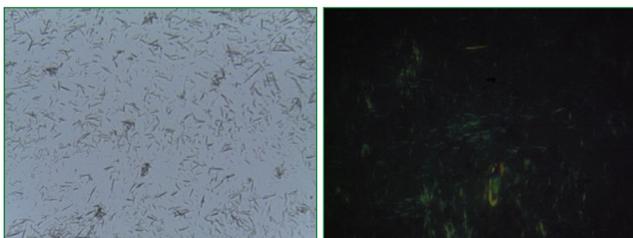
**[Table/Fig-2]:** Nodular swellings 2x1 cm and 1x1 cm in size, firm, immobile with superficial ulceration.



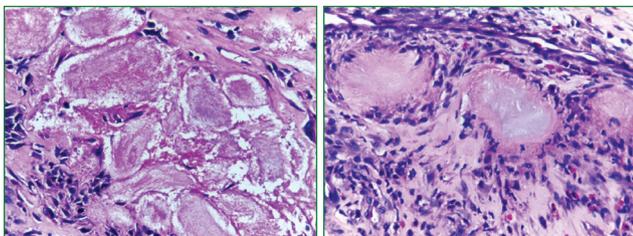
**[Table/Fig-3]:** Foreign body giant cell reaction (Papanicolaou 20X).

**[Table/Fig-4]:** Inflammatory cells in a myxoid background (Papanicolaou 20X).

negative. The nodules were clinically considered neoplastic in nature and the patient was advised FNAC. On FNAC chalky white material was aspirated. Papanicolaou staining was done and microscopy showed granular and myxoid material, multinucleated giant cells and chronic inflammatory infiltrate [Table/Fig-3,4]. Unstained cytology smears revealed needle-shaped crystals [Table/Fig-5], which on polarized microscopy showed negatively birefringent crystals, consistent with monosodium urate [Table/Fig-6]. Diagnosis was confirmed



**[Table/Fig-5]:** Elongated needle shaped crystals with pointed tips (unstained smear). **[Table/Fig-6]:** Needle shaped crystals with negative birefringence.



**[Table/Fig-7]:** Amorphous eosinophilic material and inflammatory cells (H and E 40X). **[Table/Fig-8]:** Amorphous material rimmed by inflammatory cells (H and E 40X).

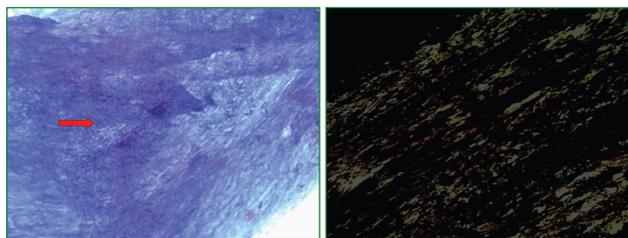
by histopathological examination of the nodule which showed extensive deposition by amorphous aggregates of urate crystals surrounded by intense inflammatory reaction composed of macrophages, lymphocytes, foreign body giant cells, and fibroblasts [Table/Fig-7,8]. Patient was treated with colchicine and allopurinol to which patient responded well.

## Case 2

A 56-year-old male patient presented fever, polyarthritis as well as pain and nodular swelling on dorsal aspect of right forearm around elbow joint. Nodules were firm, immobile and size of 4x3 cm and 3x3 cm [Table/Fig-9]. The differentials considered were rheumatoid arthritis and gouty arthritis. Patient was hypertensive, on treatment since 5 years with no other comorbidities. His haematological and biochemical examination revealed anaemia (Hb-7.8 gm/dL), normal serum uric acid (6.6 mg/dL), elevated Erythrocyte Sedimentation Rate (ESR) of 116 mm/hour. Renal function tests, liver function test, urinalysis and serum electrolytes were within normal limits. Rheumatoid factor and anti-cyclic citrullinated peptide antibody (anti CCP) were negative. The patient underwent FNAC of subcutaneous nodules and thick chalky white material was aspirated. Papanicolaou staining showed needle shaped crystals and few inflammatory cells in a myxoid



**[Table/Fig-7]:** Nodular swellings 4x3 cm and 3x3 cm in size, firm, immobile, non-tender.



**[Table/Fig-10]:** Elongated needle shaped crystals with pointed tips (Papanicolaou x 40). **[Table/Fig-11]:** Elongated needle shaped crystals with negative birefringence.

background [Table/Fig-10]. Final diagnosis was confirmed by negative birefringence using polarizing microscope [Table/Fig-11]. Patient was symptomatically treated with non steroidal anti inflammatory drugs and colchicines. Later, allopurinol 0.5 gm was started and increased to 1.0 gm to which patient responded well.

## DISCUSSION

Gout is characterised 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]. Gout caused by persistent chronic hyperuricaemia 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. Clinically, acute arthritis is the usual manifestation of gout though, it can also present as asymptomatic hyperuricaemia, chronic tophaceous gout or nephrolithiasis [2,3].

Gouty arthritis occurs when tissues have been exposed to hyperuricaemia for years. Classically, most common affected site is the first metatarsophalangeal joint. Ankles knees, wrists and the interphalangeal joints of hands and shoulder may also be affected. There is usually a time gap of around five years between arthritis and development of tophi. Tophi are commonly located in the olecranon bursa, the infrapatellar and achilles tendons and also in the subcutaneous tissue of the extensor surfaces of forearms [4,5]. Gout is a disease more commonly found in men than in women and usually occurs during the 5<sup>th</sup> and 6<sup>th</sup> decades of life as observed in the above two cases [6].

The pathogenesis underlying gout is the deposition of MSU in the synovial fluid and other tissues. These crystals in turn triggers immune activation [7]. The tophus which is the cardinal feature of advanced gout is characterised microscopically by collections of the similar MSU crystals surrounded by inflammatory cells composed of macrophages, giant cells and foreign body giant cells [8].

The crystal demonstration in FNAC smears is superior to histopathology sections where crystals are more commonly lost during processing and fixation [9]. Some studies have concluded that urate crystals are best demonstrated using air dried Giemsa/Diff-Quik stain compared to Papanicolaou stain [10]. They hypothesised that crystals were lost due to hydration steps involved in Papanicolaou staining and it was opposed by few authors. However, we could demonstrate

needle shaped crystals in Papanicolaou stain itself [11]. One of the drawbacks of FNAC is that, sometimes the crystals may be obscured by haemorrhagic background and inflammatory infiltrate. Therefore, the presence of amorphous or granular material should alert the cytopathologist. Crystals can be very clearly seen on unstained smears and the same can be employed for polarized microscopy [11].

The differential diagnosis of gouty tophi include subcutaneous or articular nodules like pseudo-gout, tumoral calcinosis, synovial cysts, osteoarthritis, rheumatoid arthritis, sarcoidosis, lymphoma and cutaneous metastases. FNAC helps in resolving the diagnostic dilemma by demonstrating needle shaped crystals. In pseudogout, Calcium Pyrophosphate Dihydrate (CPPD) crystals are deposited in soft tissue which may mimic gout. However, the crystals are positively birefringent [12,13].

Management of gout must include dietary and lifestyle modifications like restricted intake of purine rich food and limiting alcohol consumption and optimising weight. Urate lowering medications include drugs which either favour uric acid excretion like probenecid or inhibit uric acid production like allopurinol, febuxostat. Latest advancements are the Interleukin-1 (IL-1) antagonists, such as anakinra, a human recombinant IL-1 receptor antagonist and canakinumab, a monoclonal antibody against IL-1 $\beta$  used in the treatment of refractory cases or cases intolerant to classical therapy. Surgery is usually the last resort of treatment unless tophi are in a critical location, drain chronically or there is intractable joint pain, loss of motion and massive joint destruction [12,14].

## CONCLUSION

Gouty tophi which presents as peri-articular soft tissue nodules are a cause of concern and frequently mistaken as a neoplasm. FNAC of such nodules helps in straight forward diagnosis and thus is a valuable, simpler, cost effective diagnostic tool. It is also a less invasive diagnostic tool in comparison to synovial biopsy, which causes more tissue trauma. It helps to avoid unnecessary radiological and clinical investigations. The major advantage is that crystals which are commonly lost during histopathological processing can be demonstrated excellently in FNAC smears.

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