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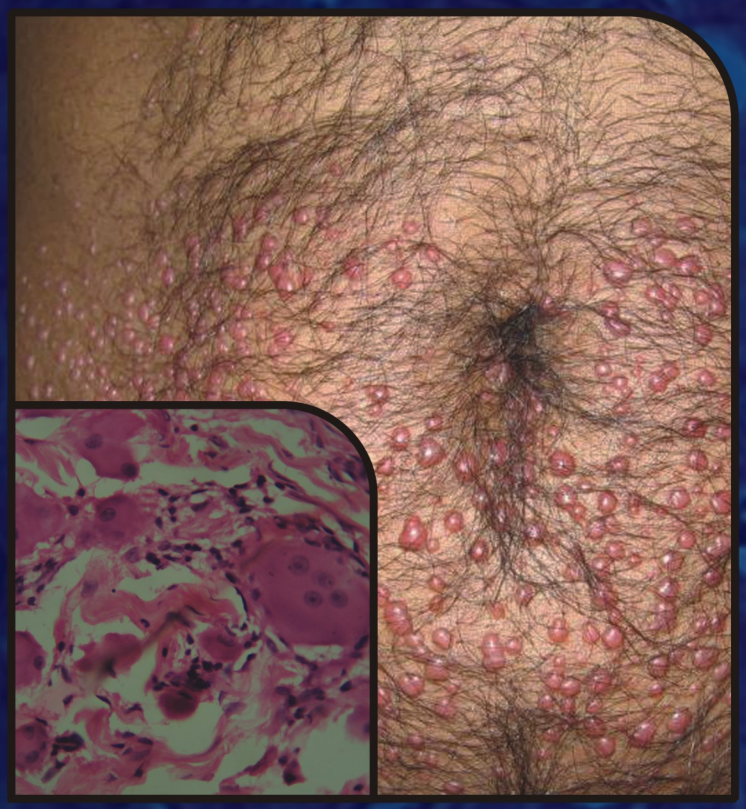

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- Lichen planus in children

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Case Report

Tophi as first manifestation of gout

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ABSTRACT

Chronic tophaceous gout classically occurs after 10 years or more of recurrent polyarticular gout. However, tophi can also occur as first sign of the disorder. Here we report a 20-year-old male presenting with multiple subcutaneous nodules on bilateral feet and toes, left palm, right elbow, helix of left ear since last one and half year prior to any other manifestation of gout. He was having mild intermittent arthritis since last six months. Fine Needle Aspiration Cytology of one tophus showed monosodium urate crystals, which are pathognomonic for gout. His serum uric acid was normal and ultrasound revealed bilateral nephrocalcinosis. So far as we know, this is the first case report from India, demonstrating tophi as the initial clinical presentation of gout.

Key words: Tophi, gout, nephrocalcinosis

INTRODUCTION

Gout is a common disease associated with monosodium urate (MSU) crystal deposition in articular or peri-articular tissues and in the renal tract. Generally it progresses through four clinical stages if 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 first sign of the disorder. Here, we report a twenty-year-old male with normal blood uric acid level who presented with tophi prior to any other manifestation of gout.

CASE REPORT

A 20-year-old non-alcoholic male presented with gradually increasing multiple subcutaneous nodules on both the lateral malleoli, lateral parts of bilateral feet and toes, left palm, right elbow, helix of left ear [Figures 1-4], ranging in size from 1-1.5 cm diameter since last one and half year. These nodules were firm, mobile and non-tender. Few of them had broken into the skin discharging whitish chalky particulate material. The same could be expressed out of the tophi with the help of a needle. He had intermittent mild pain in the great toes since last six months. Recently, it has spread to elbows. He did not receive any major medication except painkillers in the past.

Systemic examination was normal. Radiographs of both the feet and the hands showed soft tissue swellings with no involvement of bones. Fine Needle Aspiration Cytology (FNAC) was performed from subcutaneous nodules on the left leg using a 21-gauge needle. Light microscopy of the Giemsa and Papanicolaou (Pap) stained smears demonstrated abundant granular amorphous material and scattered stacks of slender needle shaped crystals, associated with chronic inflammatory infiltrate [Figure 5]. Based on the above findings, a diagnosis of gouty tophi was made. Polarizing microscopy was not used as this facility was not available in our institute. On further investigations, serum uric acid was 5.8mg/dl (normal: 2.5-7 mg/dl). His blood sugar (fasting: 142 mg/dl; postmeal: 190 mg/dl) and triglycerides were raised (212 mg/dl). Ultrasound revealed bilateral nephrocalcinosis [Figure 6]. Serum levels of calcium, phosphate, albumin, electrolytes, urea, creatinine, Parathyroid hormone, Thyroid-stimulating hormone were within

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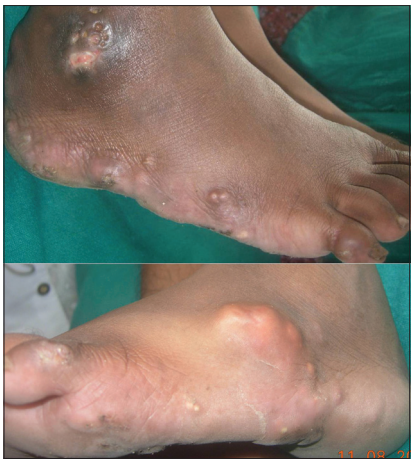

Figure 1: Tophi involving the lateral malleoli, lateral parts of feet and toes

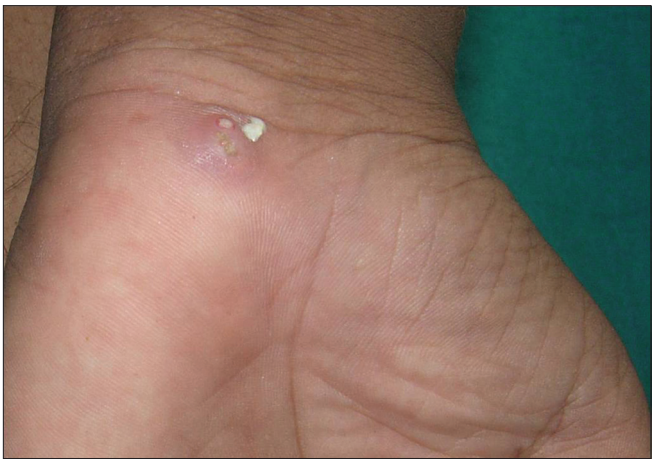

Figure 2: Tophi on proximal palm with chalky particulate material, expressed out with a needle

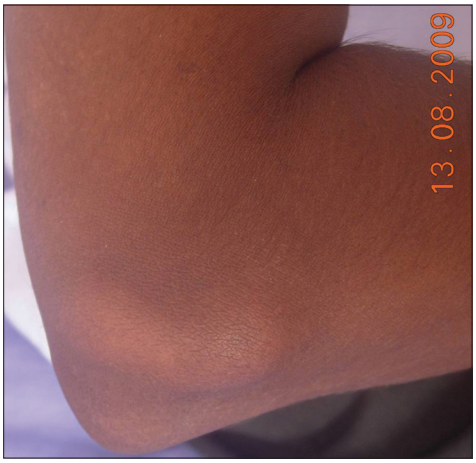

Figure 3: Tophi on right elbow

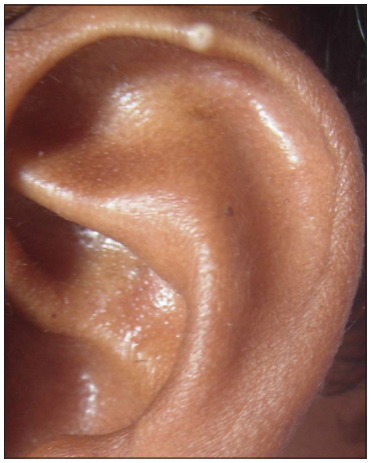

Figure 4: Tophi along left ear helix

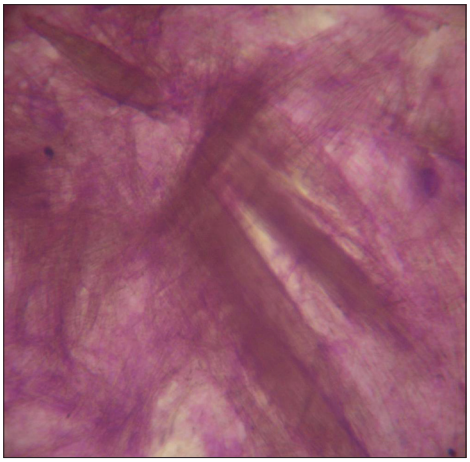

Figure 5: Photomicrograph (FNAC) shows stacks of urate crystals in tissue material (PAP×400)

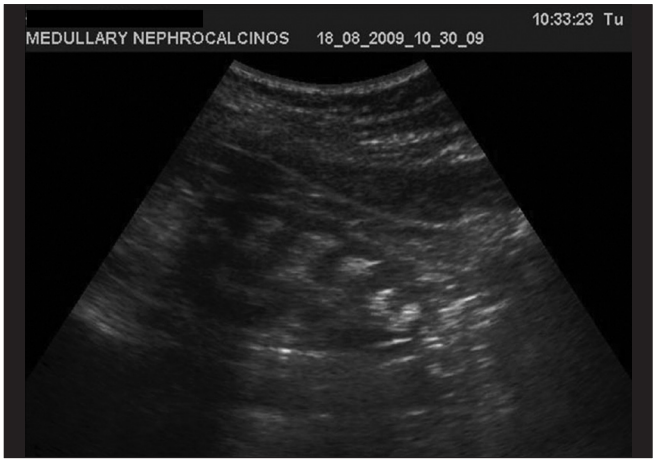

Figure 6: Ultrasonography showing medullary nephrocalcinosis

normal limits. Different tests to exclude connective tissue diseases, including that for antinuclear antibody, were performed. 24-hour urine analysis and measurement of levels of calcium, sodium, uric acid,

oxalate and citrate were done to rule out any other pathology.

DISCUSSION

Gout, one of the oldest known forms of arthritis, is characterized by chronic hyperuricemia (serum urate >450 μmol/l or 7.0 mg/dl in men; and >350 μmol/l or 6.0 mg/dl in women). The hyperuricemia may be primary (due to inborn errors of purine metabolism or diminished renal excretion of uric acid) or secondary (conditions with extensive cell turnover or acquired renal disease). In 90% cases of primary gout, hyperuricemia results mostly from relative renal urate underexcretion ('relative urate underexcretors,') while in about 10% of subjects, hyperuricemia is due to endogenous overproduction of uric acid ('urate overproducers').[1,2]

The diagnosis of gout can be made according to the American College of Rheumatology (ACR)/Wallace criteria proposed in 1977 [Table 1]. The gold standard for diagnosis is the demonstration of urate crystals in synovial fluid or in a tophus by polarized light microscopy. The presence of six or more of the 12 criterias makes a diagnosis of gout highly likely.[3] But due to changing spectrum of gout, diagnosis of gout is often difficult. Identification of urate crystals in joint aspirates is often not possible. Often the clinicians have to rely on observations of intermittent monoarthritis that begins with involvement of a single joint or multiple joints in the lower extremities (most commonly the first metatarsophalangeal i.e. podagra), associated with hyperuricemia and responsiveness to colchicine. According to newly formed European League Against Rheumatism (EULAR) recommendations, classic podagra and presence of tophi have the highest clinical diagnostic value for gout. Urate crystal identification is very likely to be positive in symptomatic gout and hyperuricemia is a major risk factor for gout although some gouty patients may have normal serum uric acid levels at the time of investigation.[4]

Table 1: American College of Rheumatology criteria for gout

American College of Rheumatology (ACR)/Wallace criteria
A. The presence of characteristic urate crystals in the joint fluid,
B. A tophus proved to contain urate crystals by chemical means or polarized light microscopy
OR
C. Six of the following 12 clinical criteria:
a. Maximum inflammation within the first day
b. More than one attack of acute arthritis
c. Monoarticular arthritis
d. Redness observed over joints
e. First metatarsophalangeal joint pain attack
f. Unilateral metatarsophalangeal joint attack
g. Unilateral tarsal joint attack
h. Suspected tophus
i. Hyperuricaemia
j. Asymmetric swelling within a joint on x-ray
k. Subcortical cysts with no erosions on x-ray
l. Negative bacterial culture of joint fluid

Hyperuricemia is the most important risk factor for the development of gout, the risk increasing with a higher urate concentration. But the level of serum uric acid (SU) may be normal in gout, specially in diabetics and alcoholics.[5] However in an Indian study of 6 normouricemic patients of gout, only one consumed alcohol.[6] In the largest studies of acute gout to date, attacks still occurred despite SU levels being below 6.8 mg/dl, the saturation level for urate. This may be attributed to persistence of tophi and an increased body uric acid pool.[7] Our patient was non-alcoholic and his serum uric acid level was within normal limits. He was never suspected to have gout before. So uric acid was never measured earlier and he never received any drugs used in treatment of gout.

Tophi are deposits of MSU crystals in soft tissue that may occur in the helix of the ear, over olecranon processes, and over interphalangeal joints. They have to be differentiated from periarticular nodules like rheumatoid nodules, ganglion cysts, pigmented villonodular synovitis, synovial chondromatosis and synovial sarcoma. The clinical differential diagnoses of acute gout are pseudogout (chondrocalcinosis articularis) and septic arthritis. Calcium pyrophosphate dehydrate (CPPD) crystals are deposited in tophaceous pseudgout and they are shorter, more rhomboid than needle shaped and show positive birefringence as compared to their counterparts in gout.

Uric acid promotes calcium oxalate crystallization in urinary tract by facilitating the formation of nuclei. Sodium acid urate also nullifies the effectiveness of naturally occurring inhibitors of calcium oxalate crystal growth. Recent prospective studies in 50000 male health professionals have confirmed that a diagnosis of gout was associated with twice the risk of incident renal calculi.[8] Toyoda *et al.*, reported 18

cases with medullary nephrocalcinosis of whom seven had gouty arthritis and one had Lesch-Nyhan syndrome.[9] According to Kuo *et al.*, gout should be considered as first differential diagnosis in male subjects with medullary nephrocalcinosis, whereas primary hyperparathyroidism should be considered first in females.[10]

Gout is often associated with hyperlipidemia (usually hypertriglyceridemia) and insulin resistance syndrome (IRS). The situation may become often tricky as the treatment of gout with a purine restricted diet that is usually rich in both carbohydrate and saturated fat may negatively influence the management of IRS.

Now FNAC is replacing other investigations due to its quick, less invasive, simpler and cost effective technique. The crystal demonstration in FNAC smears 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.[11]

Tophi generally developed after an average of 11.6 years of gouty arthritis before uric acid lowering therapy became available.[12] They were reported to occur in 12% of patients after 5 years, and 55% after 20 years of untreated disease.[13] However, they can develop without the concomitant arthritis. Iglesias *et al.*, used the term 'gout nodulosis' to describe the subcutaneous deposits of MSU in the absence of initial manifestation of gouty arthritis.[14] Recently Thissen *et al.,* reported an 85-year-old woman who was diagnosed with tophaceous gout devoid of a prior medical history of the disease.[15]

Probably tissue deposition occurs long before any symptom. When we get symptomatic disease i.e. arthritis, we recognize gout. Then we do routine tests and recognize systemic manifestations such as nephrolithiasis or interstitial deposits.

To the best of our knowledge, ours is the first case report from India where tophi were the first clinical sign of gout.

REFERENCES

1. Boss GR, Seegmiller JE. Hyperuricemia and gout: classification, complications and management. N Engl J Med 1979;300: 1459-68.
2. Fam AG. Pathogenesis of hyperuricemia in patients with primary gout. Primary Care Canada 1997;8:9-10.
3. Wallace SL, Robinson H, Masi AT, Decker JL, McCarty DJ, Yü TF. Preliminary criteria for the classification of the acute arthritis of primary gout. Arthritis Rheum 1977;20:895-900.
4. Zhang W, Doherty M, Pascual E, Bardin T, Barskova V, Conaghan P, *et al*. EULAR evidence based recommendations for gout. Part I: Diagnosis. Report of a task force of the standing committee for international clinical studies including therapeutics (ESCISIT). Ann Rheum Dis 2006;65:1301-11.
5. McCarty DJ. Gout without hyperuricemia. JAMA 1994;271: 302-3.
6. Porkodi R, Parthiban M, Rukmangatharajan S, Kanakarani P, Rajendran CP. Clinical spectrum of gout in south India. J Indian Rheumatol Assoc 2002;10:61-3.
7. Schlesinger N, Norquist JM, Watson DJ. Serum urate during acute gout. J Rheumatol 2009;36:1287-9.
8. Kramer HJ, Choi HK, Atkinson K, Stampfer M, Curhan GC. The association between gout and nephrolithiasis in men: The Health Professionals' Follow-Up Study. Kidney Int 2003;64:1022-6.
9. Toyoda K, Miyamoto Y, Ida M, Tada S, Utsunomiya M. Hyperechoic medulla of the kidneys. Radiology 1989;173:431-4.
10. Kuo CF, Ho HH, Liou LB, Luo SF, Wu YJJ, Chen JY, *et al*. Medullary nephrocalcinosis in young subjects with gout. J Rheumatol 2007;21:64-70.
11. Rege J, Shet T, Naik L. Fine needle aspiration of tophi for crystal identification in problematic cases of gout. A report of two cases. Acta Cytol 2000;44:433-6.
12. Hench PS. The diagnosis of gout and gouty arthritis. J Lab Clin Med 1936;22:48-55.
13. Wallace SL, Singer JZ. Therapy in gout. Rheum Dis Clin North Am 1988;14:441-57.
14. Iglesias A, Londono JC, Saaibi DL, Peña M, Lizarazo H, Gonzalez EB. Gout nodulosis: widespread subcutaneous deposits without gout. Arthritis Care Res 1996;9:74-7.
15. Thissen CA, Frank J, Lucker GP. Tophi as first clinical sign of gout. Int J Dermatol 2008;47:49-51.