# *Tophaceous Gout of the Ankle Presenting as a Soft Tissue Mass: A Case Report of an Uncommon Presentation of a Common Disease*

## *Ayak Bileğinde Yumuşak Doku Kitlesi Şeklinde Bulgu Veren Gut Tofüsü: Sık Gözlenen Bir Hastalığın Nadir bir Prezentasyon Şekli*

Banu Doğan GÜN, Şükrü Oğuz ÖZDAMAR, Sacide ÇOLAK, Burak BAHADIR, Gamze Mocan KUZEY*
*Zonguldak Karaelmas Üniversitesi Tıp Fakültesi Patoloji Anabilim Dalı, Zonguldak, Türkiye*
**Hacettepe Üniversitesi Tıp Fakültesi Patoloji Anabilim Dalı, Ankara, Türkiye*

### Summary

Gout is a metabolic disorder in which there is either an increase in production or a decrease in excretion of uric acid leading to hyperuricemia. Hyperuricemia results in the deposition of monosodium urate crystals in joints and visceral organs and continued deposition eventually results in chronic tophaceous gout.
We report a case of gouty tophi in a 45-year-old man who developed nodules on both lateral aspects of the malleoli with a history of arthropathy. In laboratory investigation, blood chemistry showed marked hyperuricemia (8.40 mg/dl). Macroscopically, the lesions were circumscribed whitish-gray masses. Histologically, both lesions contained areas of amorphous brown crystal deposits and they were surrounded by a foreign body type granulomatous infiltrate. The crystals revealed specific birefringence, a diagnostic characteristic of the monosodium urate crystals, with a polarizing filter.
Gout deposits in skin (tophi) are uncommon. The aim of this report is to emphasize the importance of considering this disease entity in the differential diagnosis of a soft tissue lesion in a patient with chronic arthritis. *Turk J Phys Med Rehab 2006;52:185-7*
**Key Words:** Gout, tophi, urate crystals

### Özet

Gut, ürik asit atılımında azalma ya da üretiminde artışın gözlendiği hiperürisemiye yol açan metabolik bir hastalıktır. Hiperürisemi, monosodyum ürat kristallerinin eklemlerde ve iç organlarda birikimine neden olur ve devam eden birikim nihayetinde kronik gut tofüsü ile sonuçlanır.
Bu çalışmada artropati hikayesi olan ve her iki ayak bileğinde malleol lateralinde nodüler kitleye sahip 45 yaşında erkek hasta sunulmuştur. Yapılan laboratuvar incelemesinde hastanın kan biyokimyasında belirgin hiperürisemi (8,40 mg/dl) mevcuttu. Eksize edilen lezyonlar makroskopik olarak lezyon, iyi sınırlı ve beyazımsı-gri renkte gözlendi. Histolojik olarak her iki lezyonda da amorf kahverengi kristal birikimleri içermekteydi ve yabancı cisim tipi granülomatöz infiltrasyonla çevrelenmişlerdi. Polarize filtre ile kristallerin monosodyum ürat kristalleri için diagnostik olan spesifik refle verdikleri gözlendi.
Deride gut birikimlerinin (tofüs) oldukça az gözlenmesi nedeniyle; biz bu çalışmada yumuşak doku kitlesi olan kronik artritli bir hastada bu hastalığın da akılda tutulması gerekliliğini vurgulamayı amaçladık.
*Türk Fiz Tıp Rehab Derg 2006;52:185-7*
**Anahtar Kelimeler:** Gut, tofüs, ürat kristalleri

## Introduction

Gout is first identified by the Egyptians in 2640 B.C., podogra (acute gout occurring in the first metatarsophalangeal joint) was later recognized by Hippocrates in the fifth century B.C., who referred to it as "the unwalkable disease" (1). Gout is characterized by deposition of monosodium urate (MSU) crystals in tissues that may form as a result of hyperuricemia which represents the basic underlying metabolic abnormality (2,3). The deposition of MSU crystals in and around joints as well as soft tissues, produce masses commonly referred as tophi and usually thought to be a late manifestation of gout (4).

In this report we described the clinical and histopathological features of a case of tophaceous gout in a 45-year-old man with chronic arthritis to emphasize the importance of considering this disease entity in the differential diagnosis of a soft tissue lesion.

**Address for Correspondence:** Dr. Banu Doğan Gün, Zonguldak Karaelmas Üniversitesi Tıp Fakültesi Patoloji Anabilim Dalı, Zonguldak, Türkiye
Tel.: +90 372 261 02 60 Fax: +90 372 261 01 55 E-mail: banudogangun@yahoo.com **Accepted:** October 2006

## Case Report

A 45-year-old man gave a six year history of painful arthritis at both of ankles. He had experienced recurrent swelling, severe pain occurring three or four times a year, and had been treated symptomatically. Acute attacks of arthritis were self limiting and resolved usually within 2-3 weeks. He denied any symptoms of trauma. His past medical history was significant for hypertension and diabetes mellitus. Medications included diuretics and aspirin. He reported occasional alcohol use, and had no history of renal disease, renal stones, heart failure or psoriasis. Also he had no family history of joint disease and allergies.

Physical examination revealed swollen ankles with limited mobility. Also the patient developed a mass, 2-3 cm in diameter, on both lateral aspects of the malleoli. The mass was freely mobile and did not appear attached to the underlying bony skeleton. Plain film radiographs revealed decreased bone density and mild erosive changes at the tarsal bones. MRI scans revealed a soft tissue mass and associated with erosive changes. Laboratory studies showed normal urinalysis, serum electrolytes, erythrocyte sedimentation rate, and absence of rheumatoid factor and antinuclear antibodies. His blood sugar levels and uric acid levels were high. An excisional biopsy was performed.

The resected specimens were well-circumscribed involving the dermis and subcutaneous tissue. They were fixed with formalin, stained with hematoxylin and eosin. Histopathologically skin biopsies of two lesions showed foci of brown crystaloid deposits (Figure 1). Also there were some areas of amorphous, pale staining deposits surrounded by mononuclear cells and multinucleated giant cells (Figure 2). The overlying epidermis was hyperplastic and showed parakeratosis and hyperkeratosis on its surface. On polaroscopic examination, the needle-shaped crystals revealed specific birefringence. Depending on the plane of polarization; in the appropriate position, the crystals parallel to the line drawn on the compensating filter, were bright yellow, indicative of strong negative birefringence, by contrast crystals aligned perpendicular to the compensating filter line were blue (Figure 3).

## Discussion

Gout is marked by transient attacks of acute arthritis initiated by crystallization of urates within and about joints, leading eventually to chronic gouty arthritis (5). The vast majority of first attacks are monoarticular; 50% occurs in the first metatarsophalangeal joint. Also acute attacks of ankles, heels, knees, wrists, fingers and elbows eventually occurs in about 90% of patients (2). Most common manifestation is painful arthritis afflicting the lower extremities, as in this case.

The deposition of MSU crystals in and around joint as well as soft tissues, produce masses commonly referred as tophi and usually thought to be a late cutaneous manifestation of gout (4,5). Tophi commonly appear as firm pink nodules or fusiform swellings (5,6). The overlying skin may be yellow, erythematous, or ulcerated. The lesions may drain clear fluid with flakes of urate or a thick, chalky material (6,7). Complications of tophi include pain, soft tissue damage and deformity, joint destruction and nerve compression syndromes such as carpal tunnel syndrome (7). They are the pathogonomic hallmark of the disease and develop about 10 years after the first attack of gout (2). The most common sites of the urate depositions are the synovium, articular cartilage of joints, periarticular ligaments, tendons and soft tissues including the prepatellar bursa, olecranon bursa, subcutaneous tissues overlying tendons (Achilles tendon), the helix of the ear

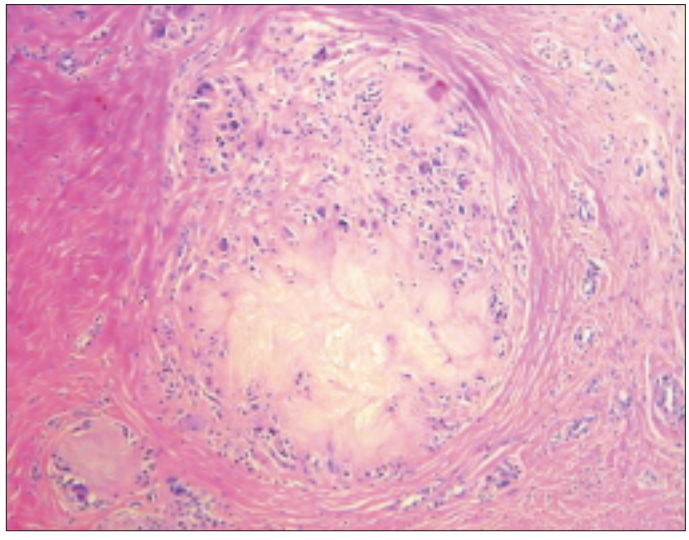

Figure 2. Foreign body-type giant cell reaction to amorphous material (HEx200).

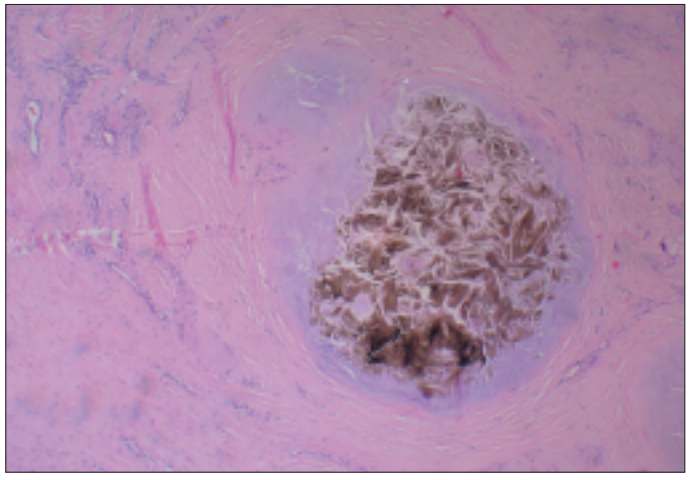

Figure 1. The apperance of the brown cyrstalline deposits under light microscopy with surrounded histiocytes and chronic inflammatory cells (HEx100).

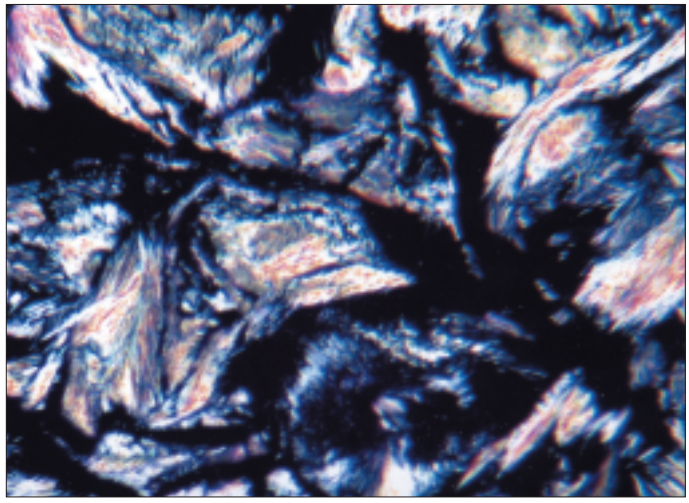

Figure 3. Polarization of the properly preserved tissue demonstrates the refractile urate crystals in these amorphous deposits (HEx400).

and the base of great toe (2,4,7). Less frequently they may appear in the kidneys, nasal cartilages, skin of the fingertips, palms and soles as well as elsewhere (2).

The histological hallmark of gout tophi is the foreign body granulomas composed of mono- and multinucleated macrophages enclosing deposits of MSU crystals. Macrophage are pivotal effectors of inflammation, the activity of which may result in phagocytosis and degradation of foreign bodies, synthesis of proinflammatory cytokines (e.g. tumor necrosis factor) and production of lytic enzymes (e.g. matrix metalloproteinases) (8,9).

The definitive diagnosis of gout is best established by demonstration of MSU crystals in the synovial fluid or biopsy (10). Measurement of serum uric acid is of little or no use in making a diagnosis of gout. In fact, those levels in some patients with gout may be low or normal (7,10). Lower serum urate levels may be observed in diabetics due to the uricosuric action of high blood glucose levels (10). Urates occur in tissue (gouty tophi), or in synovial fluids from acute gouty joints, as acid sodium urate crystals. They may be demonstrated as argentaffin with methanamine silver, or with the polarizing microscope. The deGalantha stain is particularly suited for the demonstration of crystals (11).

Tissues should be fixed in the minimum time in formal-saline otherwise urate deposits will be removed. It is safer to fix in absolute alcohol. Fixation in alcohol is important for the preservation of sodium urate monohydrate deposits that appear as needle shaped, doubly refractile crystals (11,12). In this case, because having no knowledge about the clinical prediagnosis, we fixed the material in formalin; however we still succeeded to demonstrate the negative birefringence of these crystals with polarized microscopy. During the course of routine staining of histological sections, the crystals which are water soluble, are usually removed; however examination of unstained sections by polarized light generally clearly demonstrates the crystalline nature of the deposits (11,12). Again, in spite of our staining with hematoxylin and eosin, there were presently some areas of properly preserved crystalline structures demonstrable with a polarized filter. MSU crystals are often lost after formalin fixation and during histological processing. However, they are preserved in cytological smears that are alcohol fixed (10).

Gout should be distinguished from chondrocalsinosis (pseudogut syndrom), a rare condition in which the symptoms result from diffuse deposition of calcium pyrophosphate dihydrate (CPPD) cyrstals in the articular cartilage (13). In joint fluids, particularly, it is important to differentiate between sodium urate and CPPD, which may occur in synovial fluid from acutely inflamed joints. This differentiation is relatively simple using polarizing microscopy. In contrast to MSU crystals in acute gouty arthritis, CPPD crystals are more difficult to detect because of the smaller size, rhomboid shape and only weak or no positive birefringence (10,12,13). The differential diagnosis of such a crystalline tophus would also include tumoral calcinosis (2,12). Radiographic calcification in a gouty tophus is an uncommon finding. The deposits in tumoral calcinosis are amorphous and lack a crystalline structure (2).

In gouty tophi, histiocytes may sometimes form palisating granulomas and this histopathological appearance may be a source of confusion with rheumatoid nodules and granuloma annulare (8). In these circumstances the clinical and laboratory findings will aid the differential diagnosis. Also in same cases of gouty tophi, superficial epidermis may show pseudocarcinomatous hyperplasia and clinically it may be confused with a tumoral mass (6). In this case the overlying epidermis revealed hyperkeratosis and some degree of hyperplasia, but the presence of pathogonomic features facilitated the correct diagnosis. The radiological differential diagnosis may also include; CPPD crystal deposition disease, septic arthritis, hydroxyapatite deposition disease (HADD), erosive osteoarthritis, rheumatoid arthritis and psoriatic arthritis (2,9)

In summary, when the clinical history and the presence of hyperuricemia suggest gout, the definitive diagnosis can only be made by identification of the characteristic negative birefringent needle shaped crystals obtained from synovial fluid or tophus. We here described a case of an uncommon presentation of a common disease to emphasize the importance of considering this disease entity in the differential diagnosis in a patient with chronic arthritis and also in the differential diagnosis of a soft tissue lesion.

## References

1. Nuki G, Simkin PA. A concise history of gout and hyperuricemia and their treatment. Arthritis Res Ther 2006;8:1-5.
2. Buckley TJ. Radiologic features of gout. Am Fam Physician 1996;54:1232-8.
3. Padang C, Muirden KD, Schumacher HR, Darmawan J, Nasution AR. Characteristics of chronic gout in Northern Sulawesi, Indonesia. J Rheumatol 2006;33:1813-7.
4. Fam AG, Assad D. Intradermal urate tophi. J Rheumatol 1997;24:1126-31.
5. Schumacher HR Jr, Becker MA, Palo WA, Streit J, MacDonald PA, Joseph-Ridge N. Tophaceous gout: quantitative evaluation by direct physical measurement. J Rheumatol 2005;32:2368-72.
6. Dacko A, Hardick K, McCormack P, Szaniawski W, Davis I. Gouty tophi: a squamous cell carcinoma mimicker? Dermatol Surg 2002;28:636-8.
7. Pittman JR, Bross MH. Diagnosis and management of gout. Am Fam Physician 1999;59:1799-806.
8. Schweyer S, Hemmerlein B, Radzun HJ, Fayyazi A. Continuous recruitment, co-expression of tumour necrosis factor-α and matrix metalloproteinases, and apoptosis of macrophages in gout tophi. Wirchows Arch 2000;437:534-9.
9. Cornelius R, Schneider HJ. Gouty arthritis in the adult. Radiol Clin North Am 1988;26:1267-76.
10. 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.
11. Culling CFA, Allison RT, Barr WT. Cellular Pathology Technique. 4th ed. London: Butterworth & Co. (Publishers) Ltd; 1985. p. 288-99.
12. Bullough PG. Joint Disease. In: Mills SE, Carter D, Greenson JK, Oberman HA, Reuter V, Stoler MH, editors. Stenberg's Diagnostic Surgical Pathology. 4th ed. Philadelphia: Lippincot Williams & Wilkins; 2004. p. 223-44.
13. Ahn JK, Kim HJ, Kim EH, Jeon CH, Cha HS, Ha CW et al. Idiopathic Calcium Pyrophosphate Dihydrate (CPPD) crystal deposition disease in a young male patient: A case report. J Korean Med Sci 2003;18:917-20.