

# Case of the Month: June's Diagnosis

## *Chronic Tophaceous Gout*

D. William Schlott, MD, John A. Flynn, MD,  
and Mona Z. Mofid, MD

A skin biopsy taken from the patient's elbow showed large nodular aggregates of pale amphophilic material focally containing brown needle-shaped crystals in the deep reticular dermis and subcutaneous fat. Aggregates were surrounded by histiocytes and multinucleated giant cells. Polaroscopy revealed birefringent crystals characterizing this amorphous material in the dermis. [Please place Images 1: Clinical photo, and 2 and 3: Pathology]

Any or all of the following characterizes gout:

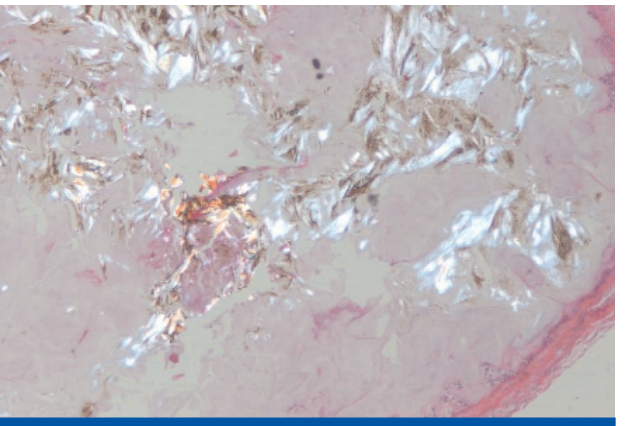
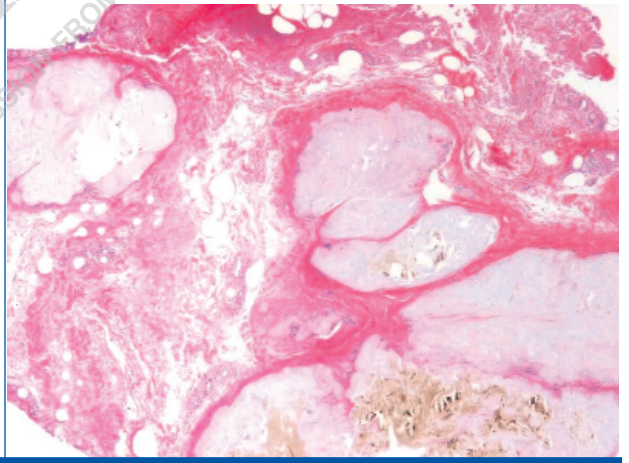
- Hyperuricemia
- Acute monoarticular and sometimes polyarticular inflammatory arthritis
- Tophaceous deposition of urate crystals in and around joints
- Renal deposition of urate crystals
- Urolithiasis

Hyperuricemia (defined as serum uric acid >7 mg/dL) can result from increased production or decreased excretion of uric acid, or both, which then leads to supersaturation of plasma and extracellular fluid—which in turn is favorable for crystal formation. The usual progression of the disease is from asymptomatic hyperuricemia (which can last decades) to acute gouty arthritis to intercritical gout and finally to chronic or tophaceous gout.

The hallmark of the disease is acute monoarticular arthritis, which is accompanied by intense inflammation and tenderness of the joint and is often explosive and quite painful. Attacks usually result from abrupt changes in serum urate levels and can be triggered by stress, trauma, infection, surgery, starvation, weight loss, excessive food and alcohol intake, and medications. Chronic gouty arthritis usually develops after a symptom-free period called interval gout (though radiographic changes do become apparent) and then becomes polyarticular arthritis—usually about 10 years after the first attack. It is at this point that tophi become apparent. Tophi usually occur in the olecranon bursa, Achilles' tendons, infrapatellar region, subcutaneous tissues on the extensor surface of the forearms, overlying joints, and less commonly around the helix of the ear.<sup>1</sup> Tophi may be confused with rheumatoid nodules and a biopsy or aspiration may be helpful.

Causes of hyperuricemia secondary to increased production of uric acid<sup>2,3</sup> include:

- Increased intake of dietary purines (eg, liver, kidney, anchovies)
- Increased rate of de novo purine biosynthesis (inborn error or PRPP synthetase)



Dr Mofid is Assistant Professor of Dermatology and Director, Outpatient Center Clinic, Johns Hopkins University School of Medicine, Baltimore, Maryland, and President, Maryland Dermatologic Society.

- Decreased rate of salvage purine synthesis (via decreased or absent HPRT, leading to de novo pathway; eg, Lesch-Nyhan syndrome)
- Accelerated purine nucleotide degradation (leukemic blast crisis, cytotoxic agents)

Causes of hyperuricemia secondary to decreased uric acid secretion<sup>2,3</sup> include:

- Decreased glomerular filtration rate
- Decreased tubular secretion
- Enhanced tubular reabsorption

*Ninety-eight percent (98%) patients with primary hyperuricemia have a defect in renal handling.*

Hyperuricemia secondary to both increased production and concomitantly decreased excretion<sup>2,3</sup> include:

- Glucose-6-phosphatase deficiency
- Hereditary fructose intolerance
- Alcohol consumption

*All result from increased ATP degradation and lactic acidosis (which inhibits uric tubular secretion).*

## TREATMENT

Patients with chronic tophaceous gout require reduction of uric acid burden. This can only be done with xanthine oxidase inhibitors in the form of allopurinol. Prolonged treatment with allopurinol will lead to resolution of tophi. To prevent attacks that may be precipitated by altering the uric acid level with medications, prophylactic colchicine is sometimes appropriate in low doses. With initiation of these medications, patients' uric acid decreased within 2 months' time and resolution of tophi was appreciated within 3 months' time.

## References

1. Sutej, Jorizzo. Rheumatoid Arthritis, Rheumatic Fever, and Gout. In: *Fitzpatrick's Dermatology in General Medicine, 5th Edition*. Freedburg et al (Eds). New York: McGraw-Hill, pp. 2061-2067, 1999.
2. Fauci, et al. Chapter 344: Gout and Other Disorders of Purine Metabolism. In: *Harrison's Principles of Internal Medicine, 14th Edition*. Fauci AS, et al (Eds). New York: McGraw-Hill, pp. 2158-2165, 1998.
3. Schapira, et al. Chronic tophaceous gouty arthritis mimicking rheumatoid arthritis. *Semin Arthritis Rheum*. 1999;29(1):56-63.

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