CHAPTER 35

Gout: Manifestations and Treatment

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The three common crystalline-induced arthropathies are gout, chondrocalcinosis (also known as pseudogout), and calcific tendinitis/bursitis. All three may manifest as lower extremity pathology, however, the latter two are not as commonly encountered in the foot as is gout.

Pseudogout is an inflammatory arthropathy caused by the deposition of calcium pyrophosphate dihydrate crystals within articular cartilage, tendons, synovium, and ligaments. It is most commonly seen in the elderly. The knee joint is most frequently involved, however, pseudogout may be found in any joint of the lower extremity including the first metatarsophalangeal joint. Therefore, a pseudogout attack may mimic a true gout attack.

The chronic deposition of calcium hydroxyapatite is associated with a periarthritis called calcific tendinitis and/or calcific bursitis. The diagnosis of this condition is usually made by the presence of calcifications in or around the joints. However, in some patients with significant crystal deposition, a white pasty material can be aspirated from tendon sheaths or joints. It is important to note that apatite deposition may be misdiagnosed as septic arthritis, since clumps of apatite crystals can be confused as leukocytes.

Gout is defined as an arthritic disease associated with the deposition of sodium urate crystals. There are three aspects of gout that will be addressed. First is the acute inflammatory phase of gout. The second is the chronic deposition of sodium urate crystals that causes tophaceous gout. Finally, we will discuss the condition of hyperuricemia which may or may not precipitate an acute gouty attack, lead to kidney stone formation, or even produce a type of cardiomyopathy.

Historically, gout was seen as an affliction of the rich. Not completely in error, it was felt that gout was a devil afflicting overweight aristocrats who over-indulged in rich foods and the consumption of alcohol.

Classically, acute gout is associated with the first metatarsophalangeal joint, and approximately 50% of the patients will have their first attack occur at this site. As many as 90% will have the first metatarsophalangeal joint involved at some time during the course of their disease (Fig. 1). The second most common site is the soft tissues of the midfoot. It is important to note, however, that any peripheral joint may be involved.

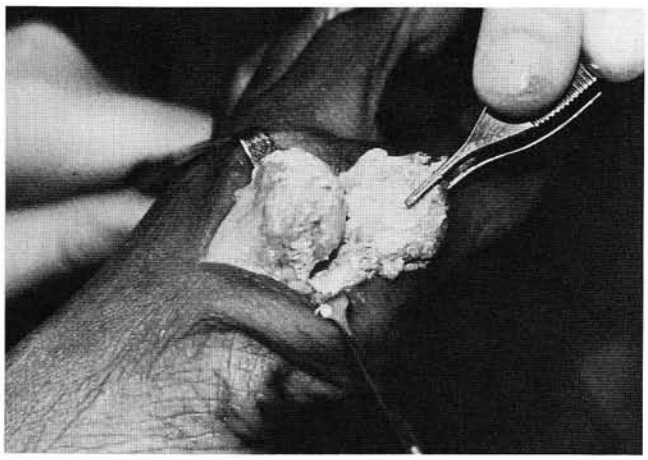

Figure 1. Although any joint of the lower extremity may be involved in an acute attack of gout, the first metatarsophalangeal joint is implicated in up to 90% of the patients.

ACUTE GOUT

Podagra, or acute gout of the first metatarsophalangeal joint, is usually described as a rapidly developing inflammatory arthropathy that awakens the patient at night or in the early morning. The reason for this presentation appears to be related to several unique characteristics of the first metatarsophalangeal joint. Osteoarthritis, commonly seen in the first metatarsophalangeal joint, causes a slight effusion of the joint to occur as the patient ambulates during the day. At night, the effusion is gradually reabsorbed. However, uric acid within the joint is reabsorbed at a much slower rate, resulting in a transient elevation of local uric acid concentration. As the concentration of uric acid rises within the joint, crystals begin to form resulting in an acute gouty attack.

Another important factor in the development of an acute gout attack relates to the temperature of the joint. The solubility of uric acid is 6.8 mg/dl at normal core body temperature, (37 degrees centigrade). However, at the level of the metatarsophalangeal joint, the temperature is typically much lower, less than 30 degrees centigrade. At that temperature, the saturation level drops to 4.8 mg/dl. This explains why approximately 30% of men have an acute attack of gout with a normal uric acid level. Proteoglycans and chondroitin sulfate in the joint provide a more soluble matrix for the uric acid. However, osteoarthritis is known to disrupt the proteoglycans and chondroitin sulfate in the joint fluid, making an acute attack more likely.

The diagnosis of gout is usually made based on the clinical presentation, history, and response to nonsteroidal anti-inflammatory therapy. Joint aspiration provides definitive diagnosis when urate crystals can be identified (Fig. 2). However, joint aspiration is difficult in the small joints of the foot. Also, it is important to remember that extra-articular involvement of the foot is often the presenting scenario. In these cases treatment is usually rendered without identification of local urate crystals. Serum uric acid levels may be drawn to aid in the diagnosis, however, normal levels of sodium urate in the blood does not rule out an acute attack in male patients. Post-menopausal women are less likely to suffer an acute gouty attack when a normal uric acid level is identified, and menstruating females almost never suffer from gout for reasons that are not clearly understood.

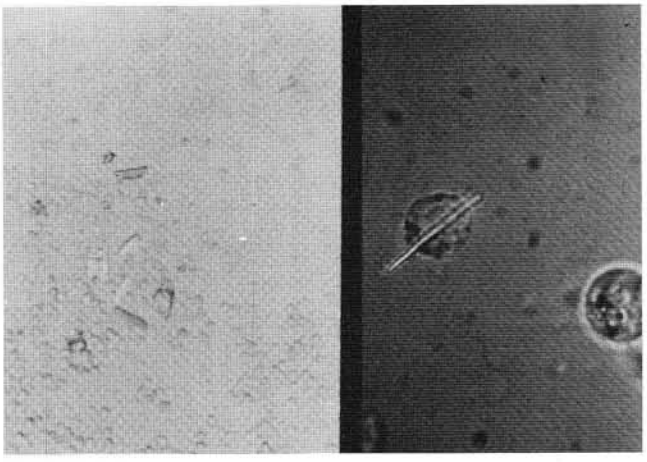

Figure 2. Negatively birefringent crystals viewed through polarized light microscopy provide definitive diagnosis of acute gouty arthritis. It is important to remember to culture all synovial fluid samples, however, since infection may also be present.

A gout attack may be precipitated by a variety of causative factors. One of the most common settings is during the postoperative period. Patients with elevated serum uric acid who become dehydrated will often suffer an acute attack. In some cases, trauma to a joint that has had chronic deposition of sodium urate will result in an acute attack, due to shearing of crystals into the joint fluid. Finally, ingestion of foods high in purines that are metabolized into uric acid, before excretion by the kidney, may raise the concentration beyond saturation resulting in crystal formation and an acute attack of gout. Foods high in purines include organ meats such as liver, kidney, and sweet breads. High protein diets, combined with the consumption of alcohol, have been associated with gout. Alcohol is metabolized into lactic acid, which blocks the excretion of uric acid by the kidneys.

TREATMENT OF ACUTE GOUT

Patients suffering from their first acute attack of gout are usually very distressed and anxious about their condition. The severity of pain is intense, and often their attack occurs during the night when medical attention is difficult to obtain. In most cases, the treatment of choice consists of nonsteroidal anti-inflammatories and rest. Abstinence from alcohol is an important adjunct to pharmaco-therapy.

Colchicine

Colchicine has been used for the treatment of gout since the sixth century A.D., and remains part of the armamentarium in both the treatment and diagnosis of gout. Unfortunately, this drug has many untoward effects that limit its use as first line therapy. At its inception, colchicine was thought to "purge the devil" of the gout since its use caused severe nausea, vomiting, and diarrhea. Today, it is thought that colchicine inhibits the migration and activity of the polymorphonuclear leukocytes which ingest the gout crystals.

Contemporary gout therapy usually reserves the use of colchicine for patients allergic to nonsteroidal anti-inflammatories, or in small doses as a prophylactic measure. Colchicine may be dosed orally or intravenously. For the acute attack of gout, a typical dosing regime for oral colchicine is one 0.6 mg tablet, every hour, until pain relief occurs or until side effects (nausea, vomiting, diarrhea)

appear. The dose should be limited to no more than 12 tablets in a 24 hour period, and must be adjusted to a lower dose in patients with renal insufficiency.

Intravenous colchicine usually produces fewer side effects and has a more rapid onset of action. Two milligrams of colchicine are diluted in at least 20 ml of normal sterile saline and infused slowly over 5 minutes. The same dosing method may be used as a preoperative prophylactic measure in patients with a tendency for acute attacks. **It is important not to give more than 4 mg of colchicine in one 24 hour period, and its use should be avoided in patients that have been on prophylactic colchicine, since bone marrow suppression can be induced.**

Colchicine has been used diagnostically for gout, since few conditions respond so rapidly and effectively to this medication. However, some cases of gout may be recalcitrant to colchicine therapy, and the other crystalline-induced arthropathies also may respond somewhat to its use.

Nonsteroidal Anti-Inflammatories

Nonsteroidal anti-inflammatories (NSAIDs) remain the mainstay of acute gout therapy today. Although any NSAID except aspirin may be used, indomethacin is felt by many to be the drug of choice due to its high potency. Aspirin in low doses interferes with the excretion of uric acid and can exacerbate or even precipitate a gouty attack. Regardless of the NSAID chosen, the maximum dose should be used as early as possible in the course of the condition. Delay in therapy will usually result in a much slower resolution in the attack, therefore requiring prolonged use of the NSAID.

Intra-articular steroids are helpful in patients with articular involvement and intolerance to nonsteroidal anti-inflammatories. Often, joint aspiration can be followed with 10 mg of triamcinolone acetate mixed with 1/2 cc of Marcaine in patients that have had a prolonged delay in therapy, and are not responding to other forms of treatment.

TREATMENT OF HYPERURICEMIA IN SYMPTOMATIC PATIENTS

Patients suffering from frequent attacks of gout or other consequences of hyperuricemia may require drug therapy to lower serum uric acid levels. It is important, however, that no attempt be made to change the uric acid concentration of the blood until the acute phase of the gouty arthritis has resolved. Fluctuations in serum urate concentration caused by the institution of uricosuric agents or allopurinol can prolong the gout attack or even cause relapse in patients recently cured. In most cases, it is best to delay anti-hyperuricemia therapy for two weeks after the resolution of acute symptoms.

Currently, there are two methods of lowering the serum level of sodium urate. The first method increases the elimination of uric acid through the kidneys with uricosuric agents. The second method involves the use of allopurinol, which competitively inhibits xanthine oxidase, the enzyme responsible for conversion of xanthine to uric acid. Both methods are effective and may be used alone or in combination depending on the clinical situation. The decision to institute therapy for hyperuricemia is usually based on the frequency of acute arthritic attacks or the development of other diseases associated with elevated serum uric acid levels.

Probenecid is a uricosuric agent that has been shown to effectively reduce serum urate levels. Its method of action is the blockage of resorption of uric acid. The increased excretion of uric acid by the kidneys must be gradually induced to prevent urolithiasis or precipitation of an acute attack of gout. Side effects of this drug include skin reactions and gastritis.

Sulfinpyrazone is a derivative of phenylbutazone that has a similar method of action as probenecid. It should be noted that the concomitant use of even small doses of aspirin with either uricosuric agent negates their effectiveness.

Allopurinol decreases the production of uric acid rather than increasing its excretion. This compound is similar in structure to hypoxanthine, a intermediate product in the metabolism of purines to uric acid. Allopurinol has been shown to effectively lower serum urate levels. As with the uricosuric agents, a gradual institution of allopurinol to therapeutic levels is used to prevent precipitation of acute gout. Allopurinol is generally used when uricosuric agents have failed to prevent hyperuricemia, or in cases of intolerance to uricosurics. In patients with significant tophaceous gout, combination therapy with both allopurinol and a uricosuric agent has proven effective.