Is It Gout? Tap the Joint!

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Gout is an inflammatory arthritis caused by the deposition of monosodium urate crystals in a joint. In the acute phase it is characterized by a monoarticular arthritis that remits after one to two weeks and recurs periodically. Joints of the lower extremity are most commonly affected. The periods between flares of the disease may shorten over time and attacks may become polyarticular. Chronic tophaceous joints develop after many years of recurrent attacks and are characterized by deposits of urate in the skin or bursa, referred to as tophi. Common sites for tophi include the pinna of the ear, the olecranon bursa and adjacent to the small joints of the fingers.

Risk Factors

The risk of developing gout is increased by obesity, renal insufficiency, hypertension, alcohol ingestion, lead ingestion (moonshine), and inherited enzyme deficiencies as outlined in Table 1. Medications may precipitate gout by interfering with renal excretion of uric acid. Common culprits are diuretics, cyclosporin, low dose salicylates, ethambutol, niacin, pyrazinamide and cytotoxic drugs.

Diagnosis

Gout usually presents in a 40-year-old male as an acute monoarthritis which affects the first metacarpal joint in approximately 60 percent of patients. It can also affect the knee and ankle. Men are more commonly affected than premenopausal women. Postmenopausal women are affected as commonly as men. The joint appears red, swollen, warm and is very tender. Although the patient may be febrile, he feels well otherwise. Even without treatment, the symptoms resolve in one to two weeks.[1]

The diagnosis of gout is based on identification of monosodium urate crystal in the synovial fluid or tophaceous deposits. Hyperuricemia does not make the diagnosis as uric acid levels can be elevated in many other conditions and is nonspecific. Many patients with hyperuricemia are asymptomatic and will never develop gout and therefore should not be treated.[2] Conversely, although patients with gout typically have elevated uric acid levels, hyperuricemia is not required to make the diagnosis.[3]

The differential diagnosis of acute monoarthritis includes gout, infection, and pseudogout as well as early manifestations of various forms of polyarthritis. Osteoarthritis usually causes a chronic rather than acute arthritis. Although gout commonly affects the first MTP joint, the coexistence of hyperuricemia with pain in the first MTP does not establish a diagnosis of gout. Frequently patients with gout with first MTP joint pain and elevated uric acid levels are diagnosed with gout and treated with allopurinol resulting in its overuse.[4] An acute monoarthritis should be aspirated and the fluid sent for cell count, crystals, gram stain and culture.[5] Frequently, acute monoarthritis is assumed to be infection without first examining the fluid for crystal and a cell count.

A septic joint is most important to consider in a patient who appears ill or has risk factors such as

Table 1. Causes of hyperuricemia

Inherited enzyme defects:	
	Glucose-6-phosphatase deficiency
	Hypoxanthine-guanine phosphoribosyltransferase deficiency
	Phosphoribosylpyrophosphate synthetase overactivity
Myeloproliferative or lymphoproliferative diseases	
Hypertension	
Diabetic ketoacidosis	
Lactic acidosis	
Intrinsic renal disease	
Other Malignancies	
Alcohol use (including lead-contaminated moonshine)	
Obesity	
Drugs:	Diuretics
	Low-dose salicylates
	Pyrazinamide
	Levodopa
	Cytotoxic drugs
	Cyclosporine

diabetes, previous joint disease or immunosuppression. Both infection and crystal arthropathy can produce an elevated white blood cell count or sedimentation rate so these laboratory tests are not helpful for differentiation. Rarely, infection and gout can co-exist in the same joint.[6]

Osteoarthritis can involve joints in a similar distribution as gout such as the first MTP joint or the knees. Joints affected by osteoarthritis are generally less swollen than those affected by gout and are not erythematous or warm.

Pseudogout is less likely to involve the first MTP joint, but may affect the ankles and knees. Affected joints may be warm, erythematous and swollen, similar to gout. Differentiation is based on examination of the synovial fluid.

The diagnosis of gout is established by observing the characteristic crystals in synovial fluid or tophaceous deposits. Aspiration of a tophus can be performed similarly to aspiration of synovial fluid. Using a 22-25 gauge needle, one can obtain deposits in the hub of the needle by quickly pulling back on the syringe and then expelling the contents onto a slide. This can be examined under a microscope just as one would examine synovial fluid.

The synovial fluid can be examined by placing a drop of the fluid on a slide and looking for the crystals under both regular light microscopy and polarizing microscopy. Under regular microscopy, one sees intracellular or extracellular needle-shaped crystals. Under a polarizing microscope, the crystals are strongly negatively birefringent which means they appear yellow when the crystals are parallel to the axis of the compensator on the microscope.

Infection and gout can coexist. Therefore, in certain clinical situations fluid may also need to be sent for gram stain and culture even if MSU crystals are identified. Recurrent gouty attacks lead to radiographic damage that appears as marginal erosions with sclerotic borders of the affected joints. Bony resorption under enlarging tophaceous deposits results in an overhanging bone margin. Unlike in rheumatoid arthritis, periarticular osteopenia is not seen with gout.

Acute Treatment

Goals of therapy include halting the acute attack, eliminating risk factors and preventing further attacks. Treatment started immediately can terminate an acute flare. NSAIDs, glucocorticoids (oral, intramuscular, or intraarticular), adrenocorticotropic hormone (ACTH), and colchicine have all been used successfully (Table 2).

Table 2. Drug Therapies for Gout

1. Acute Gouty Arthritis
   - NSAIDs
   - Glucocorticoids (oral, intramuscular, intraarticular)
   - Colchicine (oral)

2. Control of Hyperuricemia
   - Allopurinol
   - Probenecid
   - Sulfinpyrazone

Although a variety of NSAID options are available, indomethacin has been the anti-inflammatory of choice for acute gout (100-200 mg/day).[7] Likely, the newer selective COX-2 inhibitors will work well also. However, NSAIDs must be avoided in patients with chronic renal insufficiency, anticoagulation, congestive heart failure or gastric ulcers.

Glucocorticoids are useful in patients with chronic renal insufficiency or who, for the reasons mentioned, cannot tolerate NSAIDs or colchicine.[8] For patients with monoarticular involvement, an intraarticular injection of a microcrystalline glucocorticoid preparation, such as methylprednisolone or triamcinolone, will control symptoms within 1-2 days. This should be given only once infection is excluded and the diagnosis of gout is confirmed.

Patients with polyarticular gout will benefit from intramuscular injection of Glucocorticoids,[9] although oral glucocorticoids may also be used. Prednisone is begun at a dose of 20-40 mg/day and tapered off over 7-10 days (10). Although ACTH injections are another treatment option for acute gout, repeat injections may be required more often than when triamcinolone is used.[11]

Given no history of renal or liver disease, colchicine may be used both acutely and for prophylactic therapy. For acute gout, 0.6 mg is given every 2 hours orally until the patient either improves or develops side effects, the most common of which is diarrhea.[12,13]

No more than a maximum dose of 3-5 mg (6-8 tablets) is recommended due to its potential toxicity. A dose of 0.6 mg up to three times daily may be continued for the duration of the flare. Intravenous colchicine is not recommended due to its potential toxicity and the many available alternative treatments.[14]

Long-term Management

After treating the acute flare, risk factors for further gout flares should be addressed. Weight control, reduction in alcohol intake and other lifestyle medications should be advised. Adjustment of medications (such as discontinuing diuretics) is important as this may control hyperuricemia and prevent subsequent attacks without the use of additional medications.[15]

Although colchicine will not alter hyperuricemia or prevent tophi formation, it can be used to prevent future attacks. A dose of 0.6 mg is given up to three times daily with the dose adjusted for renal insufficiency. Its effect may diminish over time and therefore, addition of a drug to lower the uric acid level is usually required.

Urate-lowering therapy is indicated for patients with tophi, chronic arthritis or frequent attacks numbering more than two yearly. Additionally, patients with gout and renal stones or those who are identified as overexcretors will need urate-lowering therapy. Although this

therapy should not be started during an acute attack, once on therapy, it should not be stopped during flares. A 24-hour urine collection for uric acid will identify patients as either an underexcretors or an overproducer of uric acid. In general, overproducers will benefit from allopurinol while underexcretors may benefit form probenecid given normal renal function and no history of renal calculi.

Uricosuric agents include probenecid and sulfinpyrazone, which inhibit reabsorption of uric acid. Therefore, they should be avoided in patients with overproduction of uric acid or in patients with urate nephropathy, nephrolithiasis or renal insufficiency. Probenecid should be started at a dose of 0.5-1.0 g/day and increased gradually to 1.5-2 g/day to prevent formation of urate deposits.[1]

Allopurinol is an inhibitor of xanthine oxidase and therefore prevents conversion of xanthine to uric acid. The usual dose of 300 mg/day should be adjusted for renal insufficiency (Table 3). Patients with decreased renal function should begin taking allopurinol at a dose of 50-100 mg/day and then gradually increase the dose over a few months if it is tolerated well without fever, dermatitis or eosinophilia. The goal of urate lowering therapy is a serum uric acid level of 6 mg/dl or less.[3] Once achieved, such therapy should be continued indefinitely. Care must be taken to avoid drug interactions of allopurinol in combination with ampicillin, cyclophosphamide, azathioprine, warfarin or theophylline.

Course of Disease

The natural course of gout is variable, although the prognosis is worse in patients who are young at onset and in patients with severe renal disease.[16] Acute attacks can be treated and the frequency of attacks can be reduced by medication and lifestyle modification. In untreated gout, the average time from the initial attack to the development of tophi is 11 years. Tophi are more common in patients with a serum urate level greater than 9 mg/dl. Occasionally, tophaceous deposits may appear prior to acute gouty arthritis. Treatment of gout to maintain a normal serum urate level can prevent progression of renal disease and will prevent development of tophaceous deposits. Causes of death are similar to those in the general population.

Table 3. Allopurinol dose adjustment

Normal renal function	300 mg/day
GFR = 60 ml/min	200 mg/day
GFR = 30 ml/min	50-100 mg/day

Conclusion

Gout is an inflammatory arthritis characterized by acute attacks that, over time, can become a chronic arthritis. Untreated, progressive joint destruction occurs and tophaceous deposits develop. Gout must be diagnosed by arthrocentesis before initiating one of the many treatments that exist. Continuing drug therapy and lifestyle modifications can significantly improve patient outcome.

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