Gout: The rich man's plague

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Objectives: Describe the pathophysiology, presentations, diagnoses, and treatments of crystal arthritides, as well as the methods of arthroscopy. Briefly mention Pseudogout.

Introduction

The term gout refers to a spectrum of manifestations that can occur singly or in combination: acute inflammatory arthritis, tenosynovitis, chronic tophaceous arthritis (tophi), extraarticular tophi, urate nephrosis, acute uric acid nephropathy, and uric acid nephrolithiasis. **Hyperuricemia is the hallmark of gout.** Plasma and extracellular fluids that become supersaturated with uric acid may crystallize and result in clinical gout.
Overall, the incidence of gout has been increasing in the US; its prevalence is likely ~3% total of all adults.

The differential diagnosis for acute gouty arthritis includes septic arthritis, reactive arthritis, calcium pyrophosphate deposition disease (pseudogout), and rheumatoid arthritis.

Hyperuricemia is necessary for gout to occur, but alone is not enough. In fact, most patients with hyperuricemia do not have gout. Hyperuricemia may arise in a variety of settings that cause overproduction (e.g. cancer, genetic condition) or underexcretion (e.g. kidney disease, certain medications) or a combination of the two.

Lymphoma/leukemia or other rapidly producing neoplasm	Chronic kidney disease
Thiazide or loop diuretics	Alcohol consumption
Fatty food intake	Existing osteoarthritis
Calcineurin inhibitors	Relative dehydration

Table 1: Classic risk factors for gout.

Lifestyle features that greatly increase the risk of gout include: alcohol consumption, obesity, high purine foods (mussels, shrimp, organ meats), salty fish (sardines, herrings), sausage, red meats.

Interestingly, there has been a rise in "non-classic" gout patients, or rather, those who do not fit the classic story for acute gout. These patients are older, more female, possibly a history of an organ transplant receiving diuretics and calcineurin inhibitor (cyclosporine and tacrolimus impair urate excretion).

Presentation of acute gout flare

Acute gouty flares are exquisitely painful, with redness, warmth, and swelling of the affected joint. Maximum severity is reached in <24 hours. Attacks generally subside spontaneously in a few days.
80% of cases involve a *single* joint in the *lower extremity*. Gout flares are *twice* as likely to begin after sleeping. This is because episodes classically occur at night when the patient is supine. They wake to discover a tender, swollen joint in the most dependent area of the body. Why at night? The temperature drop reduces solubility and promotes crystallization. Therefore, one can expect to find gout flares in the ankle or first metatarsophalangeal joint (known as podagra). **The great toe is the first site of attack in half of cases.**

A mess of dietary, physical risks, as well as commodities and medications can predispose to cause a gout flare (Table 1).

In <20% of patients, multiple joints can be affected at once. This polyarticular pattern typically occurs in later flares.

Patients with recurrent gout flares may have solid tissue deposits of urate (tophi) which cause longstanding articular injury. Tophi are not painful nor tender. Tophi gradually increase in size, causing worsening soft tissue and joint injury. In the fingers, it looks like dactylitis.

Also, long term, chronic hyperuricemia causes nephrolithiasis and nephropathy, as urate itself is nephrotoxic.

Diagnosis

The only definitive method of diagnosing gouty arthritis is joint aspiration and demonstration of the characteristic crystals by polarizing microscopy. Who should undergo arthrocentesis? Anyone with suspected gout flare in whom the diagnosis has not been formally made, or those where the cause is uncertain and you need to rule out more serious causes (e.g. septic arthritis).

Cell count, gram stain, culture, and crystal analysis should be performed.

Urate crystals are *needle-shaped and negatively birefringent* under polarized light microscopy. This means that if shown a picture of the crystals, when they are lying flat they should be yellow (yel**low** when laying **low**), and if vertical they should be blue.

The sensitivity of polarized light is 85% with a specificity of 100%.

Labs cannot diagnosis gout. ESR, CRP, and WBC count are worthless for gout, but if you are concerned for septic arthritis that is a different discussion. You could argue what is the point of getting the markers if you are planning to do an arthrocentesis anyway… we would agree with that assessment.
Even worse, we still hear of a lot of people ordering uric acid levels. Please don't. Those levels don't correspond to gout flares and they do not change management. Normal serum uric acid levels do *not* rule out gout.

WBC count can range from above 10,000, but gout should *never* cause a WBC count above 100,000. If you see that, think concomitant septic arthritis. Gout may coexist with other inflammatory arthritic conditions.

X-rays don't help diagnose gout. Subcortical bone cysts and erosions might be seen, suggestive of chronic arthropathy.

What if the crystal microscopy is negative? If concern for gout is still high, we recommend close follow up with a PCP and/or rheumatologist. Missing a gout flare isn't the end of the world, missing something more serious is!

Pseudogout: Calcium pyrophosphate deposition (CPPD) disease is diagnosed when *calcium pyrophosphate* crystals are demonstrated in synovial fluid analysis. Pseudogout crystals are *rhomboid or cuboid shaped* and are weakly *positive* on polarized light microscopy. The KNEE is the most commonly affected joint in pseudogout, followed by the wrist and ankle. Calcium deposits may be seen in the articular cartilage (chondrocalcinosis), but this is not always associated with symptoms. Dietary modifications cannot prevent pseudogout flares. Treatment includes glucocorticoids or NSAIDs.

Treatment
Chronic long term therapy to prevent gout flares and reduce chronic arthropathy include allopurinol, febuxostat, and probenecid. There are a few others that are much less common.
These therapies do NOT help during gout flares, but contrary to current dogma, they are not harmful and should NOT be discontinued.

Acetaminophen and opioids do not help reduce gout inflammation. They can be used as an adjunctive but are not solutions.

Of the three major therapies (NSAIDs, glucocorticoids, and colchicine), there is no single best agent.
The best method is to review the patient's comorbidities to each medication, their preference (if this is not their first flare), and how adequate is their rheumatology follow up.

For example, if any renal disease is present, you must avoid NSAIDs. Other conditions in which we avoid NSAIDs: known coronary artery disease, peptic ulcer disease, certain anticoagulation medications, or poorly controlled diabetes mellitus.

Details of dosing
NSAIDs: naproxen, indomethacin, ibuprofen for 5-7 days
-perfect for those <60 years old who lack renal, cardiovascular, or ulcer disease.

Glucocorticoids: 30-40 mg prednisone initial dose with a 7-10 day taper.
-avoid if septic arthritis is a concern!
-great for those where NSAIDs are contraindicated or pregnant patients
-caution in those with brittle diabetes, recurrent steroid usage

Colchicine: 0.6 mg pill formulation. Patient cannot exceed 1.8 mg in 24 hours.
-should really only be used if the above two options are unavailable.
-convenient for patients who have been on it before or taking it for flare prophylaxis
-significant side effects if taken incorrectly, low dose therapy only.
-*must* be started within 36 hours or else benefit of therapy is minimal.
-contraindicated in those with severe renal or hepatic impairment, or those on significant cytochrome P450 inhibitors.
-diarrhea and abdominal cramping are the most common side effect. They are less likely at lower doses.
-more serious adverse effects are typically seen at high doses and include neutropenia, bone marrow suppression, and peripheral neuropathy.

In those with established chronic gout limited to one or two joints, we can refer these patients for outpatient intra-articular steroid injection.

References: for a complete list of references, please visit our website under this topic heading.