Crystal-induced arthritis

A variety of crystals can deposit in and around joints and cause an acute inflammatory arthritis, as well as a more chronic arthritis associated with progressive joint damage.

Crystal-associated arthritis and deposition in connective tissue:

Monosodium urate monohydrate: Acute gout, Chronic tophaceous gout

, Chronic (pyrophosphate) 'Calcium pyrophosphate dehydrate: Acute 'pseudogout arthropathy, Chondrocalcinosis (asymptomatic)

Basic calcium phosphates: Calcific periarthritis, Calcinosis

Gout:

Gout is the most common inflammatory arthritis in men and in older women. It is caused by deposition of monosodium urate monohydrate crystals in and around synovial joint.

The risk of developing gout increases with age and with serum uric acid (SUA) levels

Although hyperuricaemia is strong risk factor for gout, only a minority of hyperuricaemic individuals actually develop gout.

Pathophysiology

About one-third of the body uric acid pool is derived from dietary sources and two-thirds from endogenous purine metabolism.

Purine nucleotid synthesis and degradation are regulated by a network of enzyme pathways, but xanthine oxidase plays a pivotal role in catalyzing the conversion of hypoxanthine to xanthine and xanthine to uric acid

Causes of hyperuricaemia and gout

1- **Diminished renal excretion (90%):**

Increased renal tubular reabsorption

Drugs: Thiazide and loop diuretics

Low-dose aspirin

Ciclosporin

Pyrazinamide

2-Increased intake: red meat

Alcohol intake

3-Increased production

Myeloproliferative and lymphoproliferative disease

Psoriasis

High fructose intake

4-Inherited disorders

Lesch–Nyhan syndrome

Clinical features

The classical presentation is with an acute monoarthritis, which affects the first MTP joint in over 50% of cases.

The initial attack is oligoarticular or polyarticular in 10% to 14.5% of cases.

The axial skeleton and large proximal joints are rarely involved.

Typical features include:

Rapid onset, reaching maximum severity in 2–6 hours, and often waking the patient in the early morning.

Severe pain, often described as the ‘worst pain ever.

Extreme tenderness.

Marked swelling with overlying red, shiny skin self-limiting over 5–14 days, with complete resolution.

As the attack subsides, pruritus and desquamation of overlying skin are common. The main differential diagnosis is septic arthritis, infective cellulitis.

Some people never have a second episode and in others several years may elapse before the next one, some patients may have chronic pain and functional impairment and progress to chronic topheceous gout.

Crystals may be deposited in the joints and soft tissue to produced irregular firm nodules called tophi. These have a predilection for extensor surfaces of fingers, elbow, Achilles tendon and helix of ears

Tophi have a white colour, differentiating them from rheumatoid nodules. Tophi can ulcerate, discharging white gritty material, become infected. Occasionally, tophi may develop in the absence of previous acute attack.

In addition to causing musculoskeletal disease, chronic hyperuricaemia may be complicated by renal stone formation (Uric acid stones can occur in patients with no history of gouty arthritis) and, if severe, renal impairment due to the development of interstitial nephritis as a result of urate deposition in the kidney (does not occur in absence of gout arthropathy).

Investigations

The diagnosis of gout can be confirmed by the identification of urate crystals in the aspirate from a joint, bursa or tophus.

Between attacks, aspiration of an asymptomatic first MTP joint or knee may still reveal crystals.

A biochemical screen, including renal function, uric acid, glucose and lipid profile, should be performed because of the association with metabolic syndrome. Hyperuricaemia is usually present in gout but levels may be normal during an attack because serum urate falls during inflammation. Acute gout is characterized by an elevated ESR and CRP and with a neutrophilia.

X-rays are usually normal in acute gout but well-demarcated erosions may be seen in patients with chronic or tophaceous gout

Management

Management should focus on first dealing with the acute attack and then giving prophylaxis to lower SUA and prevent further attacks

Acute gout

Oral colchicine given in doses starting with 1.2 mg, followed by 0.6 mg 1 hour later, and then 0.6mg every 12 hours daily is the treatment of first choice in acute gout, Oral NSAIDs are also effective, Oral prednisolone (15–20 mg daily) or intramuscular methylprednisolone (80–120 mg daily) for 2–3 days are highly effective and are a

good choice in elderly patients where there is an increased risk of toxicity with colchicine and NSAID.

Joint aspiration can give pain relief, particularly if a large joint is affected, and may be combined with an intra-articular glucocorticoid injection.

Chronic prophylaxis: indicated in

Individuals who have more than one acute attack within 12 months and

Those with complications such as tophi or erosions

Nephrolithiasis

Renal impairment

The long-term therapeutic aim is to prevent attacks occurring by bringing uric acid levels below the level at which monosodium urate monohydrate crystals form. A therapeutic, target of 360 μ mol/L (6 mg/dL).

Allopurinol is the drug of first choice. It inhibits xanthine oxidase, which reduces the conversion of hypoxanthine and xanthine to uric acid. Acute flares of gout often follow initiation of urate-lowering therapy. The patient should be warned about this and told to continue therapy, even if an attack occurs. The risk of flares can be reduced by prophylaxis with oral colchicine (0.5 mg twice daily) or an NSAID for the first few months.

Febuxostat also inhibits xanthine oxidase. It is typically used in patients with an inadequate response to allopurinol, and when allopurinol is contraindicated or causes adverse effects. Febuxostat undergoes hepatic metabolism and no dose adjustment is required for renal impairment

Uricosuric drugs, such as probenecid, sulfinpyrazone and Lesinurad, inhibited renal tubular reabsorption. These drugs used only if 24hr urinary UA <800mg.

Pegloticase is a biological treatment in which the enzyme uricase, It is indicated for the treatment of tophaceous gout resistant to standard therapy and is administered as an intravenous infusion every 2 weeks for up to 6 months.

Lifestyle measures are equally important as drug therapy in the treatment of gout. Patients should be advised to lose weight where appropriate and to reduce excessive alcohol intake, especially beer. Several antihypertensive drugs, including thiazides, β -

blockers and ACE inhibitors, increase uric acid levels, whereas losartan has a uricosuric effect and should be substituted for other drugs if possible.

Calcium pyrophosphate dihydrate crystal deposition disease

This condition is associated with deposition of calcium pyrophosphate dihydrate (CPPD) crystals within articular and hyaline cartilage.

The knee (hyaline cartilage and menisci) is by far the most common site, followed by the wrist and pelvis (symphysis pubis).

In many patients, chondrocalcinosis is asymptomatic and an incidental finding on X-ray.

A proportion of patients present with an acute inflammatory arthritis (pseudogout)

Chronic inflammatory arthropathy superimposed on a background of OA.

Common causes

· Age

· Osteoarthritis

Rare

· Familial factors

· Haemochromatosis

· Hypophosphatasia

· Hypomagnesaemia

· Wilson’ s disease

· Primary hyperparathyroidism

Clinical features

The typical presentation is with a swollen tender joint that is warm and erythematous with a large effusion. Fever is common and the patient may appear confused and ill.

The knee is most commonly affected, followed by the wrist, shoulder, ankle and elbow. Trigger factors include trauma, intercurrent illness, dehydration and surgery

The presentation is with chronic pain, early morning stiffness, inactivity gelling and functional impairment.

Wrist involvement may result in carpal tunnel syndrome and second and third MCP joints can be affected give picture similar to OA

Investigations

The pivotal investigation is joint aspiration, followed by examination of synovial fluid using compensated polarised microscopy.

X-rays of the affected joint may show evidence of calcification in hyaline cartilage and/or fibrocartilage, although absence of calcification does not exclude the diagnosis. Signs of OA are frequently present.

Screening for secondary causes should be undertaken, especially in patients who present under the age of 25 and those with polyarticular disease.

Management

Joint aspiration can sometimes provide symptomatic relief in pseudogout and in a few patients no further treatment is required.

People with persistent symptoms can be treated with intra-articular glucocorticoids, colchicine or an NSAID.

Read more in:

Davidson’s Principles and Practice of Medicine, 23rd edition

Kelley & Firestein’s Textbook of Rheumatology, 10th edition