

LESSON OF THE MONTH

Crystal unclear

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Case 1

A 66 year old woman noticed a firm nodule on the volar aspect of the proximal phalanx of the left index finger. She had first noticed it 12 months previously and had watched it progressively increase in size to a diameter of five millimetres. On clinical grounds, it was thought to be a dermoid cyst. She had a history of an undifferentiated connective tissue disease with recurrent Raynaud's phenomenon, swollen fingers, a positive antinuclear antibody titre of 1:40 with an homogeneous pattern. Antibodies to extractable nuclear antigens and double stranded DNA were unable to be detected. Her other medical problems included lumbar spondylosis and osteoarthritis of the knees. Plain radiographs revealed chondrocalcinosis in the left wrist triangular fibrocartilage (see fig 1) but no calcification was noted in the nodule. Serum calcium and iron studies were normal.

As the lesion was causing some inconvenience, it was excised. At operation, a well encapsulated calcific nodule situated intradermally and extending to, but not involving the flexor tendon sheath, was excised.

On examination under polarised light, the nodule consisted of weakly positively birefringent crystals with the typical morphological characteristics of calcium pyrophosphate (CPPD). The crystals were extensively depos-

ited in fibrous tissue with only a small inflammatory infiltrate.

COMMENT

Tophaceous (tumoral) CPPD deposition is considered a relative rarity compared with its gouty equivalent. CPPD deposition is more usually visualised radiologically in the menisci, articular cartilage, ligamentum flava and intervertebral discs. Approximately 30 cases of tophaceous CPPD deposition have been reported in the literature. These deposits usually occur in elderly people. Many of these deposits occur in the vicinity of synovial tissue and develop in areas of cartilage metaplasia of the synovium. However, others may arise in subcutaneous fat. Pritzker *et al* was the first to describe a CPPD tophus.¹ The case described by him was noteworthy for arising from the left temporomandibular joint. This was followed by more reports of tophaceous CPPD deposition in a widening array of sites, including the great toe²⁻³ and the craniocervical junction.⁴⁻⁵ The seriousness of deposits at the craniocervical junction requires no further emphasis and often requires neurosurgical intervention.

More peripheral examples of soft tissue involvement have affected the digits of the hand in four other cases.⁶⁻⁹ This case report documents a fifth patient where the lesion was situated intradermally over the proximal phalanx of the finger with little surrounding inflammation. This is in contradistinction to previous reports where the clinical and radiographic appearances of the highly cellular inflammatory response to the crystal deposition were on occasions initially confused with malignancy resulting in extensive resection.² In none of the described cases⁶⁻⁹ was there evidence to suggest involvement of any other joints with CPPD. However, our case was noted to have chondrocalcinosis on previous radiographic examination of her wrist.

The precise mechanisms resulting in CPPD deposition are unclear, but tissue damage is generally considered to initiate the process. In this case, the associated connective tissue disease and Raynaud's phenomenon may have contributed to the soft tissue localisation. The patient could recall no initiating local trauma at the site of the nodule. Microcrystal deposition disease has been reported in a patient with systemic lupus erythematosus including pyrophosphate crystal deposition in articular and peri-articular locations.¹⁰ Unlike gout, which is associated with

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Figure 1 Radiograph of the left wrist showing chondrocalcinosis of the triangular fibrocartilage.



Figure 2 Lobulated soft tissue mass anterior to the left ankle.

a systemic abnormality of excess anions, CPPD seems to be driven by a local abnormality of excess anions. Leakage of nucleotide triphosphate from damaged tissue, bursts of increased pyrophosphate generation by selected chondrocytes or local synthesis of particulates stimulating CPPD crystal nucleation are all factors that may contribute to CPPD tophus formation.¹¹ A lack of crystal inhibitors, such as magnesium and chondroitin sulphate, may also contribute to CPPD deposition.

Two important points are exhibited by this case. Firstly, although tophaceous CPPD deposition is less common than tophaceous gouty deposition, it needs to be considered in the differential diagnosis. The diagnostic test is examination of the tissue under polarised light and the identification of rhomboid shaped weakly positively birefringent crystals. As the clinical and radiographic appearance of the lesion may mimic a malignancy, the diagnosis needs to be considered before biopsy is performed so that the appropriate diagnostic test may be ordered. A tophus should not necessarily be assumed to be attributable to urate deposition. Secondly, the only specific treatment for such lesions causing compression of

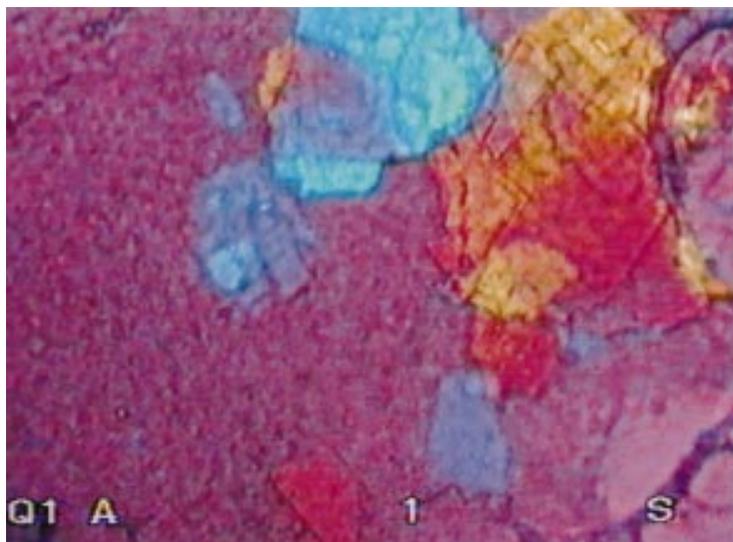


Figure 3 Cholesterol crystals viewed under polarised light.

adjacent structures is surgical resection. Even this is not necessarily curative as recurrence of the lesion may occur after surgery.¹²

Case 2

A 77 year old female Pacific Islander now resident in Australia for several years, with non-insulin dependent diabetes mellitus presented with a 20 year history of multiple non-tender large masses around both ankles, anterior to both knees and on both olecranons. These lesions were thought to be gouty tophi and she was referred to a rheumatologist for further treatment. There was no history of gouty arthritis or of significant alcohol intake. The patient's medications were allopurinol 100 mg daily and metformin 500 mg thrice daily. Her main concern was to have these multiple lesions surgically removed because they were gradually increasing in size.

On examination, she was obese and had multiple soft lesions over the above named areas (see fig 2), small Achilles tendon xanthomata, reduced pedal pulses and a left femoral bruit.

Biochemical investigation revealed a serum uric acid of 0.39 mmol/l (normal 0.25–0.42 mmol/l) and a serum creatinine of 0.08 mmol/l (normal 0.08–0.11 mmol/l). Total cholesterol was 6.4 mmol/l (target < 5.5 mmol/l) and her fasting triglyceride level was 3.23 mmol/l (target < 1.7 mmol/l). A random blood glucose was 7.5 mmol/l (normal 3.6–6.6 mmol/l).

Plain radiographs revealed osteoarthritis of the distal interphalangeal and proximal interphalangeal joints of the fingers and metacarpophalangeal joints of the thumbs. There were large lobulated, partially calcified soft tissue masses overlying the lateral malleoli of both ankles and anterior to the patella tendons. Chondrocalcinosis was seen in the right knee with evidence of marked patellofemoral and medial tibiofemoral osteoarthritis in both knees. Significantly, no erosive disease was seen. Percutaneous aspiration of one of the lesions revealed cholesterol crystals (see fig 3) indicating that the lesions were actually xanthomata.

Unfortunately, she has failed to keep her appointment with the orthopaedic surgeon to whom she had been referred for removal of some of the more troublesome lesions. She has consulted a clinical biochemist for management of her hyperlipidaemia and has been given gemfibrozil for this. This patient has subsequently been diagnosed as having type 3 dyslipidaemia or "dysbetalipoproteinaemia" and is homozygous for the apo E₂ allele.

COMMENT

Apo E is a ligand for receptors located on hepatocyte cellular membranes.¹³ These receptors mediate the uptake of lipoproteins containing apo E. Both animal and human studies have shown that subjects with the apo E₂ mutant have a markedly reduced ability to bind to hepatocyte receptors, thus resulting in reduced catabolism of apo E with accumulation in plasma and tissue deposition in the form of xanthomata. This patient's longstanding

diabetes has also contributed to her dyslipidaemia. The lipid lowering agent gemfibrozil is the agent of choice for treatment of this condition.¹⁴ However, because of the immense size of her cholesterol deposits surgical resection is the only realistic avenue for their removal.

Xanthomata often occur in dyslipidaemia types 2a and 3. This case is an example of a patient with type 3 dyslipidaemia in whom the presence of xanthomata was the presenting complaint. Approximately 10–25% of such patients will have tendon xanthomata. In type 2a dyslipidaemia or familial hypercholesterolaemia, tendon xanthomata are a prominent feature and are present in approximately half of heterozygotes by the third decade.¹⁵

While the prevalence of gout is significantly higher in Maoris and other Pacific Islanders compared with those of European extraction,¹⁶ in this case, the expected diagnosis of gout proved to be incorrect.

The lesson

- CPPD deposition and cholesterol deposits may mimic gouty tophi.
- You should attempt to determine the identity of the crystal involved by analysis of synovial fluid or tissue before making a diagnosis of a crystal arthritis.
- Needle aspiration is a simple procedure and usually provides an ample specimen for crystal identification

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