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# 'My knee is swollen'

**Case study – Sam**

'It's steadily getting worse. Over the past few days my knee has swelled up like a balloon. Now it hurts like hell and I have had to stop working'.

Sam, 59 years of age, is a builder who presents with a 3 day history of a swollen right knee (*Figure 1*). There was no preceding injury. He looks and feels well and is afebrile. He has no past history of knee or other joint swelling.

Sam is a nonsmoker, nondrinker and takes no medication. His past history includes five episodes of renal colic in the past 2 years, two of which led to hospital presentations for pain relief. He tripped and fell at a building site 6 months ago and sustained a Colles fracture of his right wrist.

Figure 1. Sam's knee

**Question 1**

What is the differential diagnosis of an acute or sub-acute monoarthritis?

**Question 2**

What is the most likely diagnosis of Sam's swollen knee?

**Question 3**

What is the most important initial investigation in someone with a new, undiagnosed joint effusion?

**Question 4**

What further investigations would be helpful?

**Question 5**

What are the potential management options for this condition?

**Answer 1**

The major differential diagnoses of an acute or sub-acute monoarthritis are:

- septic arthritis
- crystalline arthritis (gout or pseudogout), or
- trauma.

Less common causes include psoriatic and reactive arthritis. A septic arthritis must be excluded before considering any other diagnosis so antibiotic therapy (and joint wash out if necessary) can be commenced to minimise joint destruction and the likelihood of future osteoarthritis. Sometimes empirical antibiotic therapy should be started before a firm microbiological diagnosis is established.

**Answer 2**

Given the absence of systemic symptoms or signs, Sam is unlikely to have septic arthritis (although it must still be excluded). The distribution of arthritis is similar for both gout and pseudogout. Both can be precipitated by trauma, medical illness or surgery. However, gout classically affects the first metatarsophalangeal joint and the joints of the feet and hands, while pseudogout is more likely to affect the larger joints (knee, wrist or shoulder).

Sam is likely to have pseudogout. Given the combination of the monoarthritis, renal calculi and minimal trauma fracture, primary hyperparathyroidism would be a unifying diagnosis.

### Answer 3

The most important investigation for a new, undiagnosed joint effusion is joint aspiration. If you are confident, this can be performed in the surgery. Alternatively an ultrasound guided aspirate can be arranged with a radiologist. The joint fluid must be sent for both:

- microscopy, culture and sensitivity, and
- crystal identification.

A high cell count is highly suggestive of septic arthritis even if the gram stain is negative, as a gram stain has only 50% sensitivity.<sup>1</sup>

Polarised light microscopy can identify crystals in the synovial fluid and differentiate between the longer, negatively birefringent urate crystals and the shorter, stubby, positively birefringent crystals of calcium pyrophosphate (pseudogout).

Other forms of crystal arthropathy can be identified by high quality analysis of synovial fluid (eg. calcium oxalate).

Note: calcium pyrophosphate deposition is a prerequisite for pseudogout but may be associated with other forms of arthropathy more like osteoarthritis or remain asymptomatic.

### Answer 4

The underlying causes of pseudogout are listed in *Table 1*. Primary hyperparathyroidism can be confirmed by finding hypercalcaemia associated with a high or high normal level of parathyroid hormone. Hypocalciuric hypercalcaemia, which can be associated with the same

**Table 1. Causes of pseudogout**

- Familial – rare, severe, starts in childhood
- Metabolic – haemochromatosis
- Endocrine – hyperparathyroidism
- Degenerative – osteoarthritis, most common, usually age >60 years

**Figure 2. Linear calcification in the knee joint**



biochemical findings, is excluded by finding a normal or high normal fractional excretion of calcium (actual amount of calcium excreted divided by the amount filtered at the glomerulus). In Sam's case this is unlikely given his history of renal calculi.

An X-ray of Sam's knee might show calcification of the joint cartilage (chondrocalcinosis) (*Figure 2*). On its own this is not diagnostic, as the prevalence of chondrocalcinosis in the general population increases with age to 7–27% of elderly people.<sup>2–4</sup> A minimal trauma fracture in a man should trigger consideration of the three common causes of osteoporosis in men: alcohol, hypogonadism and glucocorticoids.

Bone mineral density testing and bone turnover markers (eg. beta crosslaps) will confirm osteopenia/osteoporosis and increased bone turnover, and provide a basis for future monitoring.

Interestingly, primary hyperparathyroidism disproportionately affects the bones of the wrist, perhaps the cause of Sam's Colles fracture. Changes in bone mineral density at this site are much higher than at other sites of the body.

If Sam had a family history suggestive of adenomas of the three endocrine 'Ps' (parathyroid, pituitary, pancreas) – eg. hypercalcaemia, hyperprolactinaemia, hypoglycaemia caused by hyperinsulinaemia – he might be the index case of a family with multiple endocrine neoplasia. Further investigation for other adenomas in Sam and for affected members of his family would then be indicated.

### Answer 5

Initial management of pseudogout is similar to that of gout. It aims to control the pain and inflammation with nonsteroidal anti-inflammatory medications and/or, in severe cases, prednisolone.<sup>5</sup> Intra-articular glucocorticoid can be used if these are ineffective.<sup>6</sup> If these are contraindicated, colchicine can be effective but may be associated with diarrhoea. Long term management is treatment of the underlying condition (*Table 1*).

### Case follow up

Primary hyperparathyroidism was confirmed. A single adenoma autonomously secreting parathyroid hormone is the cause in the vast majority of cases and can be identified pre-operatively by nuclear scanning and pre- and intra-operatively by ultrasound. Sam would probably have a minimally invasive parathyroidectomy by an experienced surgeon, be discharged the next day and remain asymptomatic thereafter.

Conflict of interest: none declared.

### References

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