PSEUDOGOUT SIMULATING ACUTE SUPPURATIVE ARTHRITIS

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In gout the first attack of arthritis is often acute and most painful. If the affected site is the first metatarso-phalangeal joint the diagnosis presents little difficulty. When larger joints are involved there is a risk that the condition may be mistaken for acute septic arthritis.

A more positive approach to the diagnosis has recently been made possible by Seegmiller, Howell and Malawista (1962), who showed that the presence of urate microcrystals within the synovial cavity is the direct cause of acute arthritis. McCarty and Hollander (1961) showed that they can be recognised in synovial fluid by microscopic examination. McCarty, Kohn and Faires (1962), in a study of large numbers of specimens of synovial fluid, found some to contain crystals that were not urate but calcium pyrophosphate. These specimens were obtained from patients suffering from recurrent episodes of more or less acute arthritis, with another feature in common—calcification of joint cartilage. McCarty and Gatter (1964) collected forty such cases and described the clinical features of the condition which they call "pseudogout." Žižnán and Šít‘aj (1963) collected twenty-seven cases showing similar calcification, which they termed "chondrocalcinosis articularis." Although they failed to detect crystals in the synovial fluid it appears likely that the condition they described is identical with McCarty's "pseudogout." The subject has recently been reviewed by Bundens, Brighton and Weitzman (1965). In the light of these observations it seems that both gout and pseudogout should be regarded as examples of "crystal-induced synovitis." This represents an important advance in the understanding of joint disease and there may be other examples. McCarty and Hogan (1964) suggested that reactions from intra-articular injections of corticosteroids may be caused by this mechanism.

During the last eighteen months we have diagnosed pseudogout in six patients. Two presented in the orthopaedic department with arthritis of a large joint sufficiently acute to be diagnosed as septic arthritis. It is therefore important to consider this condition in the differential diagnosis of acute monarticular arthritis. Pseudogout, tending to involve larger joints, may represent a more real source of diagnostic error in this situation than does classical uric acid gout.

Previous reports have not emphasised acute septic arthritis in the differential diagnosis of pseudogout, so we are reporting these two cases to draw attention to this mode of presentation and the steps by which the diagnosis can be established.

CASE REPORTS

Case 1—A man of fifty-four complained of swelling and tenderness of the left ankle for two days. There had been no injury, but he was recovering from a crop of boils on his neck. The left ankle was warm, swollen and tender, especially over the inner side and there was redness of the skin. Active movements were limited to one-third of the normal range but they were not very painful. The temperature was 99.5 degrees Fahrenheit. He was admitted to hospital with a provisional diagnosis of acute septic arthritis of the ankle.

Investigations and progress—The white cell count was 7,600 per cubic millimetre, with a normal differential count. The erythrocyte sedimentation rate was 49 millimetres in the first hour. The plasma uric acid level on admission (while the patient was taking salicylates) was 7 milligrams per 100 millilitres. Later estimations were 3.9 and 2 milligrams per 100 millilitres.
The latex test was negative. In addition he was found to have mild diabetes mellitus with a fasting blood sugar of 135 milligrams per 100 millilitres. Radiographs of the left ankle on admission had shown chondral calcification, but the significance of this was not immediately appreciated, and antibiotic treatment was started on the assumption that he had septic arthritis.

The pain and swelling of the ankle joint improved slowly, but he continued to run a fever of 100 degrees Fahrenheit. On the third day after admission to hospital a painful effusion developed in the left knee.

Radiographs showed fine interrupted lines of calcification in both ankles running over the surface of the articular cartilage. These were best seen in the antero-posterior view (Fig. 1). The knees showed diffuse calcification of both menisci and a line of calcification parallel with the femoral condyles (Fig. 2). A complete line of calcification was seen over both humeral heads and also in the acromio-clavicular joints. The wrists showed calcification in the region of the triangular discs and both elbows showed extensive intra-articular calcification. There were lines of calcification over both femoral heads and in the symphysis pubis. The spine showed probable calcification in the third to seventh cervical discs but not elsewhere.
radiographic appearances were characteristic of chondrocalcinosis articularis. Examination of synovial fluid from the knee revealed numerous polymorphonuclear leucocytes but no crystals. This was perhaps due to lack of experience in recognising small intracellular crystals.

The joint symptoms improved slowly on salicylates, although he continued to run a fever up to 100 degrees Fahrenheit for eight days. He was discharged on the nineteenth day almost free from symptoms.

He remained well for six months but then returned complaining of acute pain and swelling of the right ankle. Treatment was begun with phenylbutazone and the joint immobilised in a below-knee plaster-of-Paris back slab. After one week no improvement had occurred, and in addition the right knee had become painful and swollen. Aspiration of the right knee was performed and examination of the fluid on this occasion showed both intracellular and extracellular microcrystals. Local hydrocortisone injected into the knee joint gave immediate relief of his symptoms but the pain and swelling of the right ankle was slow to subside.

**Case 2**—A lorry driver of sixty attended the casualty department with an acutely painful and swollen right knee. He suffered from chronic bronchitis and had been treated with tetracycline for the past year. On the day before he had been confined to bed with bronchitis and on waking found that his knee was painful. During the next six hours the pain, swelling and tenderness became so severe that he required two injections of pethidine. There was no history of injury but he had experienced mild intermittent swelling and pain in both knees for about nine months. There was no family history of rheumatoid disease.

Examination revealed a hot, swollen, acutely tender and reddened right knee with movement restricted by pain to 10 degrees. The left knee contained a small effusion but there was no tenderness or limitation of movement. The temperature was 99 degrees Fahrenheit. He was admitted with a diagnosis of acute suppurative arthritis, partly suppressed by antibiotic administration.

**Investigations and progress**—The white cell count was 8,700 per cubic millimetre, with a normal differential count. The erythrocyte sedimentation rate was 80 millimetres in the first hour; the plasma uric acid 5 milligrams per 100 millilitres; the latex test was negative. The right knee was aspirated and 70 millilitres of turbid straw-coloured fluid were removed, and one mega-unit of soluble penicillin G solution was injected into the joint. Examination of the deposit revealed many leucocytes, predominantly polymorphic, with a few red cells, but no organisms either on Gram or Ziehl-Neelsen staining. No bacteriological growth was obtained on culture.

Treatment had been started with systemic penicillin and streptomycin and the knee immobilised in a pressure bandage with a plaster back slab. After initial improvement the effusion recurred and two days later the aspiration was repeated and 150 millilitres of turbid yellow fluid were removed and penicillin was again injected. No organisms were seen in the fluid and no bacteriological growth was obtained.

The radiograph of the right knee was now re-examined and a line of calcification was seen in the region of both menisci (Fig. 3). The lateral view showed a fine incomplete line of calcification running parallel to and three millimetres from the femoral condyles. These appearances suggested a diagnosis of pseudogout. In addition there was radiographic evidence of early osteoarthritis. A skeletal survey showed slight calcification in the lateral meniscus...
of the left knee but none elsewhere. Accordingly a further diagnostic aspiration was performed on the fifth day after admission: examination of this fluid revealed both intracellular and extracellular microcrystals showing weakly positive birefringence.

After seven days of salicylate therapy the symptoms had improved and he could flex the knee to 90 degrees. The sedimentation rate fell to 36 millimetres and he was discharged on the tenth day.

**DISCUSSION**

The work of McCarty and of Žitnjan has now clearly established pseudogout (chondrocalcinosis) as a clinical entity. As in gout, the acute attacks appear to be a reaction to the presence of microcrystals within the joint. The condition differs from classical gout in that the crystals consist of calcium pyrophosphate, not of urate. The biochemical defect is not understood and most cases show no abnormality of calcium metabolism. More than one member of a family may be affected.

Clinically the condition may present with recurrent attacks of arthritis resembling acute gout, or as chronic degenerative joint disease which may have acute exacerbations. The commonest site affected is the knee, and large rather than small joints are usually involved. Acute attacks are often associated with constitutional disturbances such as fever and malaise. This may be associated with a leucocytosis and a raised sedimentation rate. Treatment with salicylates or phenylbutazone is usually effective in the acute stage. As with true gout attacks may be precipitated by surgical procedures or by diuretic therapy.

A presumptive diagnosis of pseudogout can be made when joint symptoms are associated with the typical radiological appearance. Confirmation requires identification of crystals in the synovial fluid.

**Radiological appearances**—The fully developed radiological appearances present a characteristic picture. Fine lines of calcium deposits are seen parallel to the subchondral articular cortices, often in many synovial joints, but usually best seen in the knee, shoulder and hip. This appearance is due to calcium pyrophosphate in the superficial layers of hyaline cartilage, and when seen in several joints (as in Case 1) is highly suggestive of pseudogout. Patients with hyperparathyroid arthropathy were described by Bywaters, Dixon and Scott (1963) as occasionally showing a similar appearance but usually with additional radiological features of hyperparathyroidism. In practice it is more common for radiological calcification to involve fibrocartilage rather than hyaline cartilage. The most commonly affected site is the knee, but the significance of calcified menisci alone is uncertain. It should give rise to a suspicion of pseudogout, and the finding of a single line of hyaline calcification (as in Case 2) makes the diagnosis very likely. In pseudogout the symphysis pubis is commonly calcified. The intervertebral discs may show calcification, usually of the annulus fibrosus, but isolated dense vertebral disc calcification does not seem to be a characteristic feature.

**Identification of crystals**—Synovial fluid can be examined for the presence of microcrystals by standard light microscopy of fresh "wet" preparations. Calcium pyrophosphate may appear as rod-like crystals with parallel sides or as rhombic forms. Both types vary from 1 to 20 microns in length and may be intracellular or extracellular. Urate crystals resemble the rod forms. Once the presence of crystals within a joint has been established, the simplest method of differentiating urate from calcium pyrophosphate is by polarised light microscopy. With this technique urate crystals show strongly negative birefringence and pyrophosphate crystals weak positive birefringence. Other tests used in differentiation of these crystals include digestion by uricase, response to heating and x-ray diffraction techniques.

The concept of crystal-induced synovitis is an important advance in the understanding of joint disease, and the examination of synovial fluid for microcrystals should become a routine laboratory investigation. The incidence of pseudogout is not yet known, but we now suspect that it may be a more common cause of arthritis than classical uric acid gout. The cases
reported here show that pseudogout can mimic acute septic arthritis. It is important that this should be appreciated. Once the condition is suspected, radiological and synovial fluid examination provide a rapid and relatively simple method of making the diagnosis.

SUMMARY
1. Two cases of pseudogout are described with an onset acute enough to be mistaken for septic arthritis.
2. The radiological and laboratory investigations for diagnosis are described.

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REFERENCES