Case report

Pseudoseptic pseudogout in progressive pseudorheumatoid arthritis of childhood

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SUMMARY Progressive pseudorheumatoid arthritis of childhood is an uncommon arthropathy of unknown aetiology, which is related to spondyloepiphysyal dysplasia tarda. Previous reports have noted the absence of joint inflammation in this disease. An adult is described here with this arthropathy, who developed episodic acute inflammatory arthritis that mimicked septic arthritis, but proved to be pseudogout. The relation between pseudogout and progressive pseudorheumatoid arthritis of childhood is discussed.

Key words: spondyloepiphysyal dysplasia.

An adult with "progressive pseudorheumatoid arthritis of childhood\(^1\),\(^2\)\(^3\) a heritable, non-inflammatory arthropathy related to spondyloepiphysyal dysplasia tarda, developed three episodes of acute inflammatory arthritis simulating septic arthritis. Crystals consistent with calcium pyrophosphate dihydrate (CPPD) were present in the synovial fluid and synovial membrane, and chondrocalcinosis was noted radiographically. Pseudogout has not been reported previously in this arthropathy. We examine here the relationship of chondrocalcinosis and pseudogout with our patient's joint disease.

Case report

A 37 year old white woman developed a generalised, progressive, deforming arthropathy which was first noted when she was 2 years old. Despite a lack of clinical evidence of synovitis, and the absence of rheumatoid factor or characteristic nodules, she was diagnosed as 'juvenile rheumatoid arthritis'. She had required crutches for walking since the age of 12 because of severe coxa vara with femoris adductus and genu valgum. She underwent total joint arthroplasties of both knees and hips between November 1981 and January 1984.

The patient's arthropathy involves the spine, shoulders, elbows, wrists, hips, knees, ankles, carpal, tarsal, metacarpophalangeal, metatarsophalangeal, and interphalangeal joints of the hands and feet. She is of short stature and has a barrel shaped chest.

Roentgenographs of the hands, feet, shoulders, elbows, knees, hips, and ankles showed irregularity of the subchondral bone, marked distortion of the epiphyseal region, joint space narrowing, and bony proliferation, but no erosions (Fig 1). Platyspondyly was notable (Fig. 2), but, unlike the Morquio-Brailsford syndrome, the odontoid process was normal and the ribs were not flared. The iliac wings were mildly hypoplastic, but the mid-pelvis was not narrow, unlike the Kneist syndrome.

The patient has four similarly affected siblings, two male and two female, and four unaffected siblings, three male and one female. Neither the parents nor the children of the affected and unaffected siblings have clinical evidence of this arthropathy. The parents are first cousins. None of the other affected siblings has a history of inflammatory arthritis. Their arthropathy has been uniformly unresponsive to non-steroidal anti-inflammatory agents, and they have a strong preference for propoxyphene.

In September 1984 the patient presented with increasing pain in her right elbow. She had an oral temperature of 38.3°C. Local warmth, redness, and swelling were present about the elbow, with pain on...
scattered lymphocytes and no acute inflammatory changes.

In June 1985 the patient developed increasing pain in the left elbow over five days. Her oral temperature was 38.3°C. Heat, redness, swelling, and limited motion of the elbow were noted. The peripheral WBC was 15.4x10^9/l and the ESR was 66 mm/h. Arthrocentesis yielded synovial fluid with a WBC of 41.5x10^9/l with 90% neutrophils. No organisms or crystals were seen on routine and polarised microscopic examination of the synovial fluid. Cephapirin was administered intravenously and arthrotomy was performed. The patient defervesced after two days in hospital. After five days of intravenous antibiotic therapy a four week treatment course was completed with oral cephalaxin. Elbow mobility and pain improved over several weeks. A synovial membrane biopsy specimen obtained at the time of arthrotomy again showed densely fibrotic tissue with vascular proliferation, but no acute inflammation, and all cultures of the synovial fluid were negative.

In August 1985 the patient awoke with severe motion and further restriction of range of motion. The peripheral white blood cell count (WBC) was 20x10^9/l and the Westergren erythrocyte sedimentation rate (ESR) was 95 mm/h. Arthrocentesis yielded 4 ml of cloudy yellow fluid with poor viscosity and mucin clot. The crystal analysis by polarised microscopy and the Gram stain were negative. The synovial fluid WBC was 95x10^9/l, of which 92% were neutrophils.

Treatment with intravenous nafcillin was initiated. The following day repeat arthrocentesis showed a synovial fluid WBC of 20x10^9/l. The peripheral WBC fell to 9.5x10^9/l, and the patient became afebrile. Arthrotomy drainage with synovial biopsy was performed. Routine bacterial cultures of synovial fluid, blood, and urine, and cultures of the cervix and rectum for Neisseria gonorrhoea were all negative. The patient received two weeks’ treatment with intravenous nafcillin followed by two weeks with oral dicloxacillin. Her wound healed well, and the range of motion of the elbow gradually returned to baseline. Histological examination of the synovium showed fibrosis and vascular proliferation. Only minimal inflammation was noted, with
pain in her right elbow. On presentation she had an oral temperature of 38.3°C and heat, redness, and swelling of the elbow. The initial peripheral WBC was 18.2×10⁹/l, the ESR was 51 mm/h. Serum calcium, phosphate, uric acid, alkaline phosphatase, and serum creatinine were normal. Arthrocentesis showed a synovial fluid WBC of 68.5×10⁹/l with 96% neutrophils; the Gram stain and crystal analysis were negative. Therapy was initiated with intravenous nafcillin. Repeat arthrocentesis one day later showed a WBC of 47.5×10⁹/l with 90% neutrophils. Numerous small (2–4 μm) chisel-shaped crystals showing weakly positive birefringence were noted both intracellularly and extracellularly. Indomethacin, 150 mg/day, was added, and the patient improved rapidly. Her serum creatinine, however, rose abruptly despite a decrease in the indomethacin dose to 75 mg/day. Both indomethacin and nafcillin were discontinued after four days of therapy, and the patient recovered over one week.

Review of the patient’s roentgenographs showed chondrocalcinosis in the triangular cartilage of the wrist (Fig. 3). Review of the synovial histopathology from the previous admissions showed amorphous calcific deposits in the subsynovium, which stained with von Kossa stain, and scattered rod-shaped crystals showing weakly positive birefringence, varying from 2 to 12 μm in length.

**Discussion**

Calcium pyrophosphate dihydrate disease may mimic many diseases, including osteoarthritis, rheumatoid arthritis, and gout. Pseudogout may mask or mimic septic arthritis. Our patient had a longstanding degenerative arthritis vaguely simulating rheumatoid arthritis and developed three episodes of acute arthritis with fever, high synovial fluid and peripheral blood WBC, and intense local signs of inflammation. These episodes were each initially thought to represent sepsis and were treated as such. Cultures were negative, however, in all three episodes. Furthermore, synovial biopsy specimens obtained within days of the onset of arthritis and shortly after initiation of antibiotic therapy showed a paucity of inflammatory cells and absence of significant neutrophil infiltration. This strongly contradicts the diagnosis of septic arthritis. On the other hand, amorphous calcium deposits and positively birefringent crystals, consistent with CPPD, were found in the synovium, and chondrocalcinosis was noted in the wrist. The patient, therefore, meets criteria for ‘definite’ CPPD disease.

Chondrocalcinosis may go undetected on routine radiographs of patients with CPPD disease owing to low density of deposits, extensive loss of cartilage and joint space, and bony deformities obscuring clear view of the cartilage. The last two considerations are particularly relevant in our patient. Review of all available radiographs of our patient and her affected siblings showed calcification of intervertebral discs in several and the symphysis pubis in one. Views of the shoulders, hips, and knees uniformly showed joint space loss and deformity, which could prevent detection of chondrocalcinosis.

Our patient’s underlying arthropathy conforms to the description of ‘progressive pseudorheumatoid arthritis of childhood’, which has also been called ‘spondyloepiphyseal dysplasia tarda with progressive arthropathy’. The accelerated, generalised degenerative arthritis suffered by these patients is reminiscent of the osteoarthritis variant of CPPD disease. The extremely early age of onset, the marked bone dysplasia, the severe involvement of the axial and the appendicular skeleton, and the lack of prior reports of chondrocalcinosis and pseudogout in patients with this arthropathy all suggest that progressive pseudorheumatoid arthritis of childhood is a distinct entity and not a subset of CPPD disease.

Fig. 3 Roentgenograph of the patient’s wrist showing calcification of the triangular cartilage.
Previous series have emphasised the non-inflammatory nature of this arthropathy, with absence of soft tissue swelling, synovitis, synovial fluid leucocytosis, and radiographic erosions and periostitis. Pathological changes in the cartilage include disorganisation and hypoplasia with abnormalities of both the cellular and extracellular components. Changes suggestive of CPPD disease have not been described.

Most patients with chondrocalcinosis do not develop pseudogout. Crystal shedding from the cartilage into the synovial fluid, with subsequent phagocytosis by neutrophils and synovial macrophages, is required. Septic arthritis or gout may cause ‘enzymatic strip mining’ of the cartilage, resulting in crystal release. Ion fluxes have been proposed as a mechanism of crystal shedding, but the most obvious cause is trauma. Chondrocalcinosis and pseudogout have been reported in patients with tabes dorsalis, articular instability, and trauma. Our patient uses forearm crutches and bears weight with her severely degenerated elbows and shoulders. Trauma is the most tenable explanation for our patient’s pseudogout.

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References

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