Pseudogout in acute neuropathic arthropathy

A clue to pathogenesis?

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The association of inflammation with neuropathic joints was possibly first described by William Musgrave of Exeter (1657–1721) in his book, *Arthritia Symptomatica* (1703), in which he wrote (Kelly, 1963), ‘Though the limbs were thin and flaccid from paralysis, they had not yet completely wasted away. Quite the contrary; they were swollen and inflamed from the arthritis and clearly showed plenty of signs of vitality’.

The observation that an acute arthritic would often precede the bone collapse is referred to in Jean Martin Charcot’s frequently quoted monograph (Charcot, 1868), ‘Without any appreciable external cause we may see between one day and the next the development of a general and often enormous tumefaction of a member, most commonly without any pain whatever, or any febrile reaction. At the end of a few days the general tumefaction disappears, but more or less considerable swelling of the joint remains because of the accumulation of water in the joint and sometimes also in the periarticular bursae. On puncture being made, a transparent lemon-coloured fluid has frequently been drawn from the joint. One or two weeks after the invasion, sometimes much sooner, the existence of more or less cracking sounds may be noted betraying the alteration of the articular surfaces which at this time is already profound. The hydropneumonia resolves quickly, leaving an extreme mobility of the joint’.

We report an episode of acute neuropathic arthropathy affecting the right knee in a 67-year-old black man with chondrocalcinosis and pseudogout. To the best of our knowledge this episode is the most acute neuroarthropathy ever recorded, and affords some insight into the possible mechanism of ‘trauma induced’ pseudogout.

Case report (see Table)
The patient was seen in our clinic in January 1972, with a massive, nearly painless effusion in his left knee associated with swelling and pitting oedema of the entire leg and thigh. There was a small asymptomatic effusion in the right knee. A moderate left-sided varus deformity was noticeable on ambulation. Neurological examination showed a complete absence of deep pain sensation in all four extremities, but pressure over the eyes, pinprick and thermal stimuli all elicited pain. In addition, he had normal position sense and sluggish but reactive pupils to both light and accommodation. Romberg’s sign was absent. He had been treated for syphilis as a young man with arsenicals and this was followed up with lumbar punctures, apparently to the satisfaction of his physicians. Serological studies for syphilis in January 1972 included a weakly reactive VDRL, nonreactive Reiter’s protein, and a reactive fluorescent treponemal absorption test. Serological tests on his cerebrospinal fluid were normal, as was a colloidal gold curve, protein, glucose, and chloride. X-rays showed several small calcified loose bodies and depression of the medial tibial plateau in the left knee. There was a peaking of the tibial spines without joint space narrowing in the right knee; punctate calcification in the lateral meniscus was present (Fig. 1). Aspiration of the left knee at this time revealed a grossly bloody fluid with a low leucocyte count—no crystals were seen. An arthrogram, done 5 days later, showed fragmentation of the articular cartilage of the medial tibial plateau and more marked collapse of the medial tibial plateau (Fig. 2) which, over the next 7 months, progressed to the typical radiographic appearance of a neuropathic joint in its resorptive phase.

Synovial fluid aspirated from the right knee in December 1972 contained 350 leucocytes/mm³ and numerous intra- and extracellular calcium pyrophosphate dihydrate crystals. An x-ray taken at this time was identical to that taken a year previously. The stability of the knee was intact on clinical examination. This episode of pseudogout was treated with indomethacin 250 mg four times daily with partial success, but a few days later, when walking to the local newspaper stand, his right knee suddenly gave way with accompanying pain, he was unable to support his weight on the limb. When seen in clinic 5 days later, the whole of the right leg from groin downward was massively swollen with pitting oedema (Fig. 3). There was marked laxity of the medial collateral ligament and the knee could be angulated to 30° in the varus position. An x-ray at this time showed massive collapse of the plateau of the right medial condyle with radio-opaque debris producing an ‘auto-arthrogram’, which showed a clear outline of the suprapatellar bursa and evidence of posterior...
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<thead>
<tr>
<th>Date</th>
<th>Clinical condition</th>
<th>X-rays</th>
<th>Joint fluid</th>
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<tr>
<td>January 1972</td>
<td>Intermittent effusions</td>
<td>Mild DJD with punctate calcification of lateral meniscus</td>
<td>Group I, no CPPD</td>
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<td></td>
<td>Massive swelling left leg</td>
<td>Arthrogram showed fragmentation of articular cartilage of medial plateau</td>
<td>Bloody, no CPPD</td>
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<tr>
<td>December 1972</td>
<td>Subclinical episode of pseudogout</td>
<td>Gradual evolution of Charcot joint</td>
<td>Group I, intra- and extracellular CPPD</td>
</tr>
<tr>
<td>Nov 24, 1973</td>
<td>Episode of mild pseudogout in a clinically stable joint</td>
<td>Unchanged</td>
<td>Group I, no CPPD</td>
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<tr>
<td>Dec 1, 1973</td>
<td>Massively swollen right limb with a demonstrable varus deformity of 30° and history of sudden collapse and acute pain 5 days before</td>
<td>Gross destructive changes with 'acute' collapse of medial tibial plateau and an 'auto arthrogram' with powdered bony debris showing extravasation into calf muscle</td>
<td>Bloody fluid, no CPPD</td>
</tr>
<tr>
<td></td>
<td>No change</td>
<td>No change</td>
<td>None obtainable</td>
</tr>
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DJD = degenerative joint disease; CPPD = calcium pyrophosphate dihydrate.
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rupture into the calf muscles (Fig. 4). Aspiration revealed 6,500 leucocytes/mm³, but no crystals were seen. Over the course of several weeks the swelling gradually subsided. He was fitted with a second long leg brace and is now walking satisfactorily.

Discussion

This patient was one of four in whom the association of calcium pyrophosphate dihydrate crystal (CPPD) deposition with Charcot arthropathy was first described (Jacobelli, McCarty, Silcox, and Mall, 1973). At the time of this original report, only the left knee had exhibited neuropathic changes which had slowly evolved from a radiographic appearance, 'suspicious of early Charcot arthropathy', to a classical neuropathic joint 11 months later. In this report we document a sudden and catastrophic collapse of the medial tibial plateau of the right knee. This is of interest (1) because of the acute development of the Charcot arthropathy which, by history, literally occurred in the space of a few seconds in a joint that radiographically had remained unchanged over the course of a year, documented by an x-ray taken 4 days before the episode of collapse and an x-ray showing an acute Charcot arthropathy taken just 5 days later, this being the most acute episode of acute neuropathic arthropathy so far documented; and (2) because of the episode of pseudogout in relationship to the time course of the evolving neuropathic arthropathy. It is not surprising that a patient with known (CPPD) deposition should experience attacks of pseudogout, an apparently self-evident statement but not one that has been adequately explained. The factors responsible for the acute episode of pseudogout are poorly understood,
although postsurgical attacks (McCarty, Kohn, and Faires, 1962; O'Duffy, 1973), especially after parathyroidectomy (Bilezikian, Aurbach, Connor, Pachas, Aptekar, Wells, Freijanes, and Decker, 1973), and trauma are well known precipitating events. CPPD crystals seem to require a suitable matrix for their formation and are unlikely to crystallize de novo in synovial fluid, as has been suggested for monosodium urate crystals in classical gout (Seegmiller, 1966), as the in vitro formation of synthetic CPPD crystals requires a pH optimum of 2 (J. R. Lehr and D. J. McCarty, unpublished observations). It is therefore likely that the CPPD crystals found in pseudogout synovial fluid, both intra- and extracellularly, have come from the adjacent cartilage or synovium. Thus, factors which influence the mobilization of CPPD crystals into the joint cavity will have an important bearing on the initiation of acute pseudogout. This case report illustrates one possible mechanism of 'crystal shedding'.

The arthrogram of the left knee, in January 1972, showed fragmentation of the articular cartilage and collapse of the medial tibial plateau. Over the course of the next 11 months the subchondral bone was resorbed, leading to the typical appearance of a neuropathic joint. It is easy to visualize that during this progressive fragmentation of cartilage that any deposits of CPPD crystals would be liberated into the joint cavity. It was noted in January 1972 that the lateral meniscus of the right knee showed punctate calcification consistent with chondrocalcinosis, and in December 1972 he was observed to have subclinical pseudogout with CPPD crystals demonstrably free in the joint fluid and in joint fluid leucocytes. On November 24, 1973, he experienced a symptomatic episode of pseudogout in the right knee, although a plain x-ray taken at this time was unchanged from that taken in January 1972. However, 4 days later his right knee suddenly gave way and when he was seen 5 days later an x-ray showed massive collapse of the medial plateau with calcific joint debris producing an 'auto-arthrogram'. We speculate that the episode of pseudogout on November 24, 1973 was due to cartilaginous fragmentation resulting from microfractures of the subchondral bone which later progressed to the acute massive collapse of the medial condyle. Thus, on this occasion the shedding of CPPD crystals into the joint cavity and the
accompanying crystal synovitis was probably a harbinger of the catastrophe to follow.

The observation of intermittent joint effusions as a common early finding in neuropathic arthropathy is well documented (Soule, 1936; Steindler, 1931; Norman, Robbins, and Milgram, 1968; Key, 1932; Johnson, 1967; Katz, Rabinowitz, and Dzidziew, 1961), although one will never know what proportion of these were attacks of pseudogout. In the light of our present knowledge it seems reasonable to look specifically for CPPD crystals in such effusions, as their demonstration may be of predictive value in assessing progressive cartilaginous fragmentation. In this respect, an early arthrogram may also show such early cartilaginous changes (as in our case) enabling the alert physician to take prompt preventive action (Johnson, 1967).

By extrapolation of our hypothesis of 'crystal shedding', an explanation of the post-traumatic pseudogout attacks is possible.

**Summary**

The association of pseudogout and an acute Charcot arthropathy is described in a 67-year-old man. The sudden collapse of the medial tibial plateau of his right knee was preceded by an episode of pseudogout. Attention is drawn to the frequent occurrence in the literature of the association of an acute inflammatory arthritis and Charcot arthropathy. It is suggested that pseudogout accompanying Charcot arthropathy is due to intra-articular 'shedding' of CPPD crystals, resulting from cartilaginous microfractures, and as such is indicative of progressive joint destruction.

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