Calcium pyrophosphate dihydrate crystal deposition disease: A report of a case

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The nature of calcium pyrophosphate dihydrate (CPPD) crystal deposition disease is reviewed and illustrated with a case report. CPPD is one of several calcium-containing crystals to be found in various pathological tissues which are associated with abnormal cellular localizations of proteoglycan. Clinically and radiologically it is an age-related disorder which resembles osteoarthritis and is sometimes interspersed with attacks of acute arthritis. Diagnostic and case management aspects of relevance to chiropractic are considered. (JCCA 1988; 32(1): 23–27)

KEY WORDS: CPPD, spinal stenosis, posterior column disease, chiropractic, manipulation.

La nature de la maladie de déposition de cristaux dihydrate pyrophosphate de calcium (CDPC) est revue et illustrée par un rapport de cas. CDPC est l'un des nombreux cristaux à contenance de calcium à être trouvé dans des tissus pathologiques divers associés à une localisation cellulaire anormale de protéoglycan. Cliniquement et radiologiquement, c'est un déordre relié à l'âge qui ressemble à l'ostéoarthrite et est quelquefois entremêlé d'attaques d'arthrite aiguë. Le diagnostic et les aspects de contrôle de cas relevant de la chiropraxie sont considérés. (JCCA 1988; 32(1): 23–27)

MOTS CLÉ: CDPC, sténose dorsale, maladie de la colonne postérieure, chiropraxie, manipulation.

Introduction

Calcium pyrophospate dihydrate (CPPD) is one of several calcium-containing crystals which may be found in pathological human synovial fluid, synovium, cartilage, ligaments and tendons.[1] The other clinically important calcium containing crystals in this category are contained in the basic calcium phosphate group (BCP) which includes hydroxyapatite (HA), tricalcium phosphate (TCP) and octacalcium phosphate (OCP).[1] Within this group, HA and OCP mixture is the most commonly seen.[1] However, a mixture of CPPD and BCP crystals is also frequently encountered.[2]

Historically, the first report of radiologically observed "chondrocalcinosis articularis" was given by Zitnan and Sitaz in 1958.[3] It was, however, some years later before the nature of the crystals was identified. Chondrocalcinosis articularis later became known as "pseudogout" because of the periodic attacks of acute synovitis associated with the condition.[4] Today, the preferred name is CPPD crystal deposition disease, except in the British literature where it is frequently referred to as "pyrophosphate arthropathy".[1]

Pathogenesis

Hyaline- and fibro-cartilage have been found in vitro to secrete inorganic pyrophosphate (PPi).[5,6] When the PPi diffuses from the chondrocytes, it encounters extracellular calcium ions with which it combines. Consequently, the smallest and hence possibly the youngest CPPD crystals then form around the chondrocyte lacunae.[1]

In vitro studies have shown that with the ingestion of these CPPD crystals by synovial cells, a 3-fold increase in the secretion of collagenase and neutral protease (elastase and cathepsin (G) results and that such secretions continued until the ingested particles were completely degraded.[8] The aforementioned enzymes play important roles in the degradation of collagen, proteoglycans and other proteins.[11] McCarty noted that it took 30–90 days for a human osteoarthritic knee to clear 50% of a small dose of injected CPPD crystals.[1] Prostaglandin E2, a potent vasodilator, was released in large amounts from the synoviocytes following exposure to CPPD crystals, peaking at 6–24 hours after exposure and rapidly tapering off thereafter.[9] Such information is significant in planning the management and prognosis of the acute and post-acute phases of the condition.

It would appear, therefore, as if most CPPD is formed in cartilage, particularly fibrocartilage, as in the menisci of the knee, symphysis pubis, glenoid and acetabular labra and the articular disc of the distal radio-ulnar joint.[1] Yet, when it has formed in other tissues e.g. synovium, articular capsules, ligamentous and tendinous insertions, such tissues have invariably first undergone chondroid metaplasia.[1]

Ishikawa found abnormal cellular localization of proteoglycan around *all* immature CPPD deposits regardless of tissue type.[7] Consequently, a matrix factor may be a necessary predisposing factor in all instances of CPPD crystal deposition disease.[7]

Prevalence and classification

CPPD is an age-related disease.[10,15] This differs from BCP, in which the presence and concentration of the crystals are directly related to the amount of radiological evidence of joint degeneration.[2] Approximately 5% of 70 year old people manifest radiographic chondrocalcinosis but nearly 50% do so by the age of 90.[10] The ratio of male to female is 1.4:1.[11]

Patients with CPPD have been classified into 4 types:

1 Familial. All have been caucasians except for a few Japanese.[7]
2 Metabolic disease associated. A number of diseases may be associated with CPPD but, other than for aging, the evidence in support thereof is not strong.[1] (see Table 1). Acute attacks of "pseudogout" have been reported following gouty arthritis,[11] institution of diuretics,[15] cerebrovascular accidents,[11] myocardial infarction[11] or bacterial infections.[17]

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Table 1 Disorders thought to be associated with CPPD

Aging
Hyperparathyroidism – primary and secondary
Hypothyroidism
Hemochromatosis
Hemosiderosis
Hypomagnesemia
Hypophosphatasia
Urate Gout
Amyloidosis
Familial Hypercalcemic Hypocalciuria

3 Trauma/surgery associated. Cartilage which has been "stressed" by trauma, intra-articular fracture, surgery (e.g. meniscectomy), osteochondritis dessicans and possibly in the hypermobility syndrome, tends to develop radiographic chondrocalcinosis.[1,7] General surgery, especially parathyroidectomy, may precipitate an acute attack of "pseudogout".[17]
4 Sporadic (idiopathic). Clinically, the majority of patients are from the "traumatic" and "sporadic" groups.[1]

Clinical picture

CPPD is initiated in about 20% of cases by an acute phase, "pseudogout", more commonly in males,[12,13,14] and presents with typical symptoms and signs of synovitis accompanied by mild fever and malaise, all lasting from 1 day to 4 weeks.[15]

In the chronic form it resembles osteoarthritis and about 50% of such patients have periodic superimposed acute attacks.[14] This form accounts for about half the patients who have any form of crystal deposition disease.[15] Nearly 50% of patients with CPPD develop progressive degeneration of multiple joints[11] (see case report). The most frequently involved joints are the knees, wrists, metacarpophalangeal joints, hips, shoulders, elbows and ankles.[11] Often the involvement is symmetrical.[1]

The neurological examination is usually normal[11]. Although seven cases of cervical myelopathy due to large masses developing in the ligamentum flavum have been reported, involvement of the lumbar spine with CPPD does not appear to result in neurological symptoms.[18]

Radiological signs

Chondrocalcinosis due to CPPD is mainly an intra-articular observation, as opposed to BCP which is mainly peri-articular.[15] The calcification in the hyaline cartilage is usually linear, regular and parallels the osseous margin, whereas calcification occurring in fibrocartilage is usually clumped or granular but may be linear in the menisci, pubic symphysis or the triangular fibrocartilage of the wrist[15] (see figure 1). Patellofemoral degenerative changes which greatly exceed the changes of the tibio-femoral compartments are frequently observed[15] (see figure 2). In fact, isolated patellofemoral arthritis or isolated radiocarpal joint involvement is a radiological clue to underlying CPPD.[1] Spinal changes include disc degeneration, vacuum sign, calcification of the annulus fibrosis and degeneration of the apophyseal joints.[15] Interestingly, it has been noted that the synovial fluid levels of inorganic pyrophosphates (PPi) correlate with the degree of radiographically observed joint degeneration but not with the amount of chondrocalcinosis.[19,20]

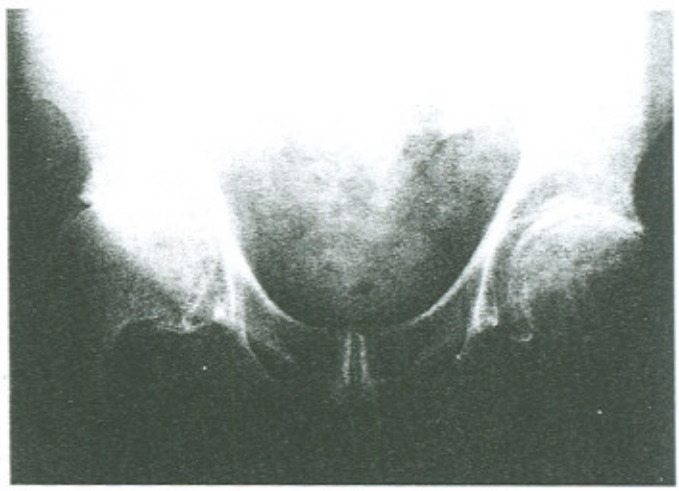

Figure 1 Note bilateral acetabulo-femoral loss of joint space; osseous proliferation about the joints; numerous acetabular and femoral head subchondral lucencies; chondrocalcinosis of the symphysis pubis.

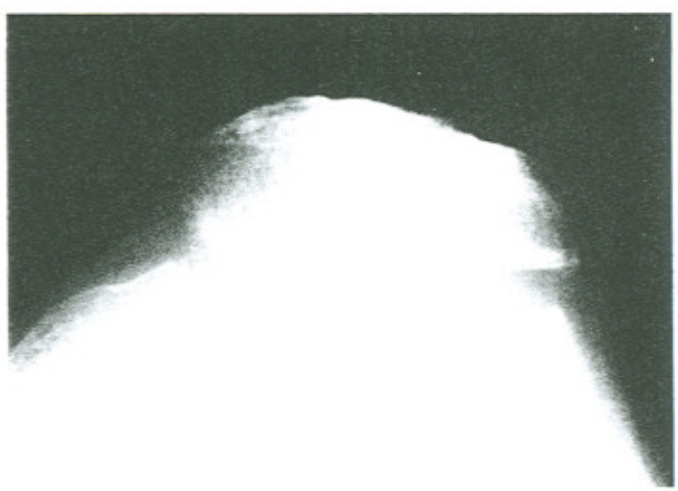

Figure 2 Note roughening of anterior aspect of patella; minimal lateral patello-femoral joint space loss; minimal spurring on lateral aspect of patella.

Differential diagnosis

CPPD must be differentiated from a number of conditions (see Table 2).[1,4,15,21]

Table 2 Conditions to be differentiated from CPPD

Differential	*Characteristic Features*
Gout	Hyperuricaemia
Rheumatoid Arthritis	Para-articular osseous erosions. However, 10% of CPPD patients are serum positive for rheumatoid factor.
Ankylosing Spondylitis	Positive HLA-B27 factor
Neurogenic Arthropathy	Hypoalgesic joints.
BCP Crystal Deposition Disease	Aggressive degenerative arthropathy not age related. Periarticular changes more likely.
Osteoarthritis	Less prominent and infrequent subchondral bony cysts; less variable osteophyte formation.

Case report

A 79 year old male caucasian complained of general sacral and bilateral sacro-iliac pain for the previous 5 to 6 years. The pain, described as a dull ache, was worse on standing or walking, on awaking, from cold weather, on changing position and would wake him at night. The pain was diminished by motion, warmth and contoured back support whilst sitting, but prolonged walking during the day resulted in cramps in the left foot and hip adductors during that night. Excessive walking for him would be 50 metres or more. Such walking resulted in a sense of "tightness" in his lower limbs especially the left. Nocturnal cramps could be relieved by walking around the bedroom. Valsalva maneuver was negative. He used a cane in his right hand which afforded him a sense of stability. He also complained of bilateral knee pain especially the left which he had sprained in his youth.

About 8 years ago he experienced an attack of acute arthritis in both hands which lasted a few weeks. No other joints were apparently involved. Nothing in his medical or surgical history was pertinent other than he took 4 to 6 coated aspirins daily. He was otherwise in good general health.

Physical examination revealed an elderly, overweight man who moved with some difficulty. Posturally, the spinal curves were normal for a person his age. All ranges of spinal motion were limited and the lumbar lordosis was maintained on forward flexion. A "clunking" crepitus was heard and felt in the lumbar spine on rotation. On palpation, there was noted paraspinal hypertonicity. Fixations were found at the right sacroiliac, thoracolumbar and midthoracic areas. Joint challenge was tender at the lumbosacral and L3 to T6 levels bilaterally. Hip joint motion was limited bilaterally in all directions and both knees were restricted in motion (0° to about 100°). Yeoman's test for the left sacroiliac joint was positive.

Tandem walking was difficult and he swayed considerably in Romberg's with his eyes open. However, Romberg's test with his eyes closed was no worse and heel to shin test was negative. Limb position sense in all extremities was normal, however, vibration from the tibial tubercles downwards was bilaterally absent. Plantar response was down-going. Achilles reflex was bilaterally absent whilst the knee and medial hamstring reflexes were 2+. Two point discrimination was 4mm on the finger tips (normal 3–5mm) and 50mm on the dorsum of the feet (normal 20–30mm). Light touch sensation was normal, however, pin-wheel sensation over the S1 dermatome was diminished on the left. Left quadriceps muscle strength was 4/5 as were the right hamstrings. SLR was positive for muscle tension only, right at 60° and left at 80°.

Posterior tibial pulses were full and equal whilst the dorsalis pedis pulses were absent. There was mild flaking of the skin of the legs with hairlessness, but inspection of the feet revealed normal temperature, colour and nails.

After 10 minutes of treadmill walking, the knee reflexes were found to be diminished and the hamstring and quardricep muscle strengths bilaterally were further reduced to 3/5.

Diagnosis of CPPD was made on the basis of the radiological features, the patient's age and the history of trauma and acute synovitis.

The diagnosis of central spinal stenosis was made on the basis of the sense of ''tightness' in his lower limbs on walking, the nocturnal pain relieved by walking and the diminished knee reflexes after treadmill walking.

Over the past 2 years, the patient has been receiving treatment at the C.M.C.C. Outpatient Clinic. This has consisted of soft tissue therapy, non-thrust mobilization, neuromuscular facilitation and electrotherapy (e.g. interferential current and ultrasound). Under this regime he has progressed from Grade IV (disabled by pain) to Grade III (improved but restricted in activities by pain).[23] The patient has been encouraged to lose further weight and a support in the form of a lumbar spine binder has been prescribed in order to add stability to the lumbar spine.

Discussion

Definitive diagnosis of CPPD crystal deposition disease is by microscopic identification of the crystals obtained from synovial fluid of an affected joint.[1] Radiological evidence of chondrocalcinosis can therefore, at best, be presumptive evidence of the condition.[24] There was no radiological evidence of spinal stenosis,[25] however, this measurement was complicated by the presence of a degenerative spondylolisthesis at L5-S1 as well as technical factors (see figure 3). Certainly CT scans would be invaluable in defining more accurately the nature and extent of the condition. It was difficult to assess how much of the hamstring and quadricep weakness after treadmill walking was neurogenic and how much was due to knee pain.

Another possible diagnosis is a posterior column disorder, but this is unlikely as the loss of vibration sense and increased two point discrimination can be explained in terms of the

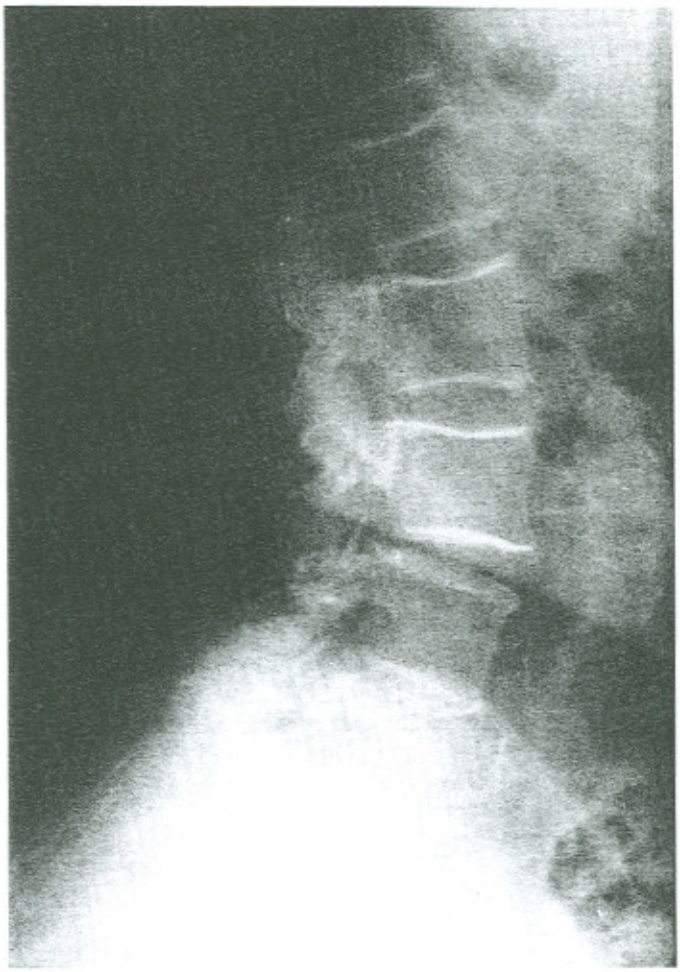

Figure 3 Note anterior slippage of L5 on S1; sacral buttressing; imbrication of lower lumbar facets with mild sclerosis and hypertrophic changes; generalized vertebral rotation; abdominal aorta arteriosclerosis.

patient's age.[26] Likewise, the difficulty he experienced with tandem walking and the positive standing Romberg's may be accounted for in terms of the degenerated state of the patient's hips and knees and/or the spinal stenosis.[27] Furthermore, his postural and gait difficulties may be due in part to the loss of cervical articular mechanoreceptor sensory input frequently associated with increasing age and degenerative or inflammatory conditions of joints.[28] All of these will be monitored.

Manipulation (high velocity thrust) was considered contra-indicated in this case as we did not wish to run the risk of precipitating an acute synovitis at this age, particularly in the light of the "clunking" crepitus which can be indicative of an unstable condition. The prevalence of adverse reactions, if any, to manipulation (micro-trauma) in cases of CPPD is not known, nor is the general response of CPPD cases to chiropractic care. However, gentle non-thrust mobilization with soft tissue therapy was helpful in maintaining joint motion and decreasing the pain. The response of this patient to treatment in the light of the findings of Cassidy, et al in cases of central stenosis, is reasonable.[23]

Summary

A brief review of CPPD crystal deposition disease is given and an illustrative case reported. The clinically important aspects of this review are:

1 that the production of CPPD crystals are related inter alia to trauma and that such should be borne in mind in any management program;
2 the approximate time taken in the degradation of the crystals with regard to the production of collegenase and neutral protease as these relate to the integrity of the articular tissues, again bearing in mind the type of treatment to be given; and
3 how consideration of the totality of the clinical picture can help unravel probable etiologies, especially when multiple clinical entities coexist.

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