Chondrocalcinosis

Last Updated: March 15, 2005

Syonyms and related keywords: calcium pyrophosphate dihydrate deposition disease, CPPD, CPPDD, calcium pyrophosphate dihydrate crystal deposition disease, pseudogout, tophaceous pseudogout, osteoarthritis, OA

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Disclosure

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Calcium pyrophosphate dihydrate deposition (CPPD) disease is an arthritis variant. CPPD actually is a chemical aberration that manifests as at least 4 separate, yet related, diseases. Chondrocalcinosis has been described as the streaking of the soft tissues with calcium. The term chondrocalcinosis sometimes is misapplied as a synonym for CPPD disease, but technically it refers to the visible presence of calcification within tissues on an imaging study.

**Problem:** CPPD consists of the deposition of calcium pyrophosphate crystals into soft tissue. It has been found in high concentrations in hyaline cartilage, synovial tissue, capsule, meniscus, labrum, ligamentum flavum, and soft tissue of the hand.

**Frequency:** Estimates vary widely on the frequency of CPPD disease in the United States. It has been described as being present in 4% to more than 25% of the population by age 80 years. Prevalence clearly increases with age. CPPD presents clinically approximately one half as often as gout in the typical practice setting. The male-to-female ratio is approximately 1.4:1.

**Etiology:** See Pathophysiology.

**Pathophysiology:** The exact physiological dysfunction is not clear, but studies appear to implicate the chondrocyte and surrounding matrix as the responsible agents. Some noxious event (perhaps chemical, perhaps physical) appears to incite a cascade that evolves toward the hypertrophy and degeneration of chondrocytes. Intracellular material escapes to the surrounding matrix and potentially alters the calcium-binding effect of the matrix proteoglycans. Calcium pyrophosphate crystals grow adjacent to these hypertrophic chondrocytes within the affected matrix. The breakdown of collagen cells has been proposed to be the source of the inorganic pyrophosphate.

**Clinical:** Four separate and distinct manifestations of this disease exist, as follows:

**Pseudogout**

An acute presentation appears very similar to gout. Technically, this is designated pseudogout, although the term often is used synonymously with all CPPD diseases. Gout can be distinguished from pseudogout in that gout crystals (sodium urate) are needle shaped and have negative birefringent, while pseudogout crystals (calcium pyrophosphate) are rhomboid shaped and have weak positive birefringent.

Pseudogout is estimated to affect a small percentage (<25%) of individuals with demonstrated CPPD disease.

Onset usually is monoarticular or pauciarticular and often is preceded by injury or surgery to the area. Not infrequently, pseudogout has been identified soon following parathyroid adenoma excision. It tends to come on in a galloping fashion, reaching a peak in hours, and creating pain, swelling, heat, and redness. Fever is present in approximately half of patients with pseudogout. The knee most often is...
affected. The shoulder, elbow, ankle, and familiar first metatarsophalangeal (MTP) joint frequently are involved as well.

The natural course is spontaneous resolution over a few days or, at most, weeks. Treatment accelerates recovery.

**Tophaceous pseudogout**

The calcium pyrophosphate material can deposit in large accumulations, producing a pseudotumor. These can be massive, with all of the consequences of any other space-filling lesion. They often are discretely painful. A review of the literature reveals reports of rare lesions in the temporomandibular joint, sternoclavicular joint, transverse ligament of C1, MTP joints, spinal facet joints, cubital tunnel, and other sites. Involvement in the spine frequently was associated with neural impingement symptoms and spinal stenosis requiring surgical decompression.

**Familial calcium pyrophosphate dihydrate deposition**

A familial pattern appears at a much earlier age, often as early as the third decade of life. It tends to be more aggressive, with a more ominous long-term prognosis. The longevity of satisfactory joint function is reduced in these individuals. Genetic studies have implicated a responsible gene with an autosomal dominant mode of inheritance. Families with a rate of sibling involvement as high as 70% have been documented.

**Osteoarthritis**

The most common presentation is that of osteoarthritis (OA) alone. Symptoms are identical to those of the typical patient with OA, with the exception that, at some point, the presence of calcium pyrophosphate crystals is appreciated. Most often, this is identified by the presence of chondrocalcinosis. Chondrocalcinosis increases in frequency with age. Injury and surgery may aggravate symptoms. Some reports of symptom onset following Hyalgan injection also are recorded in the literature.

Most patients in the typical orthopedic practice are in the latter category. Associated with the general category of CPPD diseases and, therefore, presumably including all the presentations listed above, are other metabolic diseases. Incidence of CPPD increases among those with the following conditions: hyperparathyroidism, hemochromatosis, hemosiderosis, hypomagnesemia, and hypophosphatemia.

The persistence of symptoms despite aggressive nonsurgical management should be considered the indication to perform surgical evaluation and treatment.
**Relevant Anatomy:** An intraoperative photograph (see Image 1) demonstrates extensive precipitate deposition of the calcium pyrophosphate crystals in the articular cartilage, meniscus, and synovium of a knee.

**Contraindications:** For patients demonstrating symptoms of OA and CPPD disease, no contraindication exists to performing arthroscopic surgery as needed. For persons with more advanced OA, the available surgical procedures, up to and including total knee arthroplasty, also are not contraindicated by the presence of this disease.

**Lab Studies:**

- Because of the occasional association with the metabolic conditions listed above, perform hematologic tests to exclude hyperparathyroidism (elevated serum calcium, decreased phosphate, elevated parathyroid hormone or parathormone [PTH], elevated alkaline phosphorous), hypomagnesemia, and hemochromatosis (increased serum ferritin).

**Imaging Studies:**

- Plain x-ray films are most valuable diagnostically.

- The presence of chondrocalcinosis (streaking of the soft tissues with calcium) is pathognomonic.

- Recent attempts to identify calcium pyrophosphate using MRI suggested a potential future application that is not yet suitable for routine screening.

- A 3-dimensional saturated fat gradient echo technique appeared more sensitive than plain x-ray films for identifying the presence of crystals in articular cartilage, yet it did not reveal meniscal involvement.

**Diagnostic Procedures:**

- Crystals are identified in synovial fluid analysis. Arthrocentesis yields calcium pyrophosphate crystals with their own distinct profile. These demonstrate weak positive birefringence on light microscopy and are rhomboid in shape. The fluid itself most often demonstrates an WBC count, which is indicative of inflammation (2,000-50,000 cells/mL). A WBC count exceeding 50,000 cells/mL suggests a septic joint; obtain cultures and Gram stain.

**Histologic Findings:** Soft tissues demonstrate the presence of crystal deposition with adjacent chondroid metaplasia. Synovial hyperplasia with inflammatory changes often is visualized and
mild to moderate, consisting of mononuclear cells.

In tophaceous pseudogout, giant cells often are visualized.

**TREATMENT**

Medical therapy: Treatment depends on the degree of involvement. For patients demonstrating the most common presentation (ie, arthritic symptoms), treatment should follow the algorithm assigned to patients with OA. This includes modified activity, physical therapy, and nonsteroidal anti-inflammatory drugs (NSAIDs). Surgical intervention is indicated when the response to these modalities is unsatisfactory.

For individuals with acute episodes, who usually present with an enhanced level of pain and disability, arthrocentesis associated with the administration of an intraarticular steroid provides reliable prompt relief.

NSAIDs and colchicine may be used to prevent recurrent episodes.

Surgical therapy: Arthroscopic surgery allows debridement of superficial deposits of the calcium pyrophosphate precipitate. This alone may not materially affect the course of the disease. Surgical treatment of OA with debridement, microfracture chondroplasty, radiofrequency chondroplasty, osteochondral transfers, osteotomy, and, ultimately, partial or total joint replacement complete the armamentarium.

When large space-occupying tophaceous lesions are present, surgical excision is indicated. Although the impact of crystal deposition on the viability and future performance of the articular cartilage and meniscus is not clear, many surgeons believe that the presence of this precipitate renders the tissues more fragile. Not infrequently, meniscal tears or chondral lesions are located directly at the site of the densest accumulation of crystals. Cause and effect have not been determined, yet the impression is created that the deposition is responsible for undermining the integrity of the tissue.

Intraoperative details: Changes of OA often are present. These may range from mild to severe

White crystal precipitate is identified in various locations throughout the joint. This ranges from sparse to extensive.

Tissue disruption in the form of tears (eg, meniscus) to chondral lesions (eg, articular hyaline cartilage) may or may not be present with the crystal deposition.

The white precipitate appears to be both superficially attached and deeply embedded. Often, very little effort is required to sweep the soft tissue with a blunt probe, freeing large quantities of the crystalline material into the joint fluid to be suctioned readily from the joint.

Postoperative details: Postoperative management is unchanged from that for the typical patient with OA.
**Follow-up care:** No specific moderations must be made in the postoperative period.

There is an impression among those who examine numerous joints arthroscopically that chondrocalcinosis increases susceptibility to developing osteoarthritis in those tissues exhibiting the precipitate.

The most interesting issue regarding CPPD disease is its overall impact on the progression of OA with which it coexists. The literature tends to be ambiguous on this issue. Some studies imply that the presence of CPPD disease accelerates the deterioration of OA, while other studies refute this. A Framingham OA study of 598 knee patients from 1983-1992 concluded that the presence of chondrocalcinosis had no demonstrable impact on the natural progression of the disease.

As the etiology of calcium pyrophosphate disease is clarified, more focused metabolic treatment regimens will be used. The goal will be to reduce the inflammation associated with the crystal deposition and to provide reduced frequency and intensity of symptoms.

**Caption:** Picture 1. Left images depict femoral and tibial surfaces. Right images depict anterior cruciate ligament.

**Caption:** Picture 2. Upper left image depicts anterior horn medial meniscus. Lower left image depicts undersurface of meniscus. Upper right image depicts medial
femoral condyle. Lower right image depicts synovium.