CHAPTER 13

Calcium Pyrophosphate Dihydrate, Hydroxyapatite, and Miscellaneous Crystals

GERALDINE MCCARTHY, MD, FRCPI

- The incidence and prevalence of calcium pyrophosphate dihydrate (CPPD) are unknown, though there is an increasing prevalence of radiographic chondrocalcinosis with age, and trauma may predispose to the disease. Several metabolic diseases are associated with CPPD.
- Overproduction of extracellular pyrophosphate in abnormal cartilage matrix contributes to CPPD.
- Acute pseudogout is the inflammatory host response to CPPD crystals shed from cartilaginous tissues. Because of the common occurrence of these crystals in osteoarthritic cartilage, there is a strong association of pseudogout with osteoarthritis (OA).
- There are multiple clinical manifestations of CPPD, including pseudogout, pseudo-osteoarthritis, pseudo–rheumatoid arthritis, pseudo–neuropathic arthropathy, and asymptomatic chondrocalcinosis (lanthanic CPPD).
- Diagnosis is made by identifying CPPD crystals in synovial fluid of affected joints.
- There is no practical way to remove calcium pyrophosphate crystals from the joints and symptomatic treatment is with nonsteroidal anti-inflammatory drugs (NSAIDs), colchicines, and local or systemic glucocorticoids.
- Basic calcium phosphate crystals (BCP) frequently deposit in articular tissues and may involve dysregulation of extracellular pyrophosphate homeostasis. BCP crystals can cause diverse clinical conditions including destructive arthritis (Milwaukee shoulder) and calcific periarthritis/tendonitis.

Calcium pyrophosphate dihydrate (CPPD) and hydroxyapatite crystals are the most common calcium-containing crystals associated with joint and periarticular disorders. Deposition of these crystals is frequently asymptomatic or can be intermittently symptomatic. However, common clinical manifestations of calcium crystal deposition include acute or chronic inflammatory and degenerative arthritides, and certain forms of periarthritis. In addition to these, a number of other crystalline materials have been identified less commonly in synovial or bursal fluid. These include calcium oxalate, cholesterol, lipids, and synthetic corticosteroid crystals.

CALCIUM PYROPHOSPHATE DIHYDRATE DEPOSITION DISEASE

Specific identification of calcium pyrophosphate dihydrate (CPPD) crystals ($Ca_2P_2O_7.H_2O$) in synovial fluid (SF) or articular tissue allows the clinician to differentiate between CPPD crystal deposition disease and other inflammatory and degenerative arthritides. The term *chondrocalcinosis* generally refers to the characteristic radiographic features of CPPD deposition in articular cartilage. Calcium-containing crystals other than CPPD may also deposit in articular cartilage, producing radiographically detectable densities in cartilage as well as joint inflammation or degeneration. Deposition of CPPD crystals is not limited to articular cartilage. Less frequently, CPPD crystals are deposited in synovial lining, ligaments, tendons, and, on rare occasions, periarticular soft tissue, much like gouty tophi.

Calcium pyrophosphate dihydrate crystal deposition disease may be asymptomatic or may manifest in a variety of ways. The term *pseudogout* refers to the acute, goutlike attacks of inflammation that occur in some individuals with CPPD deposition disease. CPPD deposition may also cause symptoms similar to septic arthritis, polyarticular inflammatory arthritis (which can be mistaken for rheumatoid arthritis), or osteoarthritis (OA). The incidence and prevalence of clinically important CPPD deposition disease are unknown.

Radiographic surveys show a steadily increasing prevalence of chondrocalcinosis with age. Data from the Framingham study showed an overall prevalence of radiographic chondrocalcinosis of 8.1% in the population over the age of 63, showed prevalence rates of 20% in knee joints of patients over the age of 60, and rates as high as 50% in patients over the age of 90 (1).

Classification

Categorization based on etiology results in four patient groups: hereditary, sporadic/idiopathic, associated with a metabolic abnormality, or post-traumatic. Although most cases of CPPD deposition disease are nonfamilial, many multicase families with CPPD deposition disease have been reported in the literature. Most familial cases appear to be inherited in an autosomal dominant manner, with early onset and varying severity (2). Susceptibility to familial CPPD deposition disease has been most commonly localized to the short arm of chromosome 5. Of particular interest is the gene located at the CCAL2 locus on chromosome 5p, the ANKH gene. The ANKH gene codes for the multipass transmembrane protein AHKH, which transports inorganic pyrophosphate (PPi) from the cell. Gain-of-function mutations in ANKH causes familial autosomal dominant CPPD deposition, of which several variants have been reported. Other genetic conditions are associated with chondrocalcinosis. Gitelman's and Bartter's diseases are both associated with CPPD deposition, possibly due to their association with chronic hypomagnesemia. Magnesium is a cofactor of alkaline phosphatase, and it is postulated that these conditions lead to mild functional hypophosphatasia. Iron and copper overload, associated with haemochromatosis and Wilson's disease, respectively, are thought to favor calcium crystal nucleation as well as inhibiting alkaline phosphatase activity. Genetic factors could also participate in so-called sporadic cases, as a familial pattern has been identified in some case series of apparently sporadic CPPD deposition disease. However, the late onset of the arthritis phenotype makes family studies of CPPD deposition disease difficult.

A number of metabolic disease and physiologic stresses, such as aging and trauma, have been associated with CPPD crystal deposition (Table 13-1). Only aging and previous joint surgery have been proven to be associated. Nonetheless, circumstantial evidence suggests that many of these other associations are valid. Therefore, the routine study of a patient newly diagnosed with CPPD crystal deposition should include evaluation of serum calcium, ferritin, magnesium, phosphorus, alkaline phosphatase, and thyroid-stimulating hormone. Further studies should be obtained if abnormal values are found.

TABLE 13-1. CONDITIONS ASSOCIATED WITH CALCIUM PYROPHOSPHATE DIHYDRATE CRYSTAL DEPOSITION DISEASE.

Strongly associated
Age
Previous joint surgery
Osteoarthritis
Trauma
Gout
Hyperparathyroidism
Hemochromatosis
Hypophosphatasia
Hypomagnesemia
Weakly associated
Hypothyroidism
Potentially associated
Wilson's disease
Acromegaly
Hyaluronidase deficiency
X-linked hypophosphatemic rickets
Familial hypocalciuric hypercalcemia
Ochronosis

Pathogenesis of Inflammation and Cartilage Degeneration

Acute pseudogout is believed to represent a dose-related inflammatory host response to CPPD crystals shed from cartilaginous tissues contiguous to the synovial cavity. Phagocytosis of crystals by neutrophils, as invariably demonstrated by compensated polarized light microscopy in fluids removed from acutely inflamed joints of patients with pseudogout, results in the release of lysosomal enzymes and cell-derived chemotactic factors. Phagocytosis by synovial-lining cells leads to cell proliferation and release of prostaglandins, cytokines, and matrix metalloproteases capable of matrix degradation, such as collagenase and stromelysin.

The relationship between OA and CPPD deposition is complex. A study of SF sampled at the time of knee replacement demonstrated that 60% of 53 unselected patients with a preoperative diagnosis of OA contained either CPPD or hydroxyapatite or both (3). It has been suggested that most SF from patients with OA may contain CPPD or hydroxyapatite too small or too infrequent to detect by routine microscopy. The frequency of association of CPPD crystal deposits may result from the biological effects of CPPD crystals as they interact with fibroblasts or mononuclear synovial lining cells. These include a well-documented mitogenic response, resulting in tissue hypertrophy. Stimulated lining cells secrete proteolytic enzymes and cytokine release. Proteolytic enzymes may damage cartilage and other articular structures and cytokine release can enhance further

protease production by synovial lining cells or chondrocytes. Such effects have been demonstrated for CPPD crystals in vitro.

Pathogenesis of Crystal Deposition

Overproduction of extracellular PPi, the anionic component of the crystal, contributes to CPPD crystal deposition (4). Synovial fluid PPi concentration is elevated in most joints with CPPD deposition, in contrast to plasma and urinary excretion levels. Furthermore, chondrocytes from CPPD-containing cartilage produce more extracellular PPi than normal and OA control cartilages. Articular chondrocytes likely contribute to SF PPi because they liberate PPi, an effect which can be enhanced by transforming growth factor beta (TGF-beta), ascorbate, retinoic acid, and thyroid hormones. PPi may be made de novo by chondrocyte ectoenzymes, which hydrolyze nucleoside triphosphates. In addition, intracellular PPi may be transported across cell membranes by the multipass transmembrane protein ANK or other proteins. Calcium is also necessary for CPPD crystal formation and calcium concentrations are increased in cartilages from patients with CPPD.

Changes in the pericellular matrix and matrix vesicles (MV) of articular cartilage have been implicated in CPPD crystal formation. MV are small membrane-bound extracellular organelles that bud off chondrocytes which, when isolated from articular cartilage, can produce CPPD crystals in vitro. CPPD crystals are formed in areas of abnormal pericellular matrix, but not in normal matrix. Affected cartilage matrix contains damaged collagen type II fibers and increased calcium-binding matricellular proteins. Type I collagen, not usually present in normal cartilage, is found in increased quantities in CPPD-containing cartilage and fewer large proteoglycans are present. Current data also supports a role for transglutaminases, which post-translationally modify extracellular matrix proteins in CPPD crystal formation.

Clinical Features and Diagnosis

At least five clinical presentations have been associated with articular CPPD (5).

Pseudogout

Acute pseudogout is an inflammatory process manifest by joint effusions and symptoms and signs of articular inflammation in one or more joints. These self-limited attacks can be as abrupt in onset and as severe as acute gout. Patients typically experience pain, stiffness, and swelling in the affected joint. Signs include swelling with variable erythema and warmth. Systemic manifestations during an attack may include a fever of 99°F to 103°F, leukocytosis of 12,000 to 15,000 cells/mm^3 and elevated erythrocyte sedimentation rate (ESR) and serum acute phase reactants. Compared to true gout, pseudogout attacks may take longer to reach peak intensity, and are often considerably longer lasting than gout attacks, as symptoms can last 3 to 120 days despite therapy (6). Pseudogout is more common in large than in small joints. The knee is the most commonly involved joint, followed by the wrist, ankle, elbow, toe, shoulder, and hip. As with gout, pseudogout attacks can occur spontaneously or can be provoked by trauma, surgery, or post–parathyroidectomy or severe illness, such as stroke or myocardial infarction. Patients are usually asymptomatic between episodes. Differentiation from gout or septic joint may be difficult and requires arthrocentesis followed by culture and examination of the SF for crystals. About 25% of people with CPPD deposition exhibit the pseudogout pattern of disease.

Pseudo-Osteoarthritis

Most patients with clinically apparent CPPD crystal deposition have an unusually severe, oddly distributed, degenerative arthritis resembling OA. They present with the gradual onset of joint pain and stiffness, typically involving knees, wrists, metacarpophalangeal (MCP) joints, hips, shoulders, spine, elbows, and ankles. Half of these patients will have acute attacks superimposed on their chronic symptoms. Flexion contractures of the affected joints and deformities of the knees are common. Valgus knee deformities are especially suggestive of underlying CPPD crystal deposition. This type of presentation can be difficult to differentiate from OA and consequently may be significantly underrecognized. In one series, 30% of patients diagnosed with OA had CPPD crystals in their affected joints at the time of total knee replacement (3).

Pseudo–Rheumatoid Arthritis

About 5% of patients with CPPD deposition manifest multiple joint involvement with symmetric distribution and low grade inflammation. Accompanying morning stiffness, fatigue, synovial thickening, flexion contractures, and elevated ESR often lead to a misdiagnosis of rheumatoid arthritis. In addition, 10% of individuals with CPPD crystal deposits have low titers of rheumatoid factor, which provide further diagnostic confusion. The presence of high titer rheumatoid factor, anti-cyclic citrullinated peptide (anti-CCP) antibodies, and radiographic evidence of typical rheumatoid bony erosions favor the diagnosis of true rheumatoid arthritis.

Pseudo–Neuropathic Arthropathy

Some patients with CPPD deposition disease have a severe destructive monoarthritis similar to that seen in neuropathic joints. These patients have no neurologic abnormalities and yet present with a painful monoarthritis, associated with dramatic destructive radiographic changes. The natural history of patients with this type of CPPD deposition disease is not well described.

Lanthanic

Some individuals with radiographic or pathologic evidence of articular chondrocalcinosis have no clinically apparent arthritis. This finding has been termed *lanthanic CPPD deposition* and is of uncertain significance. These patients have not been rigorously studied to see if they develop signs and symptoms of clinical arthritis with a greater frequency than the unaffected population.

Calcium pyrophosphate dihydrate crystals are not commonly found in tissue other than cartilage. Even in synovium, CPPD crystals typically form in areas of chondrometaplasia. Tophaceous CPPD crystal deposits are well described and can cause nerve compression syndromes. Neurologic manifestations of CPPD deposition in the axial skeleton can occur. Spinal ligaments seem particularly prone to CPPD crystal deposition. Affected patients may present with myelopathy. Almost 25% of patients undergoing decompressive laminectomy for lumbar spinal stenosis had CPPD crystal deposits in their ligamenta flava. Clinically, patients with CPPD crystals had more acute onset of symptoms than those without CPPD crystals.

Diagnosis of CPPD-associated disease is most commonly and accurately made by identifying CPPD crystals by polarizing light microscopy in the SF of affected joints (Figure 13-1). The weak birefringence of CPPD crystals render them more difficult to discern than monosodium urate (MSU) crystals. They can be quite sparse in number. SF characteristics can vary from inflammatory to non-inflammatory in CPPD deposition disease. In pseudogout, SF may be turbid, watery, or hemorrhagic. Average white cell counts are in the region of 12,000 cells/mm^3 in pseudogout. Histologic examination of cartilage or synovial biopsies can be helpful as long as tissue preparation methods preserve crystals. Diagnostic criteria for CPPD deposition disease have been established (Table 13-2).

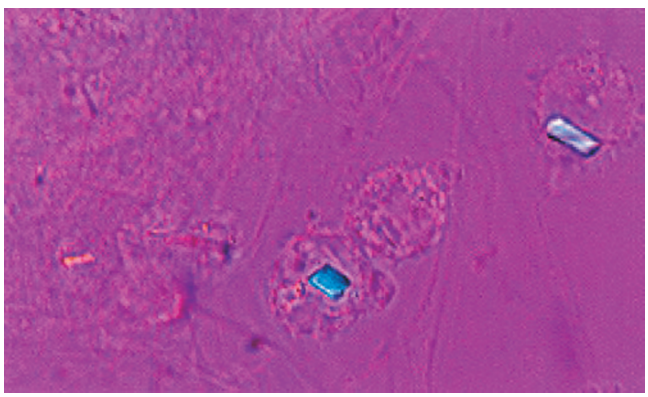

FIGURE 13-1

Rod-shaped calcium pyrophosphate dihydrate (CPPD) crystals in synovial fluid analyzed by compensated polarized light microscopy.

TABLE 13-2. REVISED DIAGNOSTIC CRITERIA FOR CALCIUM PYROPHOSPHATE DIHYDRATE CRYSTAL DEPOSITION DISEASE.

Criteria

I. Demonstration of CPPD crystals in tissue or synovial fluid by definitive means (e.g., characteristic x-ray diffraction or chemical analysis)

II. (a) Identification of monoclinic or triclinic crystals showing weakly positive or no birefringence by compensated polarized light microscopy
(b) Presence of typical radiographic calcification

III. (a) Acute arthritis, especially of knees or other large joints.
(b) Chronic arthritis, especially of knee, hip, wrist, carpus, elbow, shoulder, or metacarpophalangeal joint, especially if accompanied by acute exacerbations. The following features help differentiate chronic arthritis from osteoarthritis:
1. Uncommon site—wrist, metacarpophalangeal, elbow, and shoulder
2. Radiographic appearance—radiocarpal or patellofemoral joint space narrowing, especially if isolated (patella "wrapped around" the femur)
3. Subchondral cyst formation
4. Severity of degeneration—progressive, with subchondral bony collapse and fragmentation with formation of intra-articular radiodense bodies
5. Osteophyte formation—variable and inconstant.
6. Tendon calcifications, especially triceps, Achilles, obturators

Categories

A. Definite disease: Criteria I or II(a) plus II (b) must be fulfilled
B. Probable disease: Criteria II (a) or II (b) must be fulfilled
C. Possible disease: Criteria III (a) or III (b) should alert the clinician to the possibility of underlying CPPD crystal deposition

Radiographic Features

The typical appearance of punctate and linear densities in hyaline or fibrocartilagenous tissues is helpful diagnostically (Figure 13-2). The most characteristic sites of crystal deposition include knee articular cartilage and menisci, acetabular labrum of hip joint, fibrocartilagenous symphysis pubis, triangular cartilage of the wrist, and the annulus fibrosis of intervertebral discs. When the deposits are typical and unequivocal, the radio-

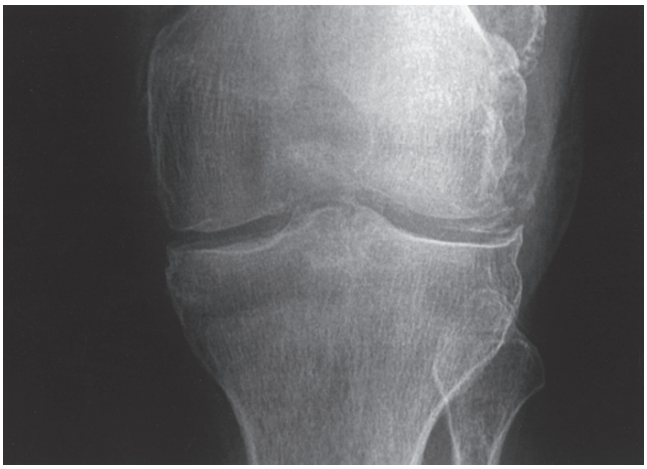

FIGURE 13-2

Chondrocalcinosis involving lateral meniscus of left knee.

graphic appearance is reasonably specific, but interpretation of atypical or faint deposits often is difficult. Calcific deposits also may appear in the articular capsule, ligaments, and tendons. Although the earliest calcific deposits occur in radiographically normal cartilage, degenerative changes often supervene. An individual can be screened for CPPD deposits with four radiographs: an anterposterior (AP) view of both knees (preferably not standing), an AP view of the pelvis for visualization of the symphysis pubis and hips, and a posteroanterior (PA) view of each hand to include the wrists. If these views show no evidence of crystal deposits, it is most unlikely that further study will prove fruitful.

Changes in the metacarpophalangeal joints, such as squaring of the bone ends, subchondral cysts, and hooklike osteophytes, are characteristic features of the arthritis associated with hemochromatosis (see Chapter 28), but are also found in patients with CPPD deposition alone. These changes occur more frequently in patients with CPPD crystal deposits and hemochromatosis than in those with only crystal deposits. In addition to the difference in pattern of affected joints, the finding of isolated patellofemoral joint space narrowing or isolated wrist degeneration differentiates CPPD from OA. Such differences may provide helpful clinical clues and are incorporated into the proposed diagnostic criteria given in Table 13-2 (7).

Treatment

In contrast to monosodium urate crystals in gout, there is no practical way to remove CPPD crystals from joints. Treatment of associated diseases, such as hyperparathyroidism, hemochromatosis, or myxedema, does not result in resorption of CPPD crystal deposits. Acute attacks in large joints can be treated through aspiration alone or aspiration combined with injection of corticosteroids. Nonsteroidal anti-inflammatory drugs (NSAIDs) are recommended for most patients. The effectiveness of oral colchicine is less predictable in pseudogout than in gout, but the number and duration of acute attacks are reduced significantly by colchicine taken on a daily basis for prophylaxis. Corticotropin or systemic corticosteroid therapy has been used successfully in patients with gout or pseudogout. Phosphocitrate is a promising agent that inhibits CPPD crystal formation and cellular responses to CPPD, but it is not currently clinically available.

Apatite/Basic Calcium Phosphates

Basic calcium phosphate crystals (BCP), consisting of carbonate-substituted hydroxyapatite, octacalcium phosphate, and, rarely, tricalcium phosphate, frequently deposit in articular tissues, but may also be found in skin, arteries, breast, and other tissues. In the musculoskeletal system, crystals may be found in tendons, intervertebral discs, joint capsule, synovium, and cartilage. Studies have suggested that dystrophic tendon calcification occurs as a consequence of local trauma, ischemia, and necrosis of tendons. Some evidence suggests that calcifying tendonitis is an active, cell-mediated process in which local vascular and mechanical changes result in focal transformation of tendinous tissues into fibrocartilagenous material containing chondrocytes. This is followed by local deposition of hydroxyapatite crystals within extracellular matrix vesiclelike structures derived from these chondrocytes. The mechanism of intra-articular BCP crystal deposition is incompletely understood but likely involves matrix vesicles and local dysregulation of extracellular PPi homeostasis. PPi is a potent inhibitor of apatite crystal nucleation.

Basic Calcium Phosphate Crystal Identification

Although BCP crystals are common, particularly in OA, their presence in SF is recognized infrequently because of the lack of a simple, reliable test for detection. Polarized light microscopy, which effectively identifies MSU and CPPD crystals, is unable to detect BCP crystals, which are too small to be resolved by light microscopy (20–100 nm). Despite the small size of individual crystals, they tend to aggregate into larger masses that occasionally may be observed by light microscopy as refractile "shiny coins" up to 5 mm in diameter. The larger BCP aggregates have been detected by Alizarin red S staining, but this method lacks sensitivity and

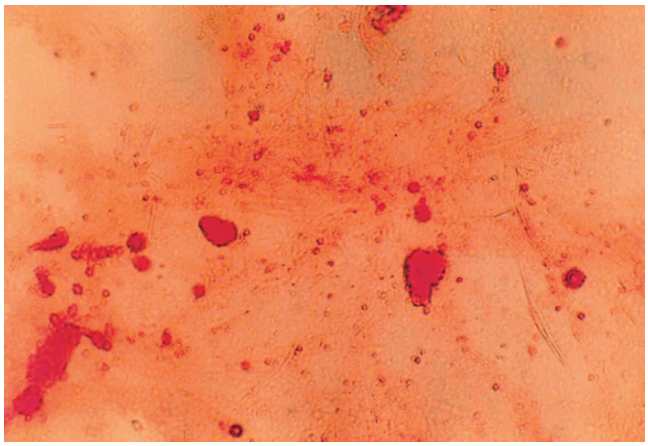

FIGURE 13-3

Alizarin red–stained clumps of apatite in joint fluid.

specificity (Figure 13-3). Techniques that are more specific for BCP crystal identification include x-ray diffraction, scanning or transmission electron microscopy with energy dispersive analysis, electron microprobe, Raman spectroscopy, atomic force microscopy, and a binding assay utilizing [^{14}C]ethane-1-hydroxy-1,1-diphosphonate. Unfortunately, these methods typically are unavailable or too costly for the handling of routine clinical specimens (8).

Clinical Features

Osteoarthritis

Concurrence of BCP crystals and OA is well established (9). The incidence of BCP crystals in SF from patients with knee OA is at least 30% to 60%. Indeed, it has recently been suggested that many OA fluids contain clusters of BCP crystals that are too small or too few in number to be identified by conventional techniques. Ample data supports the role of BCP crystals in cartilage degeneration as their presence correlates strongly with severity of radiographic OA, and larger joint effusions are seen in affected knee joints when compared with joint fluid from OA knees without crystals. Furthermore, in vitro studies of BCP crystal-induced cell activation support the active role of BCP in OA pathogenesis as they have numerous biologic effects, including the ability to induce mitogenesis in and matrix metalloproteases and prostaglandin synthesis by synovial fibroblasts and chondrocytes. Although the basis of cartilage damage by crystals has been the subject of numerous investigations, there are ongoing controversies concerning the relationship between calcium-containing crystals and OA and whether the crystals cause damage or are present as a result of joint damage. There is no known therapy for prevention or removal of BCP crystals from joints or for interfering specifically with the biological effects of BCP crystals.

Large Joint Destructive Arthritis/Milwaukee Shoulder Syndrome

A distinctive type of destructive arthropathy of the shoulder has been described in elderly individuals (10). Typically, these patients are elderly women and manifest large, non-inflammatory synovial effusions, severe radiographic damage, and large rotator cuff tears. Patients typically have pain on shoulder use and also pain at night. There is reduced active and passive range of motion, sometimes associated with pronounced joint instability. Marked bone-on-bone crepitus is typical. The rotator cuff is generally completely destroyed. Joint effusion may be massive and typically yields 5 to 130 mL of SF that is frequently blood tinged and has a low, predominantly mononuclear cell count. BCP crystals are identified in most fluids. Some contain CPPD crystals in addition. Radiographs typically show upward subluxation and deformity of the humeral head and calcification of the tendinous rotator cuff (Figure 13-4). Treatment is generally unsatisfactory. A conservative approach, including analgesics and NSAIDs and repeated shoulder aspirations with or without steroid injections, has sometimes controlled symptoms satisfactorily. Surgical intervention is sometimes successful. Pain may subside with time alone.

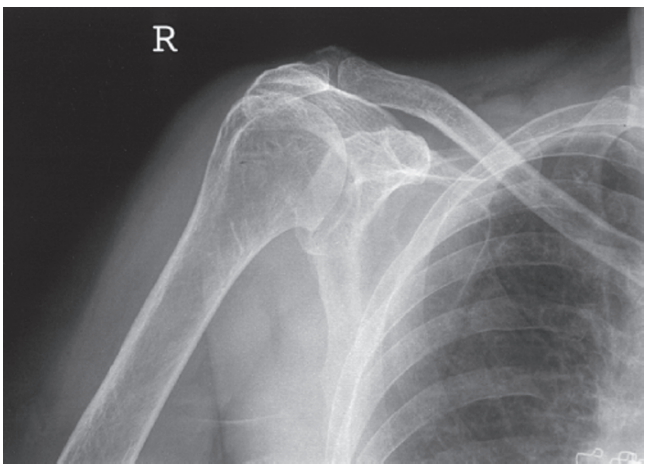

FIGURE 13-4

Anteroposterior radiograph of the shoulder joint affected by hydroxyapatite-associated destructive arthritis (Milwaukee shoulder). The extensive destruction of the periarticular tissues, including the rotator cuff, has led to instability of the shoulder with upward subluxation of the humerus. Note the associated glenohumeral degeneration and soft tissue evidence of joint effusion. Periarticular calcific deposition is noted at the acromioclavicular joint.

Calcific Periarthritis

Periarticular calcifications are occasionally observed on shoulder or other radiographs (Figure 13-4). The most common site of calcification is the rotator cuff. Most calcifications remain asymptomatic. If a patient has chronic shoulder pain, the radiographic finding of a calcification in the supraspinatus tendon or another tendon in the rotator cuff supports a diagnosis of chronic calcific tendinitis. In a few cases, particularly those with large calcific deposits, a severe attack of joint pain is precipitated by dispersal of crystals into surrounding tissues, the subdeltoid bursa, or the shoulder joint. These crystals elicit a major local inflammatory response. Patients present with severe pain and joint swelling, with warmth and erythema. The diagnosis is suspected upon radiographic observation of a rotator cuff calcification. Other diagnoses are likely to be considered, including sepsis, trauma, fracture, gout, or pseudogout. The radiographic features may evolve over time, with the calcific deposit becoming smaller, fragmenting, or disappearing. Needle aspirate of the calcific deposit may yield chalky material, and, in the case of the shoulder, may shorten the attack. Improvement also occurs following administration of NSAIDs or local corticosteroid injection. Ultrasound has been suggested as a method of breaking up calcific deposits. Untreated, the involved area may remain symptomatic for a few days or for several weeks. Smaller joints, such as the first metatarsal of the foot (hydroxyapatite pseudopodagra) and small joints of the hand, may undergo similar inflammatory attacks, particularly in younger women.

Acute Arthritis

In rare situations, BCP crystal may cause acute inflammation in joints. BCP crystal have been found in finger joints that exhibit inflammation and erosive changes. BCP crystal may have a role in inflammatory OA, a subgroup of OA associated with erythema, synovial thickening, and severe radiographic damage in proximal and distal interphalangeal joints of the hands.

Calcinosis/Idiopathic Tumoral Calcinosis

Calcinosis is the soft tissue deposition of BCP crystals. A wide variety of diseases has been associated with dystrophic calcification. Some of these conditions include the connective tissue diseases (limited scleroderma, myositis, systemic lupus erythematosus), calcification following following severe neurologic injury, and calcification following triamcinolone hexacetonide injection of joints. Idiopathic tumoral calcinosis is a rare syndrome characterized by the presence of irregular calcifying masses in periarticular soft tissue. These masses can be observed around the shoulders, hips, and elbows. They may be uni-or multifocal. Complications include skin ulceration with secondary infection, draining sinus, cachexia, and amyloidosis.

MISCELLANEOUS CRYSTALS

Oxalate Crystals

To date, oxalates have been described in joints of patients with overt renal failure only. Acute or chronic arthritis resulting from oxalate deposition can occur in a variety of joints, with the most frequently involved being the knees and hands. There are also reports of involvement of wrists, ankles, feet, tendon sheaths, and bursae. Joint fluid leukocyte counts are generally less than 2000/mm^3. Definitive diagnosis is by crystal identification in joint fluid or biopsy of joints, bones, or other tissues. SF crystals can be pleomorphic but characteristically include at least some with bipyramidal or envelopelike shapes. Sizes range from 5 to 30 μm. Most crystals are brightly birefringent although some of the smaller rod-shaped crystals could be confused with CPPD. Oxalate accumulation in hemodialysis patients may be slowed by avoiding use of vitamin C, which is metabolized to oxalate.

Depot Corticosteroid-Induced Iatrogenic Inflammation

Iatrogenic inflammation typically occurs during the first 8 hours following steroid injection. It appears more common following triamcinolone hexacetonide injection than with other preparations. Diagnosis can be supported by aspiration and identification of pleomorphic crystals that include irregular shaped rods and squares with intense positive or negative birefringence. Relief can be expedited by use of local ice packs.

Other Crystals with Possible Pathogenic Potential

These include liquid lipid crystals, cholesterol, other lipids, and foreign bodies. Management of inflammatory episodes related to these less common crystals generally involves NSAIDs when the clinical situation permits. Foreign bodies are best managed by removal.

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