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Calcium

Rebound Health
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PRINCIPLES of INTERNAL MEDICINE

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crorganisms. Synovial fluid in acute CPPD gout has inflammatory qualities. The white blood cell (WBC) count can range from several thousand cells to 100,000 cells/μL, the mean being about 24,000 cells/μL and the predominant cell being the neutrophil. Polarization microscopy usually reveals crystals with weak positive birefringence in the extracellular fluid and in neutrophils.

TREATMENT

Untreated acute attacks may last a few days to as long as a month. *Treatment* by joint aspiration (to decrease intraarticular pressure) and nonsteroidal anti-inflammatory agents or intraarticular glucocorticoid injection may result in return to prior status in 10 days or less. For patients with frequent recurrent attacks of CPPD gout, daily prophylactic treatment with low doses of colchicine may be helpful in decreasing the frequency of the attacks. Severe polyarticular attacks usually require short courses of corticosteroids. Unfortunately, there is no effective way to remove CPPD deposits from cartilage and synovium. Uncontrolled studies suggest that radioactive synovectomy (with yttrium 90) or the administration of antimalarial agents may be helpful in controlling persistent synovitis. Patients with progressive destructive large joint arthropathy usually require joint replacement. There is no subsequent increased risk of soft tissue heterotopic calcification around the prosthesis.

Table 323-2

Conditions Associated with HA Deposition Disease

Aging
Osteoarthritis
Hemorrhagic shoulder effusions in the elderly (Milwaukee shoulder)
Destructive arthropathy
Tendinitis, bursitis
Tumoral calcinosis (sporadic cases)
Disease-associated
Hyperparathyroidism
Milk alkali syndrome
Renal failure/long-term dialysis
Connective tissue diseases (e.g., progressive systemic sclerosis, CREST syndrome, idiopathic myositis)
Heterotopic calcification following neurologic catastrophes (e.g., stroke, spinal cord injury)
Hereditary
Bursitis, arthritis
Tumoral calcinosis

HA = Hydroxy-Apatite

CALCIUM HA DEPOSITION DISEASE **Pathogenesis** HA is the primary mineral of bone and teeth. Abnormal accumulation can occur in areas of tissue damage (dystrophic calcification), in hypercalcemic or hyperparathyroid states (metastatic calcification), and in certain conditions of unknown cause (Table 323-2). In chronic renal failure, hyperphosphatemia enhances HA deposition both in and around joints.

HA may be released from exposed bone and cause the acute synovitis occasionally seen in chronic stable osteoarthritis (e.g., "hot" Heberden's nodes). HA deposition is also an important factor in an extremely destructive chronic arthropathy of the elderly that occurs most often in knees and shoulders (Milwaukee shoulder). Joint destruction is associated with attenuation or rupture of supporting structures, leading to instability and deformity. Progression tends to be indolent, and synovial fluid WBC counts are usually less than 1000 cells/μL. Symptoms range from minimal to severe pain and disability that may lead to joint replacement surgery. Whether severely affected patients merely represent an extreme synovial tissue response to the HA crystals that are so common in osteoarthritis is uncertain. Observations that favor the idea that articular HA deposition and joint destruction constitute a unique entity rather than just a sequel of osteoarthritis include the following. (1) Primary osteoarthritis of the shoulders is infrequent. (2) High levels of activated collagenase and neutral protease, as well as fragments of collagen, have been found in the noninflammatory synovial fluids of patients with severe HA arthropathy; the concentration of these enzymes exceeded those found in rheumatoid arthritis and uncomplicated osteoarthritis. (3) Synovial membrane tissue cultures exposed to HA (or CPPD) crystals markedly increased release of these enzymes, underscoring the destructive potential of abnormally stimulated synovial lining cells.

Clinical Manifestations Periarticular and articular deposits may coexist and be associated with acute and/or chronic damage to the joint capsule, tendons, bursa, or articular surfaces. The most common sites of HA deposition include those in and/or around the knees, shoulders, hips, and fingers. Clinical manifestations include asymptomatic radiographic abnormalities, acute synovitis or tendinitis, and chronic destructive arthropathy. Most patients with HA arthropathy are elderly. Although the true incidence of HA arthritis is not known, 30 to 50 percent of patients with osteoarthritis have HA microcrystals in their synovial fluid. Such crystals can frequently be identified in clinically stable osteoarthritic joints, but they are more likely to come to attention in persons experiencing acute or subacute worsening of joint pain and swelling. The synovial fluid WBC count in HA arthritis is usually low (<2000 cells/μL) but may at times have as many as 50,000 cells/μL. Most synovial fluid analyses reveal a predominance of mononuclear cells. Occasionally, neutrophils may dominate.

Diagnosis Radiographic findings in HA arthropathy are not diagnostic. Intra- and/or periarticular calcifications with or without erosive, destructive, or hypertrophic changes may be present. X-ray films also may be normal.

Definitive diagnosis of HA arthropathy depends on identification of crystals from synovial fluid or tissue (Fig. 323-2). Individual crystals are very small, nonbirefringent, and can only be seen by electron microscopy. Clumps of crystals may appear as 1- to 20-μm shiny intra- or extracellular globules that stain purplish with Wright's stain and bright red with alizarin red S. Absolute identification depends on electron microscopy with energy-dispersive elemental analysis, x-ray diffraction, or infrared spectroscopy.

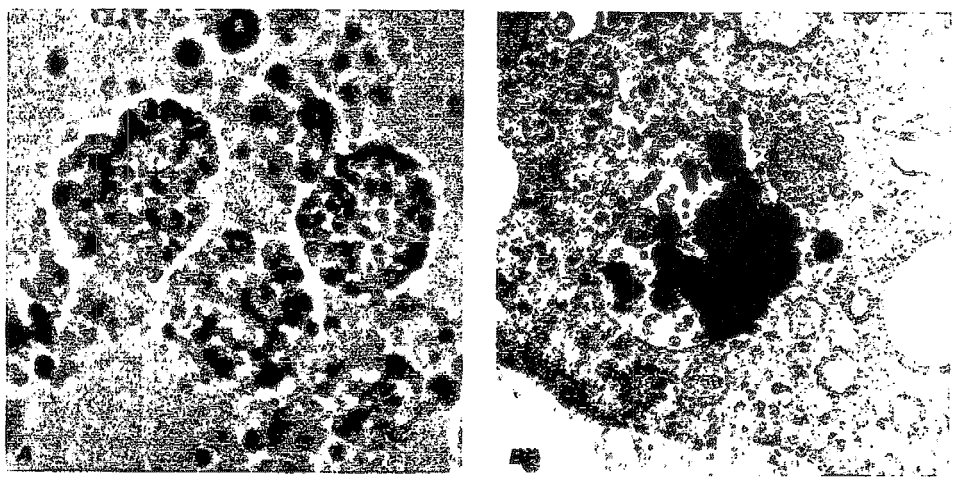

FIGURE 323-2 *A.* Cytoplasmic round inclusions inside synovial fluid cells represent aggregates of apatite crystals (fresh preparation, ordinary light microscopy; 288×). *B.* An electron micrograph demonstrates a cluster of dark apatite crystals within a synovial fluid mononuclear cell (21,600×).