ANIMAL MODEL OF HUMAN DISEASE

Calcium Pyrophosphate Deposition Disease (CPDD) in Nonhuman Primates

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Biologic Features

Calcium pyrophosphate deposition disease (CPDD) is a metabolic disease of human articular cartilage which results in a degenerative arthropathy. Other crystalline structures have been identified as important etiologic factors of acute and chronic arthropathies. Multiple joints arthropathies have been associated with urate,6 hydroxyapatite,5,9 and calcium hydrogen phosphate dihydrate2,3 crystals. Only one case of pyrophosphate crystal deposition in a dog synovial membrane has been reported.1

A naturally occurring CPDD arthropathy in a rhesus breeding colony has been identified.4 The acute form has been identified following episodes of acute trauma and involves primarily the knee and elbow joints; however, any joint may be affected. The acute disease has been identified in animals ranging in age from 6 months to 20 years. The chronic form of the disease being manifest in rhesus monkeys of all ages as joint rigidity, marked atrophy of the musculature, and a degenerative arthropathy. Mild acute synovial infiltrate consisting primarily of neutrophils and macrophages is observed with a mild degenerative arthropathy in the acutely affected animals. A moderate proliferative synovitis is present in the chronically

Figure 1—Scanning electron micrograph of an articular surface of a rhesus monkey with CPDD. A tendency to cluster around elevated chondrocyte areas is evident.

Figure 2—Scanning electron micrograph of a synovial membrane surface of a rhesus monkey with CPDD. A laminated crystal is shown (arrow).

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involved joints characterized by a prominent synovial cell layer admixed focally with neutrophils.

Birefringent crystals, perilacunar in location, can be observed by scanning electron microscopy in the articular cartilage (Figure 1) that has been processed without demineralization. These crystals are located in all zones of the cartilage. Scanning electron microscopic study of the articular surface and synovial membrane demonstrates flat lamellar crystal structures projecting into the joint cavity (Figure 2). Crystals appear to cluster, suggesting an orientation to the chondrocyte. With the use of energy-dispersive elemental X-ray analysis (EDAX), the crystal composition consists of equal amounts of calcium and phosphorous (Figures 3–5), indicating that the crystals are calcium pyrophosphate (Ca$_3$P$_2$O$_7$). The pathogenesis of CPDD has not been determined, even though all information suggests that it is related to "metabolic turnover" of the pyrophosphates (ppi), which are cellular by-products of cartilage cell metabolism. The crystals in the joint represent a "shedding" process from the articular hyaline cartilage eliciting an acute inflammatory reaction.

Figure 3 — Secondary electron image analysis of a crystal subjected to EDAX. The crystal is composed of 53.37 phosphorus and 46.63 calcium (atomic %).

Figure 4 — Surface crystal localization of phosphorus using EDAX analysis. The lighter colored areas represent higher concentrations of phosphorus.

Figure 5 — Surface crystal localization of calcium using EDAX analysis. The lighter colored areas represent higher concentrations of calcium.
Comparison With Human Disease

The common denominator in all cases of CPDD in primates suggests previous trauma as an initiating factor. This follows very closely the observation of CPDD in man, in which joint trauma antedated the joint symptoms. The crystal morphology, primary localization within hyaline cartilage, multiple joint involvement, and gross, microscopic, and scanning electron microscopic features are similar in both rhesus monkeys and man. The complete pathogenesis of the disease in either man or monkey has not been determined.

Usefulness of the Model

The identification of CPDD as a naturally occurring disease in the rhesus monkey affords an opportunity to study the pathogenesis of this disease under controlled laboratory conditions. Although the disease has been identified, it has not been experimentally reproduced. The events leading up to the acute form suggest a mechanism related to trauma and/or hemarthrosis.

Availability

The disease (CPDD) has been identified in the breeding colony at Tulane Delta Regional Primate Research Center.

References