

Calcium Pyrophosphate Disease (CPPD) / Pseudogout

Introduction:

CPPD, like gout, is a form of arthritis caused by crystals that induce inflammation within the joint space. For this reason, this condition is also known as “pseudogout” (i.e. – mimicking gout). Unlike gout, however, which is caused by uric acid crystals, CPPD is caused by calcium-containing crystals. These crystals have a tendency to accumulate along damaged cartilage surfaces within joints. Deposits of these crystals can be seen in up to 4% of the adult population at some time during life, and the prevalence of these deposits increases with age to the point that about 1/2 of those in their 80s will demonstrate evidence for these deposits on x-ray. Most individuals will experience no symptoms as a result of these calcium deposits. Those who do, however, may develop joint inflammation in a variety of different patterns. Features of CPPD: CPPD may result in different degrees of inflammation in different patients. Three basic types of arthritis are observed: acute arthritis flares of one joint, chronic inflammation of many joints, and rapidly progressive degeneration of the cartilage of an affected joint. Many patients with CPPD will develop acute episodes of joint pain, swelling, warmth, and possibly redness. Fever may also be present during these attacks. Surgery or serious illness may trigger a disease flare. It is this form of CPPD that is referred to as pseudogout because of the similarity of these episodes with gout. The most commonly affected joint is the knee, followed by the wrist. Less commonly, hand joints may be involved, or the joint at the base of the big toe may become inflamed (causing further confusion with gout). Other patients may develop inflammation of several joints at once. This inflammation is usually less intense but more widespread. When hand and wrist joints are inflamed in this manner, CPPD can resemble rheumatoid arthritis (RA), although RA generally results in more joint destruction. Finally, some individuals with CPPD appear to have a rapid progression of joint damage that resembles severe osteoarthritis (OA). Signs of inflammation are even less pronounced in this subset of patients. It is believed that the presence of the calcium crystals more rapidly strips away the lining of the cartilage. In many, it may be difficult to determine if the calcium deposits are causing any damage in the joint or are simply present by coincidence. Again, the knee is commonly affected, just as we see in those with ordinary OA. Because the wrist, elbow, and certain knuckles are rarely involved in OA alone, CPPD must be considered as a diagnosis.

Diagnosis:

CPPD should be considered as a possible diagnosis if patients exhibit any of the different patterns of joint pain or swelling noted above. The findings of swelling or warmth on physical examination suggest that any kind of inflammatory arthritis could be present. It is only by investigating further that CPPD can be sorted out from other conditions.

X-rays often demonstrate calcium deposits in involved joints, particularly the knee and the wrist. These deposits often have the appearance of a thin white rim lining the cartilage. While a swollen and inflamed joint coupled with the finding of soft tissue calcium deposits within the joint suggests the diagnosis, as mentioned above, many people over the age of 65 with no joint symptoms may demonstrate these calcium deposits on x-ray.

Examining a sample of joint fluid is a more accurate way of making a diagnosis. Not only can the diagnosis of CPPD be confirmed, but other possible problems, such as acute joint infection, can be ruled out. A drop of fluid can be examined under a device known as a polarized light microscope for calcium crystals, which can be distinguished from uric acid crystals found in gout by an experienced physician. There are certain obstacles to finding the calcium crystals within the joint fluid sample. The crystals of CPPD are more difficult to see under the microscope than the crystals found in gout. If the fluid is not examined within about 6 hours, the crystals may disappear. Also, the joints may not be as inflamed in certain patients with CPPD, and there may be less fluid to aspirate. To make matters more confusing, a certain number of patients have both gout and CPPD.

Laboratory tests do not help diagnose CPPD, but they do help investigate other diseases that may be associated with this condition. Over-activity of the parathyroid gland, which controls calcium levels in the body, under-activity of the thyroid gland, low magnesium levels, and a disease causing iron overload known as hemochromatosis are all seen in increased frequency in patients with CPPD and should be considered and screened for with blood tests. While identifying these associated diseases is important, treating them does not remove calcium crystal from the joint or reduce joint symptoms. CPPD still must be treated separately.

Therapy:

Treatment of CPPD may be either intermittent for acute flares or daily for chronic joint disease. The inflammation of CPPD can be treated much in the same way we treat gout. The major difference, however, between the two disorders is that long-term therapy for gout results in uric acid crystals being eliminated from the joint, while no such therapy exists for CPPD.

Non-steroidal anti-inflammatory drugs (NSAIDs) reduce symptoms and joint swelling in most individuals with CPPD and may be sufficient to treat the majority of patients. Ibuprofen (Motrin), naproxen (Naprosyn), and indomethacin (Indocin) are commonly used NSAIDs but increase the risk for damage to the stomach, potentially leading to ulcers in certain patients at risk. This risk is reduced when using COX-2 selective NSAIDs such as celecoxib (Celebrex) or valdecoxib (Bextra) as well as the partially COX-2 selective drug meloxicam (Mobic).

Corticosteroids may be administered in many different forms. Most often, these agents are more appropriately given during an acute flare rather than for chronic inflammatory joint disease due to the side effects of long-term therapy (thinning of the bones, elevation of blood sugar, weight gain, cataracts, etc.). While withdrawing fluid from the joint, injecting steroids directly into the joint often provides prompt relief of swelling and pain. Intravenous infusions or injections into the muscle are rarely required to treat severe flares involving multiple joints. Oral corticosteroids can also be given short-term with few side effects; when given chronically, doses of less than 10 mg/day of prednisone or its equivalent should be used.

Colchicine is usually given orally for acute flares. Intravenous colchicine may be more effective in this setting but has the potential risk of suppressing the bone marrow's production of blood cells. Low doses of oral colchicine given once to twice daily for those with frequent attacks of joint inflammation may reduce the frequency and/or severity of these episodes. The response seen in patients with chronic ongoing inflammatory arthritis is variable, and diarrhea is a side effect that may limit this approach. None-the-less, low cost and relatively few side effects make colchicine an option worth attempting in certain patients with CPPD.

Phosphocitrate is a medication in experimental stages of development that seems to prevent formation of CPPD crystals as well as other less common calcium crystals. Studies have not yet established what role this agent may have in treating CPPD long-term.