Epidemiology of Calcium Pyrophosphate Crystal Arthritis and Basic Calcium Phosphate Crystal Arthropathy

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KEYWORDS

• Calcium pyrophosphate crystal deposition • Calcium pyrophosphate crystal
• Basic calcium phosphate crystal • Epidemiology

KEY POINTS

- Calcium pyrophosphate (CPP) and basic calcium phosphate (BCP) crystal deposition may be asymptomatic, or cause arthritis, commonly in the elderly.
- CPP deposition (CPPD) is common, and strongly associates with age and osteoarthritis (OA), although it does not seem to associate with OA progression.
- Hyperparathyroidism, hemochromatosis, hypomagnesemia, and hypophosphatasia are other recognized risk factors for CPPD.

INTRODUCTION

Calcium pyrophosphate (CPP) and basic calcium phosphate (BCP) crystal deposition may be asymptomatic, or cause arthritis, commonly in the elderly. Although CPP crystals predominantly deposit intra-articularly, abnormal BCP crystal deposition occurs in both intra-articular and periarticular locations. However, it is difficult to study their epidemiology because their presence is frequently asymptomatic. Any estimate of incidence and prevalence is further impaired by the fact that synovial fluid aspiration is required to definitively establish their presence. Moreover, BCP crystals are identified with confidence only by sophisticated techniques such as electron microscopy and x-ray diffraction, which are not available routinely. Thus, the epidemiologic studies of CPP and BCP crystal deposition use radiographic calcification as a surrogate.

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Within these limitations, the epidemiology of CPP deposition (CPPD) and BCP deposition are described in this review.

Epidemiology of CPPD

The first description of articular cartilage calcification is attributed to Robert Adams, a Dublin surgeon (c. 1854).[1] Radiographic articular cartilage calcification (chondrocalcinosis [CC]) was first described in the late 1920s,[2,3] and was identified as the cardinal manifestation of a distinct disease entity (chondrocalcinosis articularis) by Zitnan and Sitaj.[4] In 1962, McCarty and colleagues[5] identified CPP crystals in joints of patients with apparently acute gouty arthritis with or without coexistent CC. Subsequently, other calcium phosphate crystals (such as hydroxyapatite, brushite, and octacalcium phosphate) were shown in joints with CC, suggesting that CC is not exclusively caused by CPPD.

Over the last 50 years, the clinical classification of CPPD has evolved from a complex system based on phenotypic similarity with several other conditions (eg, pseudogout, pseudo-rheumatoid arthritis, pseudo-osteoarthritis), to a simple system that recognizes the key manifestations of CPPD (**Box 1**).[6] Of these manifestations, the epidemiology of CC, and osteoarthritis (OA) with CC have been relatively well studied. The epidemiology of acute CPP crystal arthritis, chronic CPP crystal inflammatory arthritis, and other pseudosyndromes associated with CPPD have not been examined formally.

Joints affected by CPPD

CPPD occurs in the knees, wrists/symphysis pubis, and hips, in descending order of frequency.[7–9] Studies are conflicting as to whether the wrist or the symphysis pubis is the second most commonly affected joint. Although previous studies reported that it is rare to have CC at other joints in the absence of knee involvement, a recent cross-sectional plain radiographic study suggested that up to 40% of participants with CC do not have knee involvement.[10]

Incidence

The incidence of CPPD has not been studied in the general population. However, in middle-aged and older adults with knee OA without knee CC at baseline and followed up for 8 to 12 years, the estimated annual incidence of radiographic knee CC was 0.8% to 2.1%, and that of CPPD (CPP crystals or CC) at the knee was 2.7% to 5.5%.[11–14]

Box 1
Classification of CPPD

Asymptomatic CPPD: CPPD with no apparent clinical consequence (ie, isolated CC)

OA with CPPD: CPPD in a joint that also shows changes of OA, on imaging or histologic examination

Acute CPP crystal arthritis: acute-onset, self-limiting synovitis with CPPD (previously pseudogout)

Chronic CPP crystal inflammatory arthritis: chronic inflammatory arthritis associated with CPPD

Data from Zhang W, Doherty M, Bardin T, et al. European League Against Rheumatism recommendations for calcium pyrophosphate deposition. Part I: terminology and diagnosis. Ann Rheum Dis 2011;70(4):563–70.