OMCR

Oxford Medical Case Reports, 2019;5, 199–201

doi: 10.1093/omcr/omz030
CASE REPORT

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Calcium crystal-associated arthropathy mimicking a febrile systemic inflammatory disease in an elderly patient

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Abstract

Crystal formation and deposition in the joints is an important and common cause of acute arthritis. The disease may present with fever and systemic signs. In this report, we describe the case of a 70-year-old man, who presented with a sudden and incapacitating polyarthritis of large and small joints, fever, asthenia and leukocytosis. After extensive investigation, radiography of the joints showed the presence of chondrocalcinosis. A few days after the beginning of the treatment with colchicine, he became completely asymptomatic, drawing one's attention of calcium crystal-associated arthropathy as a cause of febrile systemic inflammatory disease particularly in elderly population.

INTRODUCTION

Crystal formation and deposition of monosodium urate or calcium pyrophosphate in the joints is an important and common cause of acute arthritis. In elderly, calcium pyrophosphate dihydrate deposition disease (CPPD) is the leading cause of acute arthritis. The highest risk groups for CPPD, besides elderly, are individuals with osteoarthritis, history of trauma, genetic and metabolic disturbances such as hemochromatosis, hyperparathyroidism and hypomagnesemia [1,2].

When the disease presents with fever and systemic signs, it can lead to a misdiagnosis and inappropriate treatment.

Herein, we report the case of a patient with an atypical clinical presentation of acute polyarthritis of large and small joints associated with fever and systemic inflammatory symptoms secondary to a calcium crystal-associated disease.

CASE REPORT

A 70-year-old man was admitted to our hospital with fever and diffuse pain, mainly in cervical area and right shoulder initiated 4 days before the admission. Soon after the hospitalization, he presented with polyarthritis in elbows, wrists, hands, knees and ankles. Three weeks before the present hospitalization, he had a self-limited diarrhea secondary to rotavirus infection. He had no remarkable family history. At physical examination, the patient was bedridden because of pain. He had tachycardia, fever (38°C) and evident polyarthritis in the right wrist, knees, elbows, shoulders, right ankle and right midfoot. The rest of the physical examination was unremarkable. Laboratory tests revealed hemoglobin of 14 mg/dL, total white blood count of 26.690 cells/mm^3 with no shift deviation, erythrocyte sedimentation rate of 120 mm and c-reactive protein of 5.14 mg/dL (normal

Received: November 20, 2018. **Revised:** February 7, 2019. **Accepted:** February 24, 2019

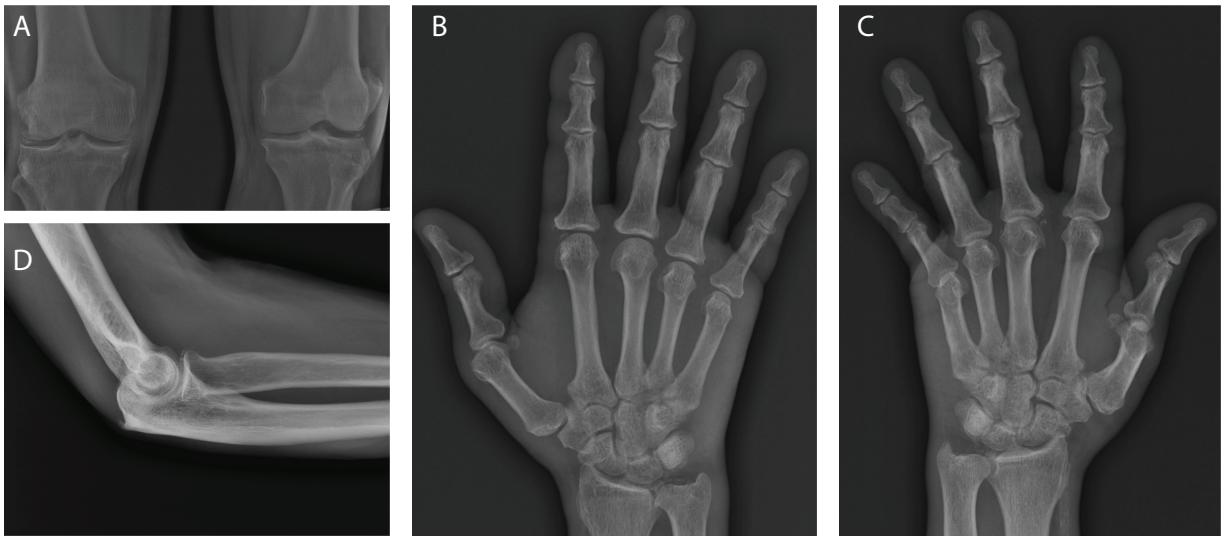

Figure 1: Radiographs showing chondrocalcinosis in meniscus of the knee, fibrocartilage of the wrist and elbow.

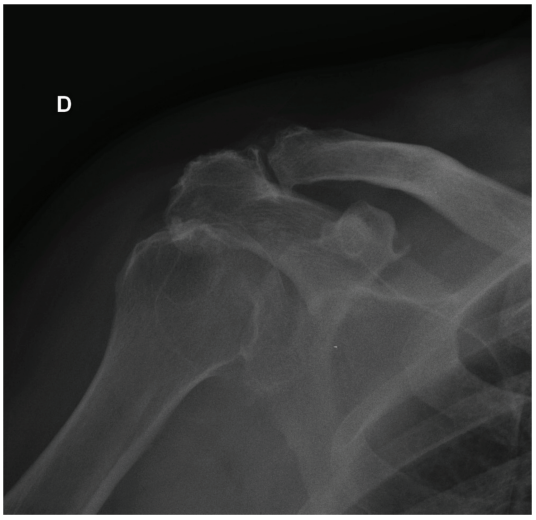

Figure 2: Radiograph of the right shoulder revealing joint space narrowing and irregularity of the glenohumeral bone surface compatible with 'Milwaukee shoulder'.

range up to 0.5 mg/dL). He had negative serology for dengue, B and C hepatitis, human immunodeficiency virus and syphilis. Urine culture was negative. Serum uric acid was within the normal range, and the patient had no history of hyperuricemia. The renal function (cretinine = 0.7 mg/dL; creatinine clearance estimate by Cockcroft–Gault = 104.17 mL/min), electrolytes (calcium, phosphorus and magnesium) as well as thyroid function and parathyroid hormone were normal. Transesophageal echocardiography had no evidence of vegetation. Plane radiographs of the joints demonstrated chondrocalcinosis in meniscus of the knees, fibrocartilage of the wrists, metacarpophalangeal joints and elbows articular cartilage (Fig. 1). The right shoulder had joint space narrowing and irregularity of the glenohumeral bone surface resembling the one observed in the Milwaukee shoulder syndrome (Fig. 2). Unfortunately, we were not able to perform a study to define the type of crystal present in his joints because polarized light microscopy for crystal search was not available in this service.

A regimen of 20 mg/day prednisone was initiated for symptomatic relief of the pain, with only partial improvement. Assuming a presumptive diagnosis of CCPD, colchicine 1 mg/day was started. The patient presented rapid improvement of his arthritis and fever within 48 h of the introduction of colchicine even with the suspension of the corticosteroids. He was discharged in use of colchicine, walking normally without fever and no other complaints.

DISCUSSION

CPPD is a prevalent and important differential diagnosis of acute arthritis in the elderly [2,3]. The most common sites for crystal deposition are the fibrocartilages and hyaline cartilages (e.g. knee menisci, wrist triangular cartilage, hip and glenohumeral joint). Less commonly, CPP can be found in periarticular tissues as spinal ligaments and Achilles tendon [4].

When the crystals are formed, they can interact with plasma cell membrane, leading to activation of NLRP3 inflammasome-IL-1β pathway, the main mechanism of inflammation [5]. Once released, IL-1β will lead to endothelial cells activation, neutrophils recruitment and release of other inflammatory mediators, such as TNF-α, which may contribute for the development of arthritis and systemic manifestation of CPPD [6,7].

The acute form of the disease is characterized by sudden onset of monoarthritis, generally in elderly women, usually of large joints, most commonly knees, wrists, shoulders or elbows. Acute attacks are self-limiting similar to what occurs in acute gout, which is the reason why CPPD has also been known as pseudogout [2]. On the other hand, sometimes, CPPD can present as polyarthritis, and it can be associated with systemic manifestations such as fever, increased acute phase reactant levels and leukocytosis mimicking an infectious disease as was observed in the present case [8–10]. Moreover, some case reports have shown CPPD as a cause of altered mental status in elderly, which improved after treatment [9–11]. In this scenario, the presence of infection should always be excluded due to its potential morbidity.

Another febrile syndrome associated with crystal deposition is called crowned dens syndrome, which is caused by the deposition of crystal around the odontoid process. It manifests as

recurrent attacks of fever, neck stiffness and is an important differential diagnosis with meningitis, spinal tumor or infectious spondylitis [12].

The destructive arthropathy-type Milwaukee shoulder syndrome observed in our patient has been classically related to deposition of basic calcium phosphate (BCP) crystals, but it has also been described in association with CPPD [13,14]. In our case, the presence of chondrocalcinosis in meniscus of the knees and in the fibrocartilage of the wrist would corroborate the diagnosis of CPPD. Moreover, to the best our knowledge, there is no description of polyarticular systemic form of BCP crystal deposition. However, a study performed in cadavers demonstrated that radiological chondrocalcinosis is not specific for the chemical composition of the crystal as a high prevalence of BCP crystals was observed in joints with chondrocalcinosis [13]. Thus, we cannot exclude the possibility of the presence of two types of crystals simultaneously in the joints of our patient [14].

The diagnosis of febrile CPPD polyarthritis in elderly largely relies on the examination, medical history and musculoskeletal exam by the attending physician in addition to joint aspiration and search for crystals. A detailed study of the synovial fluid and the type of crystal in this clinical scenario is recommended as part of the investigation of unexplained arthritis [15,16]. Not having performed a synovial fluid analysis is a limitation of our study. However, polarized light microscopy is available only in a few specialized laboratories in our region. In this particular case, it was an elderly patient that had acute polyarticular arthritis and calcifications in fibrocartilage complex in wrists and knees, suggesting calcium pyrophosphate deposition. Besides that, from the practical point of view, the therapeutic strategy is similar for both CPPD and BCP crystal deposition. Indeed, the good response to colchicine reinforces the diagnosis of disease for deposition of crystals although not discriminating the type of crystal.

ACKNOWLEDGEMENTS

M.S. is currently receiving a scholarship from Conselho Nacional de Desenvolvimento Científico e Tecnológico.

CONFLICT OF INTEREST STATEMENT

None declared.

ETHICAL APPROVAL

The case report did not require the ethical board approval.

CONSENT

Consent has been obtained from the patient.

GUARANTOR

Mittermayer Santiago is a guarantor of the article.

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