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Case Report / Olgu Sunumu

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CPPD-related pseudoneuroarthropathy in a patient with myelodysplastic syndrome

Miyelodisplastik sendromlu bir olguda CPPD ilişkili psödonöroartropati

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Abstract

The calcium pyrophosphate deposition (CPPD) disease is a common form of crystal arthropathy. It usually affects elderly patients. The clinical and radiological features of CPPD vary widely, so CPPD is a great mimicker of other musculoskeletal conditions. Asymptomatic and destructive forms can present at the same time in the same patients. Several diseases have been proposed to be related to CPPD, but hematologic disorders have not been reported to occur concurrently. Charcot arthropathy (CA) is associated with neuropathy and is characterized by erosive joint disease. Here, we report an interesting CPPD case presenting as pseudo-CA in a patient with myelodysplastic syndrome.

Keywords: Chondrocalcinosis, pseudoneuroarthropathy, myelodysplastic syndromes, pyrophosphate arthropathy, pseudogout

Öz

Kalsiyum pirofosfat depozisyon (CPPD) hastalığı kristal artropatilerin yaygın bir formudur. Genellikle yaşlı bireyleri etkiler. CPPD'nin radyolojik ve klinik özellikleri değişken olup bu yüzden kas-iskelet sistemi hastalıklarının iyi bir taklitçisidir. Asemptomatik ve destrüktif formları aynı hastada aynı anda bulunabilir. CPPD ilişkili birçok hastalık tanımlanmış olup hematolojik hastalıklarla ilişkisine dair kanıt yoktur. Charcot artropatisi (CA) nöropatik hastalıklarla ilişkisi olup eklem erozyonları ile karakterizedir. Makalemizde miyelodisplastik sendromlu bir hastada psödo-CA ile prezente olan enteresan bir CPPD olgusunu sunuyoruz.

Anahtar Kelimeler: Kondrokalsinozis, psödonöroartropati, miyelodisplastik sendrom, pirofosfat artropatisi, psödogut

Introduction

The calcium pyrophosphate deposition (CPPD) disease is a crystal arthropathy that is caused by calcium pyrophosphate dihydrate (CPP) crystals. The clinical spectrum varies widely among patients; acute or chronic, monoarticular or polyarticular, and destructive or non-destructive patterns are possible.[1] CPPD prevalence is 4.5% in the adult United Kingdom population and correlates with increasing age (aged 55-59: 3.7%, aged 80-84: 17.5%); the presentation is uncommon in patients younger than 50 years of age. There was no difference in prevalence between men and women.[2] In the literature, the first patient with CPPD is reported by McCarty DJ and coworkers in 1961 by the identification of CPP crystals from arthritic knee joints.[3]

In the following years, the other clinical forms were defined and two characteristic issues stood out for CPPD; it has a heterogeneous clinical spectrum and is a good mimicked for other rheumatic diseases. McCarty DJ classified CPPD into 6 forms; type A: Pseudogout, type B: Pseudorheumatoid arthritis, type C or D: Pseudoosteoarthritis with acute attacks or without inflammation, type E: Asymptomatic CPPD, and type F: Pseudoneuropathic form.[4] In 2011, Europan League Against Rheumatism (EULAR) suggested "asymptomatic CPPD, osteoarthritis with CPPD, acute CPP crystal arthritis, and chronic CPP crystal arthritis" as a definitions because the term "pseudo" may confuse.[5] For example, some patients can have different clinical forms of CPPD simultaneously according to McCarty's classification.[1] Chondrocalcinosis (hyaline cartilage or fibrocartilage) is

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the main hallmark of CPPD and usually appears; synovial/capsule/tendons/ligaments/bursae calcifications, tumoral deposition, joint space narrowing, subchondral sclerosis and cysts, osteophytes, osseous fragmentation, and bone erosions are the other signs of CPPD. The most commonly affected joint is the knee, but the ankle is an uncommon site for CPPD.[6] In this article, we report an intriguing CPPD case who of bilateral ankle/foot arthritis.

Case Report

In May 2021, a 64 years-old male hematology inpatient with a recent diagnosis of myelodysplastic syndrome (MDS) presented with a two month history of swollen ankles and consulted with our rheumatology department. He was an asymptomatic hepatitis-B virus (HBV) carrier. His family history was unremarkable. He never smoked and did not use alcohol or any illicit drug.

On physical examination, bilateral warm, erythematous, very painful ankle arthritis and pale conjunctiva were examined; there were no other signs or symptoms. Vital signs were normal. Arthritis began acutely and progressed during the two months. There wasn't any history of gastrointestinal or genitourinary tract infection in the last month. Serum laboratory tests were as follows: Glucose, urea, creatinine, electrolytes (including sodium, calcium, potassium, phosphate, and magnesium), procalcitonin, total protein, albumin, aspartate aminotransferase, alanine aminotransferase, direct and indirect bilirubin levels were in normal ranges; white blood cell count: 1.390/µL (with 26.6% neutrophils and 71.4% lymphocytes), hemoglobin (Hb): 7.1 g/dL and platelet count: 89.000/µL; uric acid: 3 mg/dL, erythrocyte sedimentation rate: 64 mm/h and C-reactive protein (CRP): 150 mg/L; rheumatoid factor, anti-cyclic citrulline peptide antibody, and antinuclear antibody were negative (which were assessed by ELISA); HBsAg: Positive and HBV-DNA: Negative; other viral serology tests for hepatitis C virus and HIV were negative. Complete urinalysis and plain chest X-ray were normal. The feet's X-rays (Figure 1) showed bilateral destructive and erosive changes suggesting Charcot arthropathy (CA).

To identify the cause of neuroarthropathy, some laboratory tests were performed; the serological test for syphilis was negative and electromyography was normal. Pedal pulses were easily palpable. Anteroposterior radiography of the knees was performed since the knee is the most affected joint for CPPD disease; bilateral (asymptomatic) knee chondrocalcinosis and meniscal calcification were detected (Figure 1). There was no family history of CPPD, and CPPD-associated metabolic diseases such as hemochromatosis, hyperparathyroidism, hypothyroidism, hypomagnesemia, or hypophosphatasia[7] were detected in additional tests. In conclusion, we diagnosed our patient as 'pseudoneuropathic form of CPPD according to McCarthy's definition and as chronic CPP arthritis according to the EULAR definition. In the first-line treatment, methylprednisolone 16 mg/day (P.O.) treatment was initiated for two weeks but the patient had no response to corticosteroid therapy. Therefore, colchicine 1 mg/day (P.O.) was given as a second-line option. After two weeks of colchicine therapy; the arthritis completely resolved and he could walk unaided. The erythrocyte sedimentation rate regressed to 36 mm/h and CRP regressed to 24 mg/L. Written informed consent was obtained from the patient.

Discussion

CA is associated with neuropathy and is characterized by bone and joint erosions, which may cause deformities. The most common etiological disease for CA is diabetes mellitus (DM); syphilis (tabes dorsalis), leprosy, alcoholism, syringomyelia, peripheral nerve injuries, or congenital absence of pain sensation is the other associated factors and joint involvement can vary according to etiology.[8] The absence of other CA-associated factors was the greatest clue in this study and joint involvement was similar to DM, but fasting blood glucose and glycosylated hemoglobin (HbA1C) levels were within normal ranges.

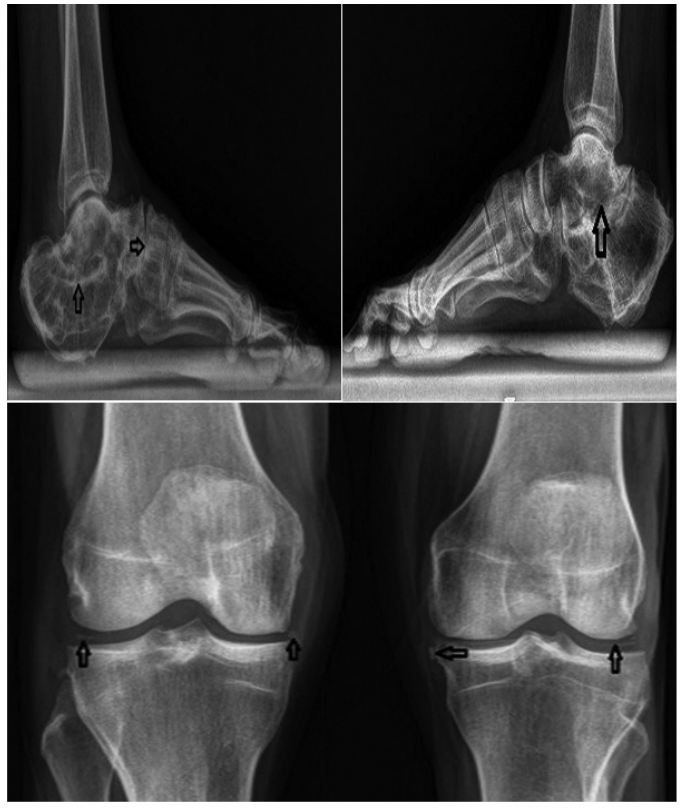

Figure 1. Right food, left foot, and knee radiographies of patient

In a study with 105 patients with CPPD; progressive and destructive joint involvement was present in 15.2% of cases, the hip was the most common site of destructive joint involvement but ankle/foot involvement was not present. Severe destructive changes are common in the knees and especially in women, but our patient did not have any severe damage to knee joints.[1] In another study with 113 patients with CPPD, the destructive arthropathy was 13.5% (n=15) with female predominance and a bilateral symmetrical pattern was observed in only two of 15 cases (other cases are generally polyarticular); knee, shoulder, wrist, and hip were the most common sites in a total of 38 destructive joints, only 5% of them presented in the ankle but hip or shoulder X-rays of our patients did not show destructive feature.[9] The talocalcaneal joint is the most common site for CPPD-related structural changes and CPPD-related joint destruction (especially in the hip, knee, ankle, and cervical spine) can simulate neuropathic arthropathy.[10] In 2015, Lomax et al.[11] reported nine patients (5 female and 4 male, median age: 66) with CPPD-related pseudoneuroarthropathy in foot and ankle joints who were unreported previously; six had bilateral involvement, all cases had multiple joint involvements, and affected joints were talonavicular: 9, tarsometatarsal: 9, subtalar: 6, naviculocuneiform: 6, calcaneocuboid: 3 and ankle: 2. Subtalar, and talonavicular joints of the left foot and subtalar joint of the right foot were affected in our patient.

We found two cases as the coexistence of MDS and CPPD in the literature: Iqbal et al.[12] reported an 83 years-old male patient with radiocarpal joint chondrocalcinosis, knee joint chondrocalcinosis, and degenerative changes in the lumbar spine; Tedeschi et al.[13] reported a 75 years-old male patient with knee, ankle and cervical spine (crowned dens syndrome) involvement. Treatment of CPPD is uncertain; cool packs, temporary rest, non-steroidal anti-inflammatory drugs, colchicine, and intra-articular or oral corticosteroid are recommended for acute attacks; a low-dose corticosteroid, hydroxychloroquine, and methotrexate are recommended for chronic CPPD by the EULAR Task Force.[14] Disease-modifying antirheumatic drugs are not part of the care (such as gout and allopurinol).

Currently, we couldn't diagnose our patient as "MDS-related pseudoneuroarthropathy" because of insufficient evidence: First, MDS-related arthritis is typically polyarticular, symmetric, and non-erosive; second, arthritis resolved with only colchicine treatment in this study but increasing evidence suggests that MDS-directed therapy is effective for the paraneoplastic autoimmune complications;[15] third, there is no any proven relationship between MDS and CPPD.[7] We did not consider HBV-related arthropathy since serum HBV-DNA was negative, liver function tests, and bilirubin levels were within normal ranges.

Conclusion

CPPD disease is a common rheumatic disease in the elderly population and a great mimicked for other musculoskeletal diseases. Our case is the first for the coexistence of MDS and destructive CPPD arthropathy in foot joints (like diabetic CA). The absence of neuropathic causes was the major clue for us. Patients with CPPD may not simultaneously have acute attacks at all affected joints simultaneously, so frequently affected joints (especially the knee) should be reviewed in the presence of suspicion. Rheumatologists should keep in mind the many clinical and radiological manifestations of CPPD in daily practice.

Ethics

Informed Consent: Written informed consent was obtained from the patient.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Concept: M.P., G.K., Design: M.P., G.K., Data Collection or Processing: M.P., G.K., Analysis or Interpretation: M.P., G.K., Literature Search: M.P., G.K., Writing: M.P., G.K.

Conflict of Interest: No conflict of interest was declared by the authors.

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