Kato K, et al., HSOA J Gerontol Geriatr Med 2025, 11: 245
DOI: 10.24966/GGM-8662/100245

HSOA Journal of Gerontology and Geriatric Medicine

Case report

A Case of Pseudo-Rheumatoid Arthritis Mimicking Remitting Seronegative Symmetrical Synovitis with Pitting Edema (RS3PE) Syndrome

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Abstract

We report a Calcium Pyrophosphate Deposition Disease (CPPD) case confusingly similar to Remitting Seronegative Symmetrical Synovitis with Pitting Edema (RS3PE) syndrome. An elderly woman presented with generalized pain, symmetrical digital edema of Metacarpophalangeal (MCP) and Proximal Interphalangeal (PIP) joints, and bilateral ankle arthritis. Initial diagnosis of RS3PE syndrome was reconsidered due to atypical steroid response. Radiographic examination revealed chondrocalcinosis in multiple joints, leading to a final diagnosis of pseudo-rheumatoid arthritis (pseudo-RA) type CPPD. This case highlights that pseudo-RA type CPPD can present with clinical features remarkably similar to RS3PE syndrome, underscoring the importance of considering pseudo-RA type CPPD in the differential diagnosis of RS3PE syndrome and emphasizing the value of radiographic assessment when evaluating RS3PE-like presentations.

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Citation: Kato K, Umezawa Y, Imai Y, Asai K, Noguchi Y, et al. (2025) A Case of Pseudo-Rheumatoid Arthritis Mimicking Remitting Seronegative Symmetrical Synovitis with Pitting Edema (RS3PE) Syndrome. HSOA J Gerontol Geriatr Med 11: 245.

Received: March 11, 2025; **Accepted:** March 13, 2025; **Published:** March 20, 2025

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Keywords: Chondrocalcinosis in multiple joints; Pseudo-rheumatoid arthritis type CPPD; RS3PE syndrome

Introduction

RS3PE syndrome, first described by McCarty et al., in 1985, presents with dramatic symmetrical distal synovitis and pitting edema of the hands and/or feet [1]. The condition characteristically demonstrates a rapid and sustained response to low-dose corticosteroids. Our case initially presented with clinical features highly suggestive of RS3PE syndrome, but the incomplete response to corticosteroids prompted further investigation.

Case Presentation

A 79-year-old woman presented to an outpatient clinic with a 1-week history of generalized pain. She had a 2-month history of symmetrical digital edema involving the MCP and PIP joints of both hands and a 1-month history of bilateral ankle arthritis. Her medical history included left breast cancer status post resection and dementia. Her family physician detected anemia and elevated inflammatory markers and referred her to our outpatient clinic in the general medicine department. On examination, her vital signs were as follows: blood pressure 128/78 mmHg, pulse rate 91 beats/min, respiratory rate 20 breaths/min, and oxygen saturation 99% (room air). She was afebrile, awake, and alert. Physical examination revealed bilateral pitting edema of the MCP and PIP joints and the dorsal surface of both hands, along with swelling of both ankle joints. Tenderness was notable on the right index finger involving the MCP joint, the right elbow joint, and both ankle joints. There was no evidence of thoracoabdominal abnormalities, spinal tenderness, or skin findings suggestive of psoriasis or other dermatological conditions.

Investigations

Laboratory results were as follows: white blood cells, 5.3 × 10^3/μL (reference range: 4.0-10.0 × 10^3/μL); hemoglobin, 8.0 g/dL (reference range: 12.0-16.0 g/dL); mean corpuscular volume, 85 fL (reference range: 80-100 fL), suggesting normocytic anemia; platelets, 54.8 × 10^4/μL (reference range: 15.0-35.0 × 10^4/μL); blood urea nitrogen, 21.8 mg/dL (reference range: 8.0-20.0 mg/dL); creatinine, 0.84 mg/dL (reference range: 0.5-1.0 mg/dL); and C-Reactive Protein (CRP) level, 5.83 mg/dL (reference range: <0.3 mg/dL). The Erythrocyte Sedimentation Rate (ESR) was 143 mm/hr (reference range: 3.0-15.0 mm/hr), and Antinuclear Antibody (ANA) titer was 1:40 (homogeneous and speckled patterns). The Rheumatoid Factor (RF), anti-cyclic citrullinated peptide antibodies, Proteinase-3-Antineutrophil Cytoplasmic Antibodies (PR3-ANCA), Myeloperoxidase-Antineutrophil Cytoplasmic Antibodies (MPO-ANCA), and blood culture were negative. Her thyroid function and serum ferritin levels were also normal.

The findings of symmetrical pitting edema of predominantly peripheral joints with elevated acute phase reactants (ESR, CRP) in an

older adult led to an initial impression of RS3PE syndrome, based on the McCarty criteria [1] which include: 1) bilateral pitting edema of the hands, 2) sudden onset of polyarthritis, 3) age >50 years and 4) seronegative RF. We tested for ANCA due to the multisystem nature of her presentation and to rule out vasculitis. We then began treating her with oral prednisolone (10 mg/day) with immediate improvement of the bilateral hand edema. However, arthritis symptoms in the right MCP joint, right wrist, and both ankle joints became more prominent after a 10-day treatment course.

Because the response to low-dose steroids was not typical for RS3PE syndrome, we reviewed the diagnosis. A plain radiograph of the right hand revealed chondrocalcinosis at the MCP joint of the second and third fingers and the wrist joint, with no erosive changes suggestive of Rheumatoid Arthritis (RA) (Figure 1). These radiographic findings were not obtained prior to steroid initiation as the initial clinical presentation strongly suggested RS3PE syndrome, which typically responds dramatically to low-dose steroids. These symptomatic characteristics, laboratory and imaging findings, and clinical course were consistent with pseudo-RA CPPD, which was our final diagnosis. Although synovial fluid analysis would have been the gold standard for confirming CPPD diagnosis, the characteristic radiographic findings of chondrocalcinosis in conjunction with the clinical presentation were considered sufficient for diagnosis in this case.

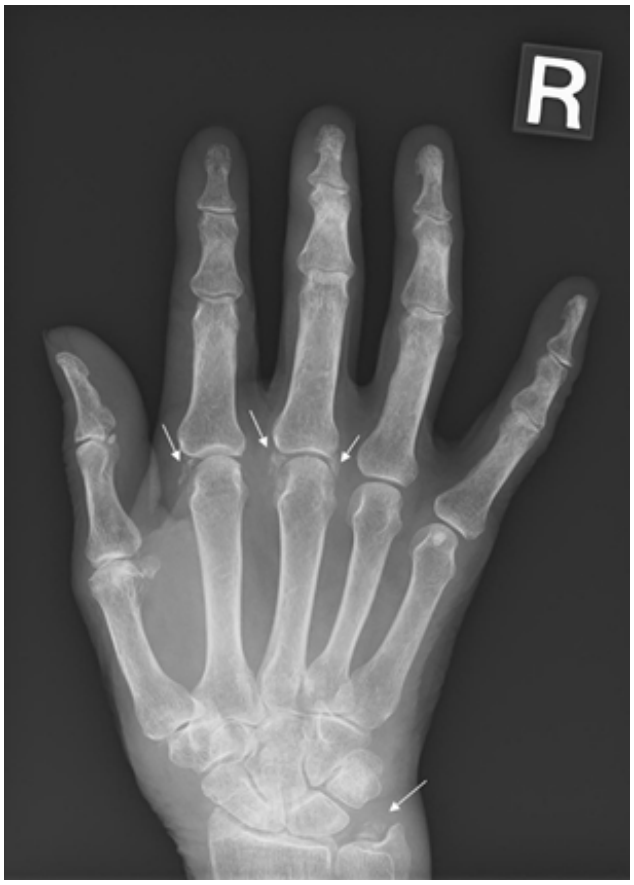

Figure 1: Plain radiography of the right hand showing calcified lesions at the MP joint of the second and third fingers, and the wrist joint (arrows), with no supportive findings of rheumatoid arthritis. Additionally, mild osteoarthritis changes are observed at the DIP and PIP joints of the third, fourth, and fifth fingers as age-related changes.

Differential Diagnosis

Differential diagnoses of RS3PE syndrome

RS3PE syndrome is a rare inflammatory arthritis marked by symmetrical distal synovitis, pitting edema of the hands and feet, and absence of RF. This condition is relatively common in older men. Treatment with 10-20 mg/day of prednisolone generally results in rapid improvement and a good prognosis [2]. Diseases with a similar presentation to RS3PE syndrome include polymyalgia rheumatica, Elderly-Onset Rheumatoid Arthritis (EORA), Calcium Pyrophosphate Deposition Disease (CPPD), vasculitis, infectious diseases such as infective endocarditis, paraneoplastic syndromes, fibromyalgia, psoriatic arthritis, ankylosing spondylitis and hypothyroidism. In these differential diagnoses, the characteristics of high acute phase reactants, RF negativity, and systemic manifestations resembling RS3PE led us to focus on EORA.

RA generally develops at 30-50 years of age, but if it develops at an older age, it is called EORA. EORA has a lower frequency of positive RF rate than younger-onset RA (80%), and both small and large joints are commonly affected in EORA. This disease often resembles RS3PE syndrome, with peripheral edema and relatively high levels of acute phase reactants. As a feature of the imaging examination, plain radiographs can confirm bone erosion of affected joints [3]. While evaluating for bone erosion of EORA, a plain radiograph of the right hand revealed synovial calcification in multiple joints, which were distinctive of pseudo-RA CPPD (Type B CPPD) [4].

CPPD can be classified into six types, from Type A to Type F. Type A is the so-called pseudogout, which is the most common pattern in symptomatic CPPD. This feature is marked by acute or subacute arthritic attacks lasting approximately 1 day to 4 weeks. One or a few arthritis symptoms may occur, but many of these symptoms are self-limiting, and the pain is somewhat less severe than that in gout. Knee joints are most commonly affected, and medical disease or trauma may be the triggering factor. Type B CPPD has clinical features that are completely different from pseudogout; instead, it more closely resembles RA, leading to it being termed pseudo-RA. Approximately 5% of patients with Type B CPPD have multiple joint involvement with subacute attacks lasting 4 weeks to several months. Nonspecific symptoms, such as morning stiffness and general fatigue, are common. Clinically, it closely resembles RA, with synovial thickening, localized edema, arthritis, and abnormal CRP or ESR [5].

Psoriatic arthritis was considered in the differential diagnosis due to the presence of dactylitis-like findings. However, the absence of psoriatic skin lesions, nail changes, and the characteristic radiographic findings of CPPD instead of the pencil-in-cup deformities typically seen in psoriatic arthritis made this diagnosis less likely.

Outcome and Follow-Up

Oral celecoxib (200 mg/day) treatment was initiated. As a result, the arthritic findings in the right fingers, wrist, and ankle joints, and the inflammatory response in blood tests improved within 1 week. No relapse was observed after the discontinuation of celecoxib. The normocytic anemia was thoroughly evaluated, with no evidence of hemolysis, gastrointestinal bleeding, or nutritional deficiencies, suggesting it was anemia of chronic inflammation related to the inflammatory arthritis. The good response to Nonsteroidal Anti-Inflammatory Drugs (NSAIDs) without relapse was compatible with CPPD.

NSAIDs were chosen as the treatment for pseudo-RA CPPD based on evidence suggesting that they are effective for symptomatic relief in CPPD, particularly for chronic forms of the disease [6].

Discussion

The literature describes several cases where CPPD has mimicked various inflammatory rheumatic diseases. Kano et al. reported a case of pseudo-RA CPPD that exhibited polyarthritis and calcified lesions in multiple joints similar to our case, but peripheral pitting edema was absent [7]. Thus, the prominent presence of peripheral edema in our case represents an unusual clinical presentation for pseudo-RA CPPD and highlights how closely it can mimic RS3PE syndrome, potentially leading to misdiagnosis. The association between CPPD and RS3PE-like presentations may be explained by the inflammatory response to calcium pyrophosphate crystals in the synovial tissue, leading to increased vascular permeability and subsequent edema. This mechanism differs from the pathophysiology of true RS3PE syndrome, which is thought to involve Vascular Endothelial Growth Factor (VEGF) and Interleukin-6 (IL-6) mediated vascular permeability [8].

Radiographic evidence of chondrocalcinosis is a key diagnostic feature in differentiating pseudo-RA type CPPD from RS3PE syndrome. In our case, the failure to obtain radiographic imaging prior to initiating treatment may have delayed the correct diagnosis, emphasizing that radiographic assessment should be considered an essential component of the diagnostic workup for suspected RS3PE syndrome. While the gold standard remains synovial fluid analysis for calcium pyrophosphate crystals under polarized light microscopy, characteristic radiographic findings of chondrocalcinosis can provide crucial diagnostic clues when clinical presentation is ambiguous or response to therapy is atypical [9].

Treatment approaches differ between RS3PE syndrome and CPPD. While RS3PE syndrome typically demonstrates a dramatic and sustained response to low-dose corticosteroids, CPPD often responds well to NSAIDs, as seen in our case. For chronic forms of CPPD, NSAIDs are considered first-line therapy, with colchicine, low-dose corticosteroids, and methotrexate as alternatives for refractory cases [10].

Conclusion

Remitting Seronegative Symmetrical Synovitis with Pitting Edema (RS3PE) syndrome is characterized by acute onset symmetrical polyarthritis, dramatic pitting edema of the hands and/or feet, negative rheumatoid factor, and excellent response to low-dose corticosteroids. Pseudo-rheumatoid arthritis type CPPD can mimic RS3PE syndrome, with an important distinguishing feature being the presence of chondrocalcinosis on radiographic imaging. When the initial diagnosis of RS3PE syndrome is questioned due to atypical steroid response, radiographic imaging should be promptly performed to evaluate for alternative diagnoses such as CPPD.

While synovial fluid analysis remains the gold standard for diagnosing CPPD, characteristic radiographic findings of chondrocalcinosis in conjunction with appropriate clinical presentation can support the diagnosis. NSAIDs are typically effective in managing pseudo-RA type CPPD, whereas RS3PE syndrome generally demonstrates a dramatic and sustained response to low-dose corticosteroids.

Ethics

Written informed consent was obtained from the patient for publication of this case report and accompanying images.

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