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Pseudogout Overlapping with Pre-Existing Joint Pathologies: A Case Series

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A B S T R A C T

Background: Pseudogout, or calcium pyrophosphate deposition disease (CPPD), is a crystal-induced arthritis frequently mistaken for gout or septic arthritis, particularly in elderly patients or those with inflammatory disorders. **Case Presentation:** We present two cases highlighting the diagnostic value of synovial fluid analysis and musculoskeletal ultrasonography (MSUS). An 34-year-old man diagnosed with ankylosing spondylitis presented with acute right knee pain after running; synovial fluid revealed rhomboid-shaped crystals with high leukocyte count, confirming pseudogout, while MSUS showed intra-cartilaginous crystal deposits. An 87-year-old man presented with mild right knee pain and swelling; synovial fluid again demonstrated rhomboid-shaped crystals, and MSUS confirmed intra-cartilaginous crystal deposition, consistent with pseudogout coexisting with osteoarthritis. Both patients received intra-articular triamcinolone acetonide 40 mg and showed favourable clinical outcomes, with improvement in pain and swelling. **Conclusion:** These cases highlight the diagnostic challenges of acute monoarthritis in chronic inflammatory disease and advanced age, where inflammatory markers may mislead. Synovial fluid crystal analysis remains crucial, while MSUS offers a non-invasive alternative when aspiration poses challenges, ensuring accurate diagnosis and appropriate anti-inflammatory therapy.

1. Introduction

Pseudogout, also known as calcium pyrophosphate dihydrate (CPPD) crystal deposition disease, is an arthritic condition characterized by the acute onset of joint inflammation resembling gout or septic arthritis.[1] Unlike gout, which is caused by monosodium urate (MSU) crystals, pseudogout results from the accumulation of calcium pyrophosphate crystals and predominantly affects older adults, although it may also be associated with metabolic disorders such as hyperparathyroidism, hemochromatosis, and hypomagnesemia.[2-6] This clinical overlap can lead to misdiagnosis, inappropriate treatment, and delayed initiation of anti-inflammatory therapy. Diagnosis relies on the identification of rhomboid-shaped crystals in synovial fluid using polarized light,[7] while management is primarily directed toward symptom control, as no treatment currently reduces crystal burden.[8,9] We present two cases of pseudogout with distinct clinical histories, a young patient with ankylosing spondylitis and an elderly patient with coexisting knee osteoarthritis, to highlight the diagnostic value of synovial fluid analysis and crystal identification and emphasize the importance of

considering CPPD in atypical presentations of acute monoarthritis.

2. Case Presentation

a. Case 1

Clinical Course

A 34-year-old male with a history of ankylosing spondylitis (AS) on maintenance therapy with Infliximab presented with acute pain and swelling of the right knee for five days following an intense running activity. Symptoms progressed to sharp pain on knee flexion, fever (peak 38.1°C), and difficulty ambulating. Synovial fluid analysis revealed a turbid, yellow fluid with a high leukocyte count (37,790 cells/µL, 85.8% of PMNs), negative for monosodium urate crystals (MSU), and positive for rhomboid-shaped crystals under polarized light microscopy, confirming pseudogout (Figure 2). Synovial fluid analysis revealed elevated leukocytes (Figure 3). Ultrasound examination showed intra-cartilaginous crystal deposition consistent with CPPD (Figure 1).

Treatment and Outcome

The patient received an intra-articular injection of triamcinolone acetonide 40 mg. On follow-up, knee pain and swelling improved substantially, with resolution of the acute inflammatory episode. No treatment-related complications were observed.

b. Case 2

Clinical Course

An 87-year-old Man presented with mild pain and swelling in the right knee. Synovial fluid analysis showed rhomboid-shaped crystals with polarized light microscopy, with a cell count >13,000/µL (Figure 2). He was also diagnosed with right knee osteoarthritis (Kellgren–Lawrence grade II). MSUS revealed intra-cartilaginous crystals consistent with CPPD (Figure 1). The final diagnosis was pseudogout overlapping with osteoarthritis. Clinical examination showed visible swelling compared to the contralateral knee (Figure 4).

Treatment and Outcome

The patient was treated with an intra-articular injection of triamcinolone acetonide 40 mg. On follow-up, knee pain and swelling improved, accompanied by functional recovery. No treatment-related complications were observed.

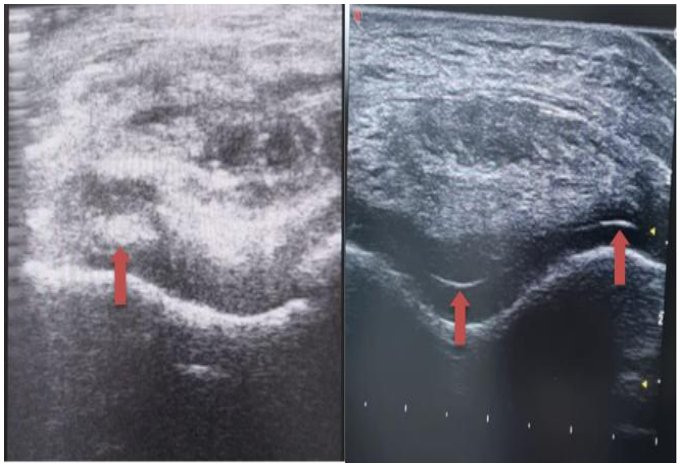

Figure 1. Musculoskeletal ultrasonography showing intra-cartilaginous crystal deposition consistent with CPPD on case 1 (A) and case 2 (B).

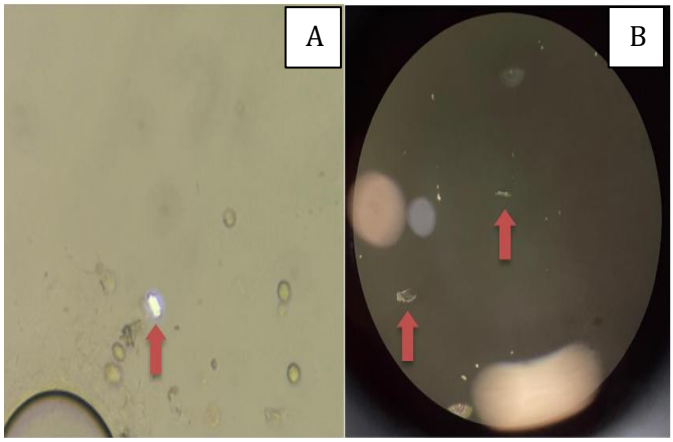

Figure 2. Polarized microscopy shows no monosodium urate crystals (MSU) but reveals rhomboid-shaped crystals, confirming pseudogout on case 1 (A) and case 2 (B).

Figure 3. Synovial fluid was turbid yellow with elevated leukocytes (37,790/μL; 85.8% PMNs) in case 1.

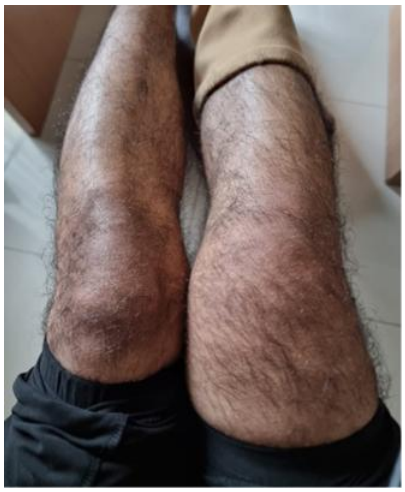

Figure 4. Swelling of the right knee compared to the left knee in case 2.

3. Discussion

Recognition of CPPD crystals through synovial fluid analysis and polarized light microscopy is critical, as it directly influences diagnostic and treatment decisions. Our first case shows the importance of considering pseudogout even in younger patients with underlying inflammatory arthritis conditions like ankylosing spondylitis (AS).[1] Similar reports, such as those by Rondon et al., describe CPPD in younger individuals with autoimmune diseases where crystal arthritis mimics infectious or gouty arthritis, emphasizing the importance of synovial fluid analysis, which could prevent unnecessary antibiotic use and invasive procedures.[11] The use of musculoskeletal ultrasonography (MSUS) further supported the diagnosis by identifying characteristic intra-cartilaginous crystal deposits. Filippou et al., demonstrated that ultrasound improves diagnostic accuracy by detecting CPPD deposits within cartilage and periarticular tissues.[12,13] In contrast, oMur second case highlights the frequent coexistence of pseudogout with osteoarthritis (OA).[14] McCarthy et al. indicate that CPPD crystals may exacerbate osteoarthritic symptoms, complicating clinical management[15] The mild pain but significant inflammatory response seen here aligns with findings from previous studies suggesting that CPPD can induce variable inflammatory intensities, necessitating tailored treatment such as intra-articular corticosteroids for effective symptom control.[16,17]

Taken together, these cases showed the broad clinical spectrum of CPPD and the importance of maintaining a high index of suspicion when evaluating acute monoarthritis. The first case demonstrates that CPPD may occur even in younger patients with underlying inflammatory rheumatic diseases, whereas the second illustrates how CPPD can coexist with osteoarthritis and be overlooked as a purely degenerative process.[18] Both cases underscore that definitive diagnosis relies on the identification of calcium pyrophosphate crystals in synovial fluid using polarized light microscopy.[19] Musculoskeletal ultrasound (MSUS) provides a valuable, non-invasive tool that can support diagnosis by detecting crystal deposition in joints and periarticular tissues.[5]

A deeper understanding of the mechanisms underlying CPPD crystal formation may open the door to future treatments that go beyond symptom control. CPPD arises from excess extracellular pyrophosphate, which promotes calcium pyrophosphate crystal deposition within cartilage. Subsequent activation of the NLRP3 inflammasome and interleukin-1β (IL-1β) signalling induces neutrophil-mediated synovitis, explaining the pronounced inflammatory response observed in our first case despite concomitant infliximab therapy. This pathogenic pathway also provides a rationale for emerging therapeutic strategies targeting IL-1 signalling in refractory CPPD,

extending treatment approaches beyond conventional symptomatic control.[19]

4. Conclusion

In summary, a thorough understanding of the clinical presentation, supported by synovial fluid analysis and musculoskeletal ultrasonography (MSUS), is essential for the accurate diagnosis of pseudogout, especially in cases with atypical features or coexisting rheumatologic conditions. MSUS provides a valuable non-invasive adjunct and may be particularly useful when joint aspiration is technically difficult, contraindicated, or unsuccessful. These diagnostic approaches help differentiate pseudogout from similar conditions such as gout and septic arthritis, enabling more precise treatment decisions and improving patient outcomes. Further prospective studies and registry-based data are needed to better characterize CPPD overlap syndromes and refine diagnostic strategies in patients presenting with acute monoarthritis.

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Data availability

The datasets and materials generated and/or analyzed during the current study are available from the corresponding author on reasonable request.

Ethics approval and consent to participate

The research was conducted based on the principles outlined in the Declaration of Helsinki. Consent to participate was obtained from patients from case series.

Consent for publication

Not applicable.

Competing interest

The authors report no conflict of interest in this work.

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