Letter to the Editor

A rare case of atypical tumoral presentation of calcium pyrophosphate dihydrate crystal deposition disease

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Introduction

The term *calcium pyrophosphate dihydrate crystal* was first used by McCarty in 1961 (1). The main pathological changes in calcium pyrophosphate dihydrate crystal deposition disease (CPPDCD) is the deposition of calcium pyrophosphate dihydrate (CPPD) crystals and damage to joint structures (2). This disease mainly affects middle-aged and older adult patients, and the incidence and severity increase with age (3). Studies have shown that calcium pyrophosphate crystal formation occurs in the presence of excess extracellular inorganic pyrophosphate in the cartilage pericellular matrix (4). CPPD can deposit in the joint's hyaline cartilage, fibrous cartilage, synovium, joint capsule, tendon, or ligament, causing calcification of articular cartilage or the soft tissue adjacent to the joint (5).

Tumoral CPPDCD (TCPPDCD) is a distinct and uncommon lesion that should be differentiated from CPPD. As a tumoral lesion, TCPPDCD may cause tumor-related symptoms, such as localized mass as well as a risk of joint dysfunction. Despite being a nonneoplastic lesion, it can imitate bone or soft tissue tumors on radiological or pathological examination (6). TCPPDCD is frequently observed in the temporomandibular joint or paraspinal tissues, while its occurrence in extremity joints is infrequent (7). Through electronic database searches, we identified 59 reported cases of TCPPDCD affecting the extremity joints in the English-language literature. Based on tumor location, the patients were categorized into upper extremity (40 patients) and lower extremity (19 patients) groups. Among the lower limb cases, the hip was the most commonly affected site (8 cases), followed by the metatarsal or metatarsophalangeal joint (7 cases) and the knee (3 cases). The ankle was affected in 1 case.

We present an intriguing case of TCPPDCD at the tarsal joint site, which, to our knowledge, represents the first reported instance in this region. The imaging findings were characterized by the presence of a calcified mass within the soft tissue secondary to significant bone invasion. Throughout disease progression, there was gradual enlargement of the lesion. Initially, this patient was misdiagnosed as having a neoplastic lesion due to overlapping clinical and imaging findings indicative of both benign and malignant tumors.

Case presentation

All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee(s) and with the Helsinki Declaration (as revised in 2013). Written informed consent was obtained from the patient for publication of this article and accompanying images. A copy of the written consent is available for review by the editorial office of this journal.

Medical history

The patient, a female aged 82 years old, complained of a painful, hard, and palpable mass on her left foot. All levels of serum calcium, phosphorus, magnesium, alkaline phosphatase, and uric acid were within the normal range. All blood cell counts were negative except for a brief increase in C-reactive protein (CRP) and the erythrocyte sedimentation

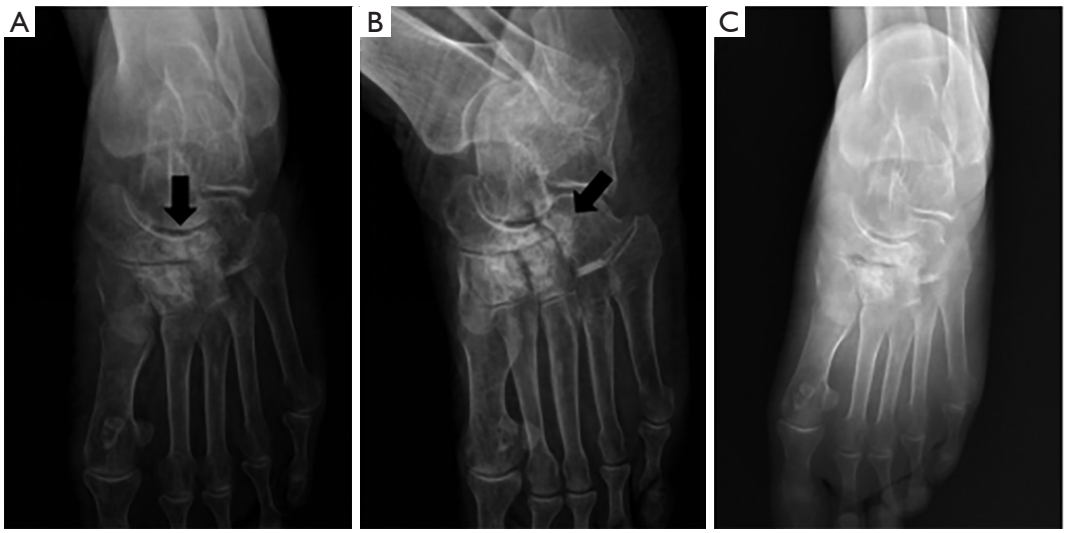

Figure 1 Radiographs of the left foot. (A) Anteroposterior and (B) oblique radiographs of the left foot revealed a noticeable mass (arrows) adjacent to the tarsal joint, accompanied by internal calcifications and obvious signs of osseous erosion. (C) An anteroposterior radiograph revealed the postoperative manifestations of the lesion.

rate. Hyperparathyroidism, hemochromatosis, diabetes mellitus, rheumatoid arthritis, and gout were not present. The patient's left foot had not been injured, and the pain was affecting her normal activities. No relevant family history or genetic history was identified.

Imaging assessment

Radiographs of the left foot in the antero-oblique view revealed a calcified mass in the tarsal region (*Figure 1A*,*1B*). Postoperative X-ray imaging revealed complete resection of the lesion (*Figure 1C*).

Computed tomography (CT) demonstrated an expansive and invasive calcified mass with significant intraosseous involvement, prominent pressure erosion, and scattered curly calcifications (*Figure 2*).

Magnetic resonance imaging (MRI) showed a well-defined, lobular mass with low signal intensity on sagittal T1-weighted imaging (T1WI-S). Proton density-weighted imaging (PDWI) revealed nonuniform signal intensity in the mass, with multiple low-intensity foci (*Figure 3*).

Intraoperative findings

The mass was completely removed. Under the naked eye, the mass appeared as a chalky white material with a well-preserved capsule measuring 4.0 cm × 2.0 cm × 2.0 cm in size. On histological examination of the excised tissue via hematoxylin and eosin staining (HE) staining, rhomboid-shaped crystals were found to be surrounded by fibroblasts and macrophages. Under polarized light, the calcified deposits showed weakly positive birefringent polarized light, suggestive of CPPD crystals, and these findings were consistent with those of TCPPDCD (*Figure 4*).

Discussion

A rare and lesser-known variant, TCPPDCD, is a distinct entity characterized by the development of a periarticular mass that leads to local erosion of adjacent bones (8). TCPPD has a relatively low overall incidence, and there are significant variations in its distribution across different anatomical sites. The anatomic distribution of TCPPDCD differs from that of common forms of CPPDCD, which typically affect the knee and wrist. However, the temporomandibular joint is the most common location for TCPPDCD, followed by paraspinal tissues. Other less common locations included the foot (7).

On radiological examination, the CPPD deposits appear radiologically dense. Calcium deposits can be observed in the meniscus, articular cartilage, yellow ligament, and intervertebral disc. They are typically distributed as spots or lines within the meniscus or parallel to the subchondral bone plate. However, TCPPDCD presents with granular or

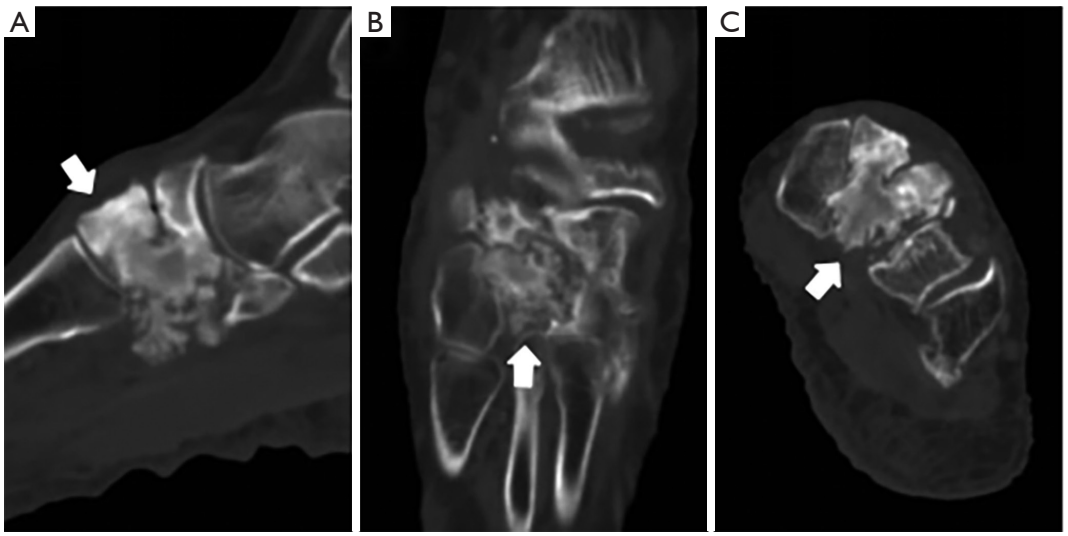

Figure 2 Preoperative CT image of the left foot. The (A) sagittal, (B) coronal, and (C) axial bone window CT scans of the left foot revealed a 3.8×2.0×2.2 cm mass (arrows) with expansive and invasive characteristics, clearly affecting the bone. Additionally, there was evident pressure erosion with well-defined boundaries, accompanied by scattered villous arc-shaped calcification. CT, computed tomography.

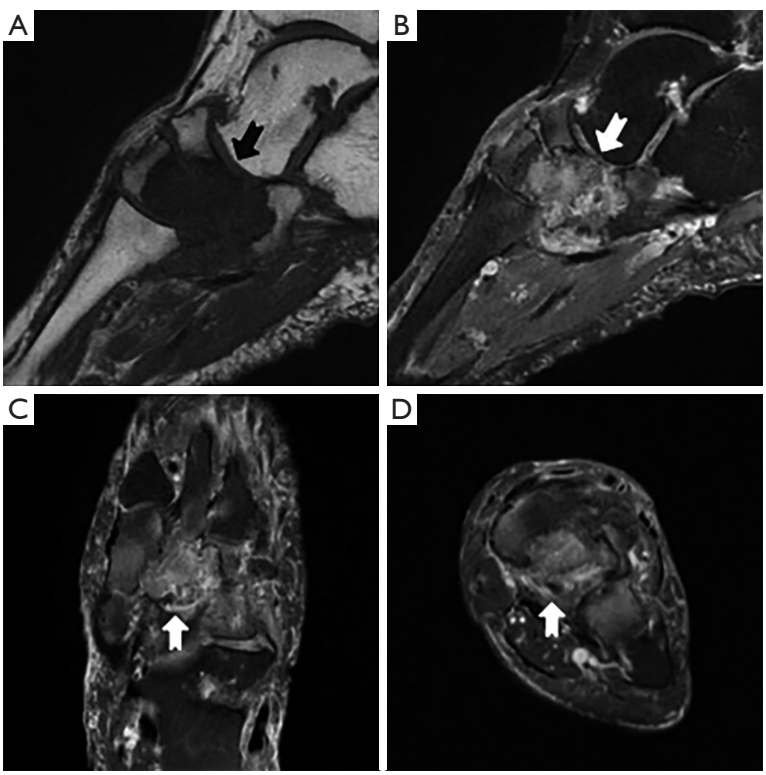

Figure 3 MRI of the left foot revealed a 3.8×2.0×2.2 cm mass (arrows) in the tarsal region. (A) The mass showed an overall low signal in sagittal T1WI. PDWI included heterogeneous signal intensity in (B) sagittal, (C) coronal, and (D) axial images, exhibiting multifocal hypointensity. The image clearly depicted the deep penetration of the mass into the cuneiform bone, scaphoid bone, and surrounding soft tissue, accompanied by a significant amount of bone edema adjacent to the mass. Furthermore, it is worth noting that the mass was responsible for cortical thinning and pressure erosion of the proximal metatarsals. MRI, magnetic resonance imaging; T1WI, T1-weighted imaging; PDWI, proton density-weighted imaging.

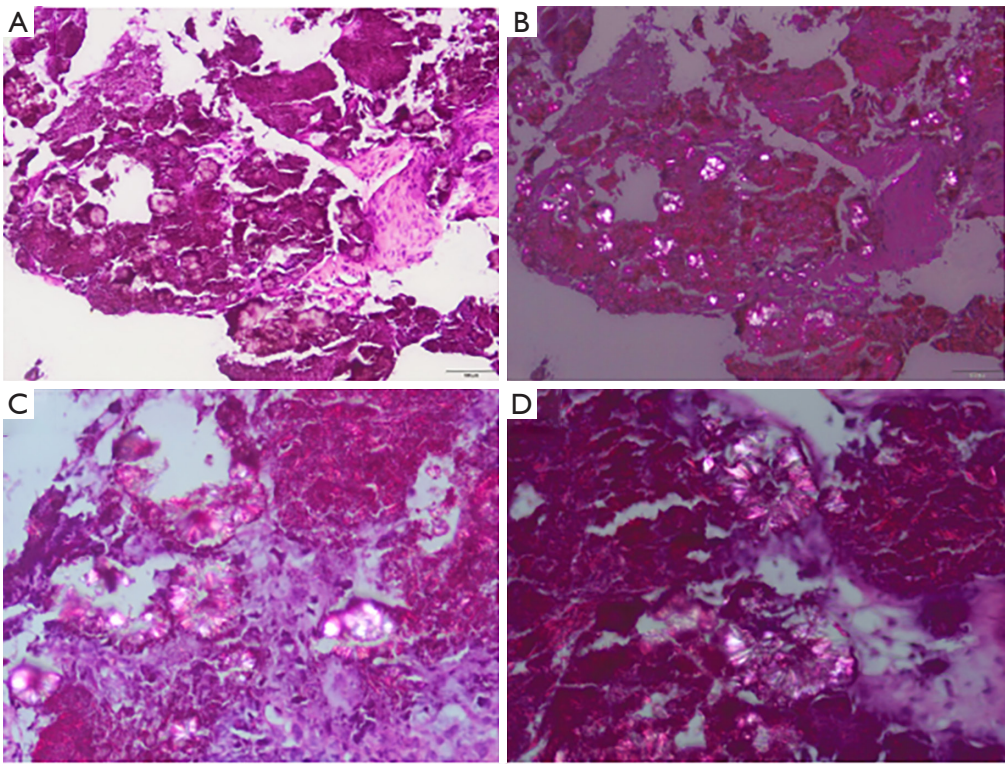

Figure 4 Pathological biopsy. (A) Photomicrograph of the tumoral mass showed deposits of crystals surrounded by fibroblasts and macrophages (HE, 100×). (B-D) Upon HE staining with polarization gating, the calcified deposits showed pathognomonic positively birefringent rhomboidal crystals on (B) low-power view (100×) and (C,D) high-power view (200×). HE, hematoxylin and eosin.

fluffy pattern calcifications. In some cases, pressure erosion may occur near the calcified mass (9). On CT, an irregular calcified density mass is present, and on MRI, a low signal intensity mass on T1-weighted imaging (T1WI) and a mixed high-low signal intensity on T2WI are apparent (10). These typical manifestations are consistent with those observed in our case. In addition, there were more visible low signal areas on MRI T2WI, which might have been related to the varying degrees of calcium phosphate crystal deposition.

Differential diagnosis and typical features

Radiologically, this condition should be distinguished from malignant tumors or benign diseases, such as chondrosarcoma, synovial chondromatosis, tumorous calcification, and bizarre parosteal osteochondromatous proliferation. In this case of TCPPDCD, the lesion appeared as a dense, enlarged mass around the joint with bone erosion. The malignant transformation of chondroid-like tumors (i.e., chondrosarcoma) has similar characteristics (11). Chondrosarcoma originates from mesenchymal tissue that undergoes differentiation toward cartilage cells or chondrogenesis. On X-ray and CT images, chondrosarcomas typically manifest as regions of variable sizes and exhibit osteolysis. These areas often feature clusters or a diffuse distribution of punctate and ring-like calcifications, which are indicative of cartilaginous tumors. Notably, there have been previous reports of chondrosarcomas occurring in the foot (12). Synovial chondromatosis is another concern for potential differential diagnosis and is characterized by the presence of multiple cartilaginous nodules within the synovium, synovial membrane, or bursae of the joint. This condition is marked by the multiple formations of free bodies within the joint. Primary synovial chondromatosis typically affects adults, with males constituting the majority of the affected individuals (13). Because the TCPPDCD lesion appears as a mass with amorphous calcification, it requires differentiation from the tumoral calcification. Tumoral

calcification often involves soft tissues near the joint with variably sized calcified nodules, which can appear as amorphous, lobular, or clustered calcifications. However, it mainly occurs in young people and is more common in multiple forms (14). Bizarre parosteal osteochondromatous proliferation is a benign skeletal tumor composed of differentiated bone, cartilage, and fibers. This lesion is most commonly encountered in the hands and feet. On radiographic examination, there are well-defined, mushroom-like, or lobulated bony processes attached to the bone cortex (15).

TCPPD disease affecting the tarsal joint is an uncommon medical condition. For radiologists, the rarity of lesions in the tarsal joint and the indistinctness of some imaging features, as well as the potential overlap or association of CPPD with other age-related diseases, make differential diagnosis challenging and can lead to misdiagnosis. Misdiagnosis may not only result in unnecessary overtreatment, such as chemotherapy and radiotherapy, but also potentially harm healthy tissues and lead to side effects such as compromised immunity in the eradication the tumor. Moreover, misdiagnosis can also impose a significant psychological burden on patients, potentially triggering anxiety, depression, and other psychological complications. Even if it is later confirmed as a misdiagnosis, patients still have to confront the physical and mental trauma, as well as the resulting challenges of recovery.

Currently, the treatment strategy for TCPPDCD varies based on the clinical presentation. Similar to acute forms of CPPDCD, TCPPDCD can be symptomatically managed with therapies that address local inflammation, including colchicine, nonsteroidal anti-inflammatory drugs, corticosteroids, and interleukin-1 inhibitors (16). For patients with severe symptoms, conservative surgical resection (10,12) is recommended. Most patients have a good prognosis, and due to the potential for recurrence of TCPPDCD after surgical resection, further follow-up may be necessary in these patients. As the mechanism of TCPPDCD is not fully understood, there are currently no clear medical interventions available to prevent the formation of CPPD crystals or promote their dissolution in affected joints or tissues (16). The prognosis and optimal treatment regimen for TCPPDCD remain to be further studied.

There are many challenges in the diagnosis and treatment of TCPPDCD, and establishing the correct diagnosis is the first obstacle. This case suggests that doctors should gain a deeper understanding of the disease's pathogenesis and clinical manifestations to improve the accuracy of diagnosis and treatment.

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Footnote

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://qims.amegroups.com/article/view/10.21037/qims-24-328/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee(s) and with the Helsinki Declaration (as revised in 2013). Written informed consent was obtained from the patient for publication of this article and accompanying images. A copy of the written consent is available for review by the editorial office of this journal.

References

1. Abhishek A, Tedeschi SK, Pascart T, Latourte A, Dalbeth N, Neogi T, et al. The 2023 ACR/EULAR Classification Criteria for Calcium Pyrophosphate Deposition Disease. Arthritis Rheumatol 2023;75:1703-13.
2. Rosenthal AK, Ryan LM. Calcium Pyrophosphate Deposition Disease. N Engl J Med 2016;374:2575-84.
3. Andrés M, Sivera F, Pascual E. Progresses in the imaging of calcium pyrophosphate crystal disease. Curr Opin Rheumatol 2020;32:140-5.
4. Williams CJ, Rosenthal AK. Pathogenesis of calcium

pyrophosphate deposition disease. Best Pract Res Clin Rheumatol 2021;35:101718.
5. Krochak R, Culbertson MD, Vigorita V, Goodman H. Atypical Tumoral Presentation of Calcium Pyrophosphate Deposition Disease: A Case Report. JBJS Case Connect 2016;6:e86.
6. Lo PC, Yue CT, Kung WM. Lumbar Extradural Pseudogout Mass Manifesting as Radiculopathy: A Case Report. J Multidiscip Healthc 2021;14:1593-8.
7. Nakamura O, Kaji Y, Yamagami Y, Yamaguchi K, Nishimura H, Fukuoka N, Yamamoto T. A Rare Case of Tumoral Calcium Pyrophosphate Dihydrate Crystal Deposition Disease of the Wrist Joint. Case Rep Orthop 2015;2015:313291.
8. Tantillo TJ, Chang K, Tan S, Sirotnikov S, Goodman HJ. An Unusual Pathologic Ulna Fracture Induced by Intraosseous Tumoral Calcium Pyrophosphate Dihydrate Crystal Deposition Disease. J Hand Surg Glob Online 2022;4:233-8.
9. Bullough P, editor. Orthopedic pathology, 4th ed. Edinburgh, London, New York, Oxford, Philadelphia, St. Louis, Sydney, Toronto: Mosby Publication, 2004.
10. Park HJ, Chung HW, Oh TS, Lee JS, Song JS, Park YK. Tumoral pseudogout of the proximal interphalangeal joint of a finger: a case report and literature review. Skeletal Radiol 2016;45:1007-12.
11. Nakagawa M, Endo M, Susuki Y, Yokoyama N, Maekawa A, Nabeshima A, Iida K, Fujiwara T, Setsu N, Matsunobu T, Matsumoto Y, Yokoyama R, Yamada Y, Kohashi K, Yamamoto H, Oda Y, Iwamoto Y, Nakashima Y. Clinical, Radiological, and Histopathological Characteristics of Periosteal Chondrosarcoma with a Focus on the Frequency of Medullary Invasion. J Clin Med 2022;11:2062.
12. Zhou LB, Zhang HC, Dong ZG, Wang CC. Chondrosarcoma of the toe: A case report and literature review. World J Clin Cases 2022;10:9132-41.
13. Padhan P, Ahmed S. Synovial Chondromatosis. N Engl J Med 2019;381:1364.
14. Anilkumar A, Högler W, Bursell J, Nadar R, Ryan F, Randell T, Shaw NJ, Uday S. Successful treatment approaches for tumoral calcinosis in children and young people: A condition of diverse pathogenesis. Bone 2024;182:117049.
15. Gitto S, Serpi F, Messina C, Albano D, Di Bernardo A, Armiraglio E, Cannavò L, Mazzoli S, Luzzati A, Parafioriti A, Sconfienza LM. Bizarre parosteal osteochondromatous proliferation: an educational review. Insights Imaging 2023;14:109.
16. Mandl P, D'Agostino MA, Navarro-Compán V, Geßl I, Sakellariou G, Abhishek A, et al. 2023 EULAR recommendations on imaging in diagnosis and management of crystal-induced arthropathies in clinical practice. Ann Rheum Dis 2024;83:752-9.

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