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Case Report

An Unusual Pathologic Ulna Fracture Induced by Intraosseous Tumoral Calcium Pyrophosphate Dihydrate Crystal Deposition Disease

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In this case report, we describe a novel occurrence of tumoral calcium pyrophosphate dihydrate crystal deposition disease (TCPPDCD) in a 76-year-old man that presented as an unusual, intraosseous, metadiaphyseal lesion of a long bone causing a pathologic fracture. A routine intralesional biopsy was performed, demonstrating granular deposits composed of polarizing, overlapping rhomboid crystals consistent with TCPPDCD. With limited numbers of reported cases of TCPPDCD, and the atypical intraosseous origin seen in this case, it is paramount to thoroughly evaluate all cases of TCPPDCD to clearly differentiate key findings that are essential in diagnosing and managing TCPPDCD.

Calcium pyrophosphate dihydrate crystal (CPPD) deposition disease (CPPDCD) encompasses a spectrum of disorders, including pseudogout and chondrocalcinosis. The pathophysiology of CPPDCD commonly involves the intra-articular deposition of CPPD crystals, leading to a localized inflammatory response, resulting in joint pain, swelling, and erythema.[1] Risk factors for CPPD include joint trauma, a family history of CPPD, increased age, a history of urate gout, hypothyroidism, hyperparathyroidism, hemochromatosis, hemophilia, and metabolic derangements.[1] First-line therapies for typical cases of CPPD include nonsteroidal anti-inflammatory drugs with progression to steroids, which remains an effective treatment protocol for acute flares.[1]

In rare instances, however, the focal deposition of CPPD crystals can coalesce, forming a discernible mass or lesion, known as tumoral CPPDCD (TCPPDCD). Tumoral CPPDCD most frequently occurs in the temporomandibular joint; however, cases have also been reported in the hands, wrists, hips, knees, ankles, and feet.[2] Given similar radiographic characteristics, including fine, stippled calcifications within a soft tissue mass, differentiating TCPPDCD from malignancy can be difficult, often requiring a histologic diagnosis.[3,4] As TCPPDCD can be associated with severe bone destruction, patients may initially present with a pathologic fracture, especially after a traumatic injury.[3] Owing to this crossover in presentation, the diagnosis and treatment of TCPPDCD remains a challenge for clinicians, warranting a thorough understanding of the condition to improve patient outcomes.

Case Report

A 76-year-old man presented to the Northwell Health musculoskeletal oncology clinic after being referred from another orthopedist with a chief complaint of a swollen and painful right, dominant wrist following a minor mechanical fall. At presentation, plain radiographs revealed a suspicious intraosseous lesion in his ulna. The patient was subsequently referred for magnetic resonance imaging and was instructed to follow-up with the musculoskeletal oncology specialist (H.J.G.).

The patient's history was considerable for lung cancer treated with a partial lobectomy 17 years prior to presentation, with no further sequelae. He denied having any antecedent pain or symptoms in his right wrist. On physical examination, the patient had an

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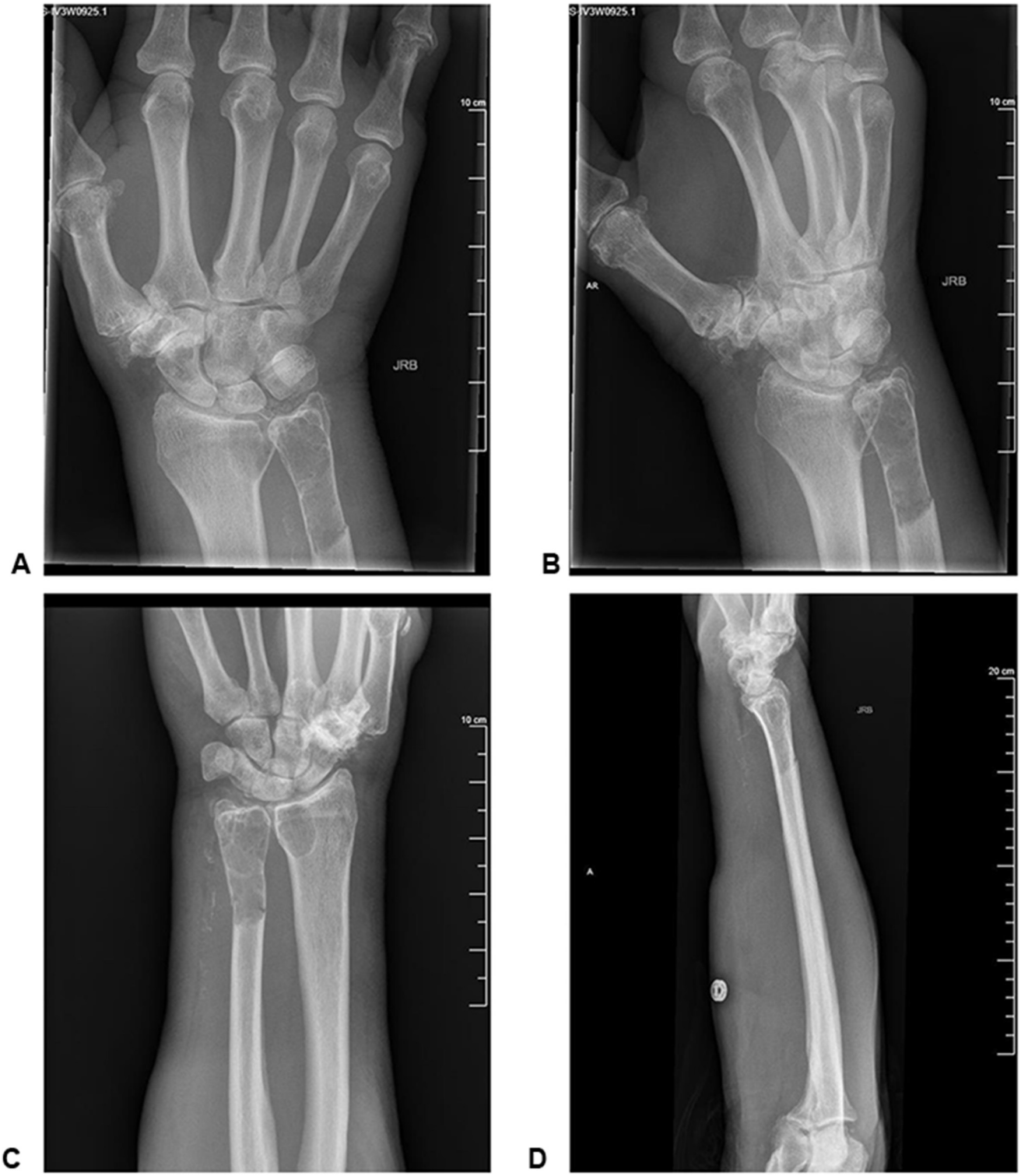

Figure 1. Posterior-anterior, oblique, and lateral x-rays of the right wrist and forearm, demonstrating a well-demarcated, radiolucent lesion within the medullary canal of the ulna, extending across the distal radioulnar joint into the ulnar half of the radius, and a minimally displaced, transverse fracture of the distal ulna around the lesion.

acutely swollen wrist with tenderness over the distal ulna. His range of motion was limited, secondary to pain, but was otherwise neurovascularly intact.

A review of the radiographs demonstrated a diffusely radiolucent lesion in the distal ulna and lunate fossa of the distal radius. A pathologic fracture of the metadiaphysis region of the ulna was also noted (Fig 1). Magnetic resonance imaging revealed a large intramedullary T2 hyperintense and T1 hypointense lytic lesion within the distal ulnar metaphysis extending to the distal epiphysis and ulnar styloid, measuring approximately 4 cm. Few septations/residual trabeculae through the region of cystic change were also apparent. Endosteal scalloping and focal cortical permeation with adjacent, periosteal, T2-hyperintense foci along the radial and ulnar margins at the distal metadiaphysis region, measuring

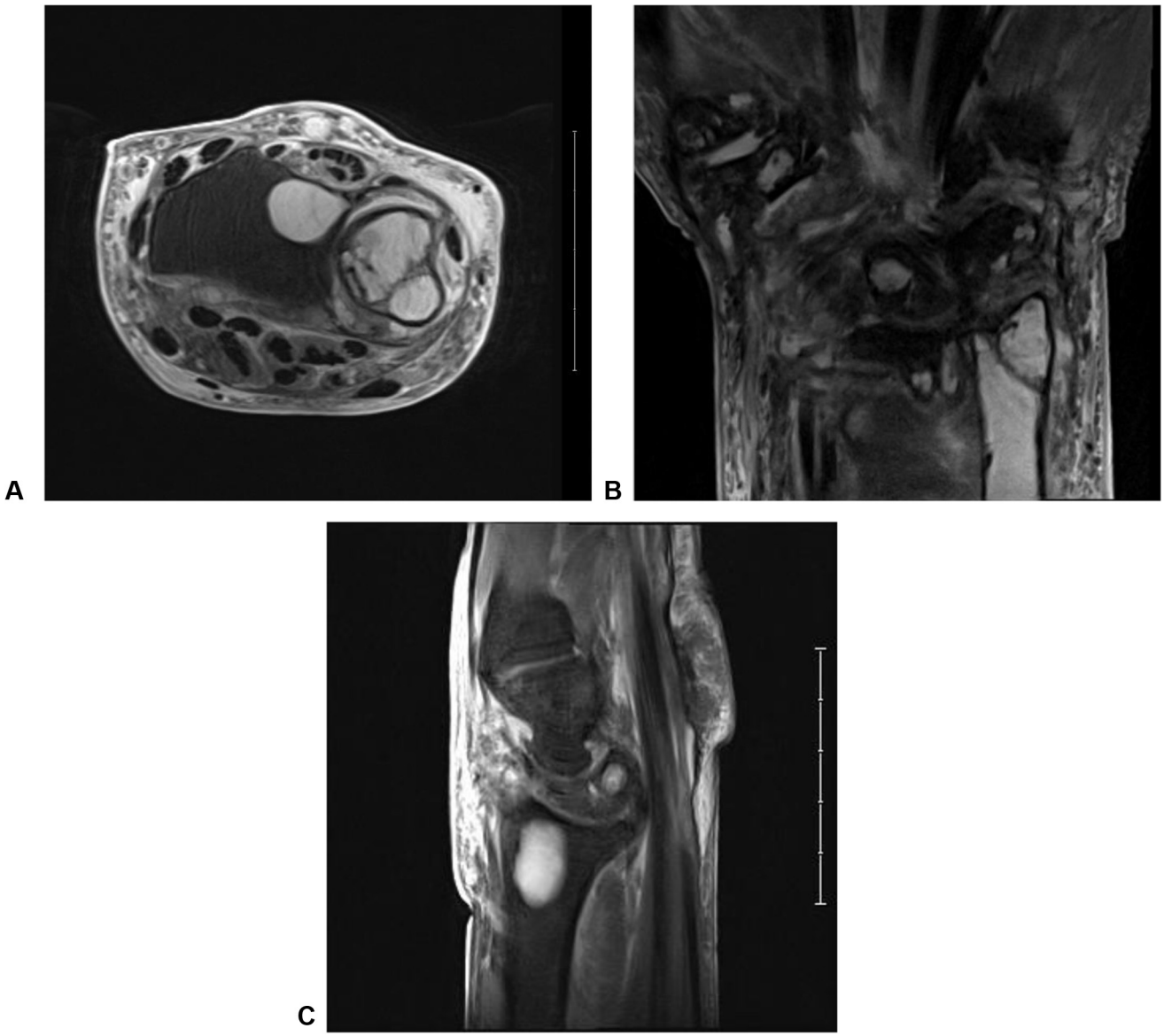

Figure 2. T2-weighted axial, coronal, and sagittal magnetic resonance images demonstrating a septated, hyperintense lesion within the medullary cavity of the distal ulna and a well-demarcated, hyperintense lesion of the ulnar aspect of the intramedullary canal of the radius.

approximately 2 and 3 mm, respectively, were noted. No intrinsic fluid-fluid levels were noted. Additionally, a prominent intraosseous T2 hyperintense or cystic change within the distal radius along the ulnar margin of the metaphysis, measuring approximately 2 cm in length, was visualized (Fig 2). Aside from a faintly positive immunoglobulin G–Kappa monoclonal protein band found on serum protein electrophoresis, laboratory testing did not reveal any notable abnormalities.

The patient subsequently underwent an incisional biopsy of the right distal ulna. Under local anesthesia, a cortical window was made in the distal ulna, and 2 samples measuring approximately $1.0 \times 0.5 \times 0.3$ cm and $1.5 \times 1.1 \times 0.2$ cm of aggregate tan-brown, rubbery to slightly firm tissue fragments were obtained and sent for pathologic analysis. On hematoxylin-eosin staining, fragments of fibrous tissue with embedded granular, purple deposits composed of overlapping rhomboid crystals were noted, along with associated granulation tissue. Under polarizing light microscopy, rhomboid-shaped calcium pyrophosphate crystals were visualized (Fig 3). Gram staining and cultures of the samples were negative.

Following the biopsy, which confirmed a nonmalignant process consistent with TCPPDCD, the patient was advised to undergo curettage and bone grafting of the lesion; however, he elected for nonsurgical management with a wrist immobilizer.

At the patient's 4-week appointment, he reported considerably less pain compared to his preinjury period and was only using pain medication once every 3–4 days. On physical examination, the patient had markedly decreased swelling over the wrist, with a well-healed surgical incision and increased range of motion at the wrist and hand. He was again offered curettage with bone grafting but continued to defer operative management. Brace use was subsequently discontinued after 2 months, and the patient's physical examination, fracture healing on radiographs, and function continued to improve until his 8-month postoperative visit, after which he was lost to follow-up.

Five years following his biopsy, the patient re-presented with a complaint of worsening contralateral wrist pain. On physical examination, he had no edema or erythema of the left upper extremity. He was found to have mild tenderness over his wrist, left

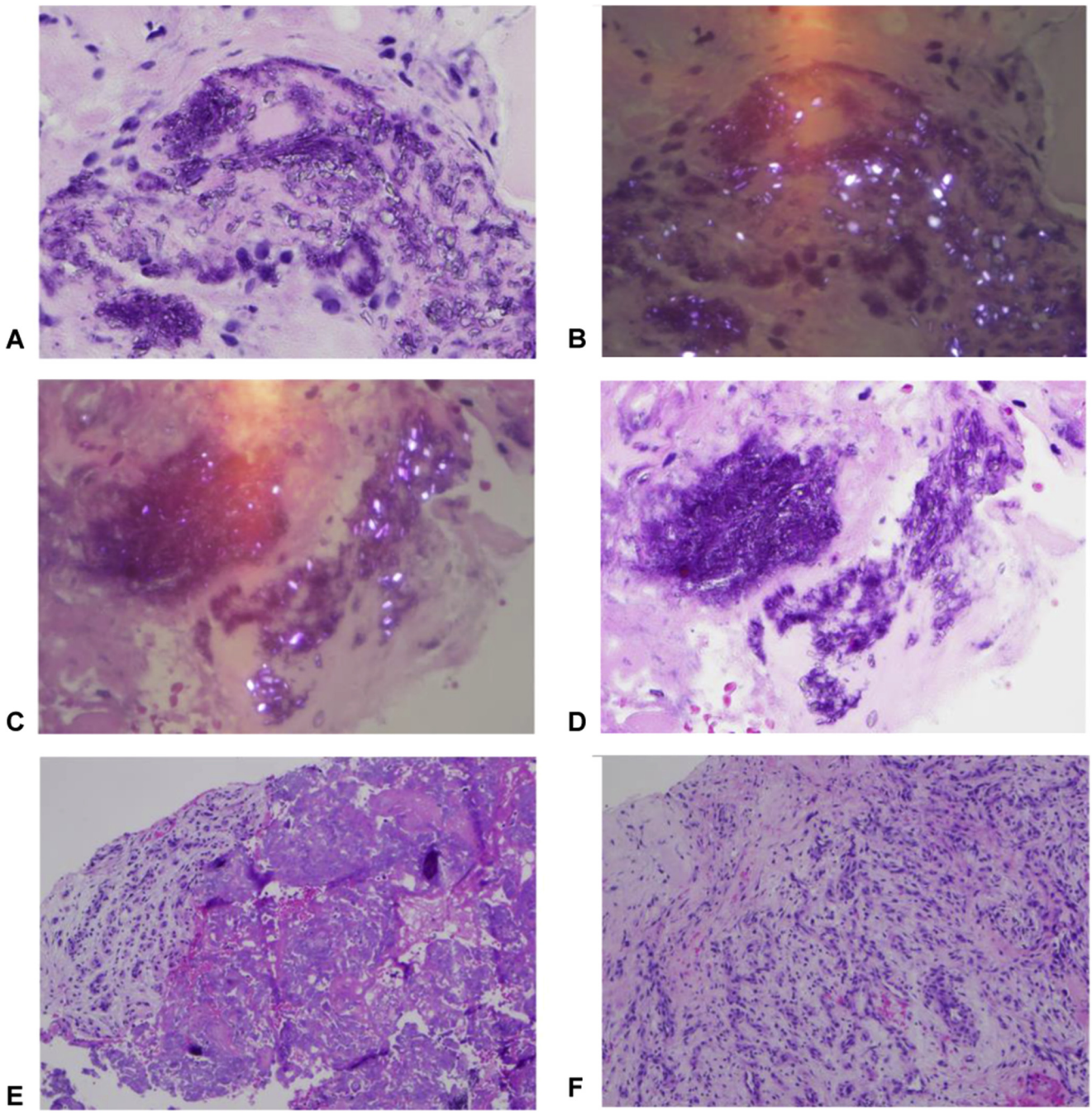

Figure 3. **A, C** The rhomboid crystals, which do not stain. **B, D** Polarized light images highlight the individual rhomboid crystals. There are coalescing aggregates of granular, purple material, composed of overlapping rhomboid crystals with adjacent plump vessels and chronic inflammation, consistent with granular tissue.

index finger, and basal joint. His wrist range of motion had approximately 70° of flexion and extension and full pronosupination. In his right, postoperative wrist, he had no tenderness over the distal ulna pathologic fracture site. The x-rays of the bilateral wrists demonstrated increased mineralization in the ulnar gutter along the left triangular fibrocartilage complex, consistent with chondrocalcinosis. There was a mild lucency in the left ulna without fracture; however, this lucency was less prominent than the lucency previously identified in the right wrist. Radiographs of the right wrist demonstrated a healed distal ulnar fracture (Fig 4). Based on his history, examination, and radiology findings, it was determined that the patient's new left wrist findings were consistent with TCPPDCD; given his lack of notable pain or risk for pathologic fracture, conservative management with referral for rheumatology was recommended.

Discussion

Calcium pyrophosphate dihydrate crystal deposition disease, formerly called pseudogout, is a common inflammatory arthropathy found in individuals over the age of 60.[5] A lesser-known, rare variant, TCPPDCD, is a unique entity characterized by the formation of a periarticular mass leading to the local erosion of adjacent bones.[6,7] With limited cases of TCPPDCD reported, we describe an

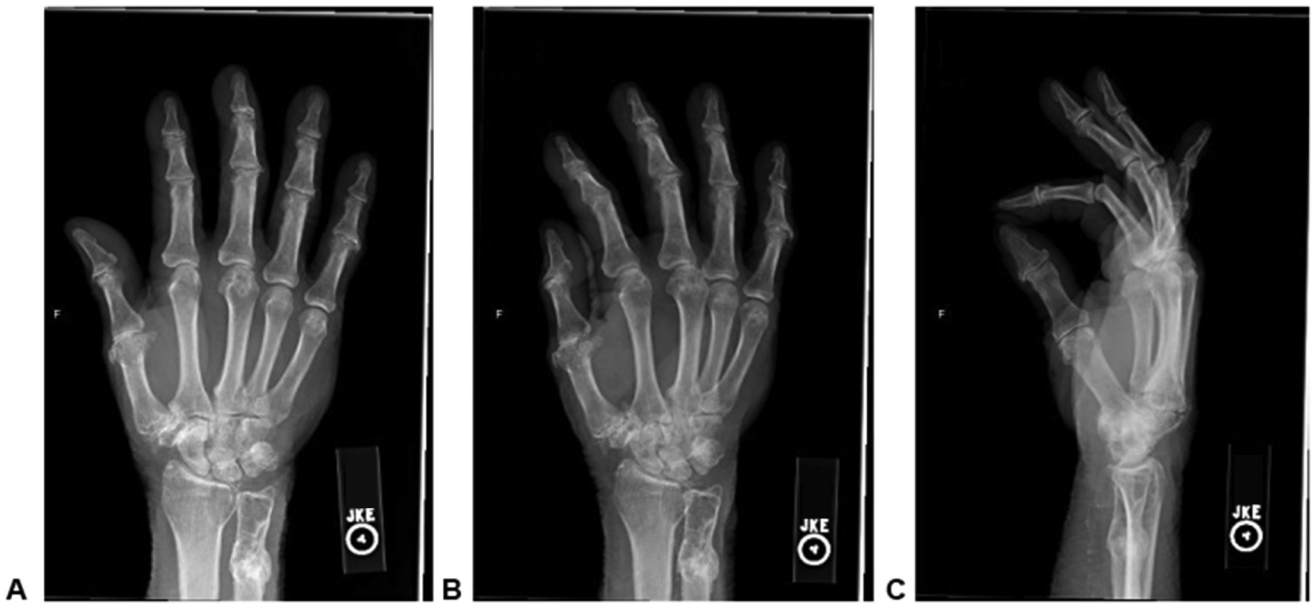

Figure 4. Posterior-anterior, oblique, and lateral x-rays of the right wrist and forearm, redemonstrating the radiolucent lesion of the distal ulna with extension across the distal radioulnar joint into the radius. In this image series, a radio-opaque region of bony callus formation is present on the distal ulna where the transverse fracture had been identified in previous images.

interesting case of TCPPDCD, differentiated by its unusual, intraosseous, long-bone origin, resulting in a pathologic fracture.[8]

Although the developmental mechanisms remain largely unknown, TCPPDCD is thought to originate through the accumulation of intracellular proteoglycans by hypertrophic metaplastic chondrocytes creating a site for crystal deposition.[9] Often located in the temporomandibular joint or paraspinal tissues, the finding of TCPPDCD in the joints of extremities is rare, with only 3 reported cases occurring at the wrist.[10,11] Of the documented cases of TCPPDCD, a predilection for women and patients aged between 31 and 86 years old has been seen.[6] Other risk factors include previous traumas or surgery to the affected joint, osteoarthritis, metabolic conditions (hyperparathyroidism, hypothyroidism, hemochromatosis), and familial CPPDCD.[10,12–14]

One hallmark of TCPPDCD is the difficulty in differentiating this condition from other disease processes, specifically malignancies. In a study by Yamakawa et al,[8] it was reported that 14 patients with a final diagnosis of TCPPDCD initially had a provisional diagnosis of a malignant tumor. Our patient presented a similar diagnostic challenge, given his risk factors for malignancy, including a 50 pack-year smoking history, age > 40, male sex, and previous diagnosis of lung cancer. Consequently, as with any potential neoplasm, a thorough diagnostic workup, including laboratory, radiographic, and pathologic analyses, was indicated.

With regards to the laboratory analysis, our patient underwent routine testing for oncologic workup of a radiolucent lesion. All laboratory studies were unremarkable except for serum protein electrophoresis, which was ordered to exclude plasma cell neoplasms from the differential. Although our patient was found to have faint monoclonal bands in the immunoglobulin G–Kappa region, this result was likely attributable to the patient's stage 3 chronic kidney disease, as an elevated glomerular filtration rate has been associated with decreased specificity of elevated serum-free light chains.[15]

On radiographs, TCPPDCD presents as periarticular, radio-opaque, amorphous, granular calcifications with pressure erosion of adjacent bones.[7,16] Radiolucent septae, which were identified on our patient's imaging, can also be seen and may be specific to TCPPDCD.[7] On magnetic resonance images, TCPPDCD characteristically displays low-intensity or hypointense signals on T1 sequences and medium to high signal intensity on T2-weighted images.[7,8,10] These findings were also consistent with the magnetic resonance imaging findings seen in our patient.

Owing to the overlapping similarities in imaging findings between TCPPDCD and other conditions, such as myositis ossificans, tumoral calcinosis, chondrosarcoma, and extra skeletal osteosarcoma, a biopsy is essential in confirming the diagnosis. Although variations exist, the typical histologic findings of TCPPDCD include a surrounding fibrous stroma admixed with basophilic, granular, calcific deposits, and the pathognomonic, positive, birefringent, rhomboid crystals.[8] Most commonly misdiagnosed as either chondrosarcoma or synovial chondromatosis owing to the analogous appearance of cytologic atypia, TCPPDCD can be histologically differentiated by identifying foreign body-type granuloma formations containing giant cells and histiocytes, as well as positively birefringent, rhomboid crystals. The presence of crystalline structures can help distinguish TCPPDCD from tumoral calcinosis and chondrosarcoma even in the absence of birefringence.[8] In our patient, the biopsy confirmed positively birefringent crystals among a background of fibrous tissue and basophilic deposits, excluding the possibility of malignancy.

As a paucity of reported cases exists, the treatment recommendations for TCPPDCD remain limited. Similar to acute and chronic forms of CPPDCD, TCPPDCD can be symptomatically managed with therapies that address the local inflammation, including intra-articular glucocorticoids and nonsteroidal anti-inflammatory drugs.[1] Typically, patients are initially trialed with nonsteroidal anti-inflammatory drugs and colchicine. However, if these therapies fail, the patient can be transitioned to a trial of glucocorticoids.[1] Disease-modifying anti-rheumatic drugs, interleukin-1β inhibitors, and biologics have been investigated for their potential roles in treating CPPDCD; however, the evidence for these agents is equivocal. In a randomized crossover trial evaluating the efficacy of methotrexate for CPPDCD, no significant benefit was demonstrated over a placebo ($P = 0.44$).[13,17,18] Thus, in most cases, the recommendation for TCPPDCD is surgical excision.[6]

Notwithstanding, even with a complete surgical excision, 1 study reported a recurrence rate of approximately 85%.[6]

Despite the intraosseous origin of the TCPPDCD lesion in this case, our recommendation was to perform an intralesional curettage with bone grafting. As a pathologic fracture was also present, the fracture was successfully treated with a period of immobilization; however, more studies in this exceedingly rare clinical entity are needed to fully elucidate the best treatment protocol.

Conclusions

Tumoral CPPDCD remains a rare entity among the pyrophosphate arthropathy spectrum. In this atypical, intraosseous presentation of TCPPDCD, with an associated pathologic fracture of a long bone, we demonstrate the role of conservative treatment in managing this condition. More research is needed to better understand this complex disease process and to direct future treatment guidelines.

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