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A Case Study of Pseudo-Neuropathic Pseudogout

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A Case Study of Pseudo-Neuropathic Pseudogout

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A CASE STUDY OF PSEUDO-NEUROPATHIC PSEUDOGOUT

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Background

This interesting case highlights the clinical progression of a rare disease process and the important role of a multi-disciplinary team in achieving a diagnosis and successful management plan.

Case Presentation

A 76-year-old male with a history of coronary artery disease, hypertension and hyperlipidemia presented as an outpatient with left foot pain and swelling. He had spent a week bicycling in Colorado one month prior to presentation. The pain was initially localized to the plantar surface of his foot and progressed to involve the lateral and dorsal aspects of the foot, as well as his great toe. The pain was accompanied by swelling of the midfoot without erythema and he was unable to bear weight. His podiatrist prescribed Ibuprofen and a foot brace for empiric treatment of tendonitis. An outpatient MRI demonstrated extensive bony edema and synovial enhancement within the midfoot, as well as severe superficial edema and peroneal tendonitis with mild subluxation. The patient was sent to the emergency department to be evaluated for osteomyelitis.

On exam, the patient was afebrile with normal vital signs. The left foot was warm and edematous without erythema or discrete fluid collection. There were no ulcers or breaks in the skin. The dorsal portion of the foot was exquisitely tender to palpation. The ankle had decreased active and passive range of motion. Pedal pulses were equal, and sensation was intact. Initial chemistries were significant for an erythrocyte sedimentation rate (ESR) of 81 mm/hr and C reactive protein (CRP) of 1.1 mg/dL. Foot and ankle x-rays were negative for fracture or dislocation. Venous ultrasound of the lower extremities was negative for deep venous thrombosis.

The patient was evaluated by orthopedic surgery and was diagnosed with severe bony stress and trauma from his prolonged bike trip. A full rheumatologic evaluation was normal. A fluid collection amenable to arthrocentesis was not identifiable. Based on imaging and physical exam, the Infectious Disease team did not feel there was evidence of osteomyelitis. The patient was prescribed high-dose Ibuprofen to treat inflammation caused by bony trauma and placed in an air boot. The patient's pain and edema improved and he was discharged.

Two weeks later, the patient presented with worsening left foot pain, edema, and continued inability to bear weight. He was noted to have new left calf atrophy, but proximal and distal muscles of the legs had full strength. Laboratory results were significant for a leukocytosis of 11.7 B/L, CRP of 2.2 mg/dL, and ESR of 94 mm/hr. A left foot x-ray demonstrated progression

of left foot swelling, osteoporosis, and intertarsal joint erosions. An MRI of the lumbosacral spine to evaluate for nerve root compression did not identify any mass or abnormal signal along the lumbosacral plexus. An MRI of the left foot and ankle demonstrated unchanged bone marrow edema. No drainable fluid collection was identified, and there was no evidence of osteomyelitis. A bone scan demonstrated abnormal activity within the left midfoot consistent with neuropathic joint disease and synovitis of the left knee. Orthopedic surgery was consulted, and additionally diagnosed micro-fractures of the midfoot, visible on the left foot x-ray and MRI. Their diagnosis was neuropathic joint disease and they recommended non-weight-bearing status for joint preservation.

The patient developed progressive left knee edema and posterior tenderness to palpation. An ultrasound of the left leg and ankle demonstrated a Baker cyst, as well as chondrocalcinosis in the cartilage of the talar dome and extensive synovitis of the talonavicular and tarsometatarsal joints (Figures 1,2). Results were discussed with Neurology and Radiology and a diagnosis of pseudogout of the left knee, foot and ankle was made. Rheumatology recommended high dose scheduled Naproxen. The patient's pain and edema improved, and he was discharged home with Naproxen and an orthopedic boot.

Outcome and Follow-up

Two weeks after discharge, rheumatology aspirated three milliliters of straw-colored fluid from the left ankle, which contained calcium pyrophosphate crystals, consistent with pseudogout. An ultrasound four months later demonstrated improvement in the left talonavicular and tarsometatarsal joint synovitis, and a small tibiotalar joint effusion with persistent chondrocalcinosis. The patient's outpatient orthopedic surgeon confirmed the diagnosis of pseudogout, with associated pseudo-neuropathic joint disease. The patient is currently being maintained on low dose scheduled Naproxen and Methotrexate as an outpatient. He is no longer wearing an orthopedic boot, and is progressively regaining his mobility.

Discussion

This case highlights the importance of an evolving differential diagnosis, based on physical exam, laboratory and radiological tests. The initial outpatient differential diagnosis included severe multifocal stress response, osteomyelitis, and early neuropathic change, and evolved to include reflex sympathetic dystrophy, osteoporosis and finally pseudogout with associated neuropathic joint disease.

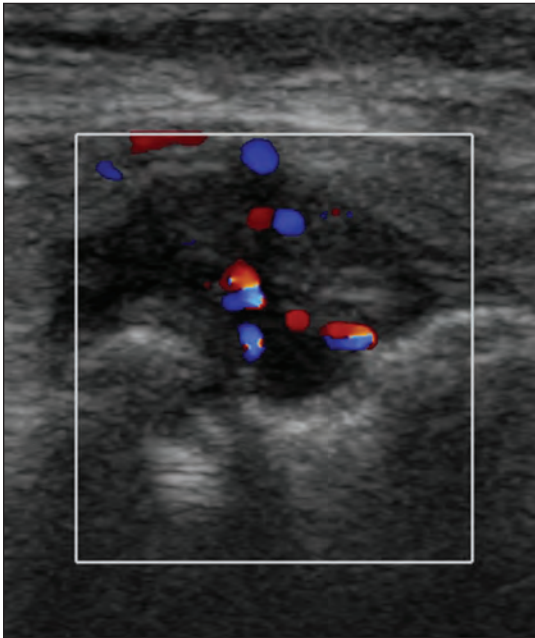


Figure 1. Color Doppler Ultrasound, sagittal view of the talonavicular joint, showing thickened synovium and increased color Doppler flow, indicating synovitis.

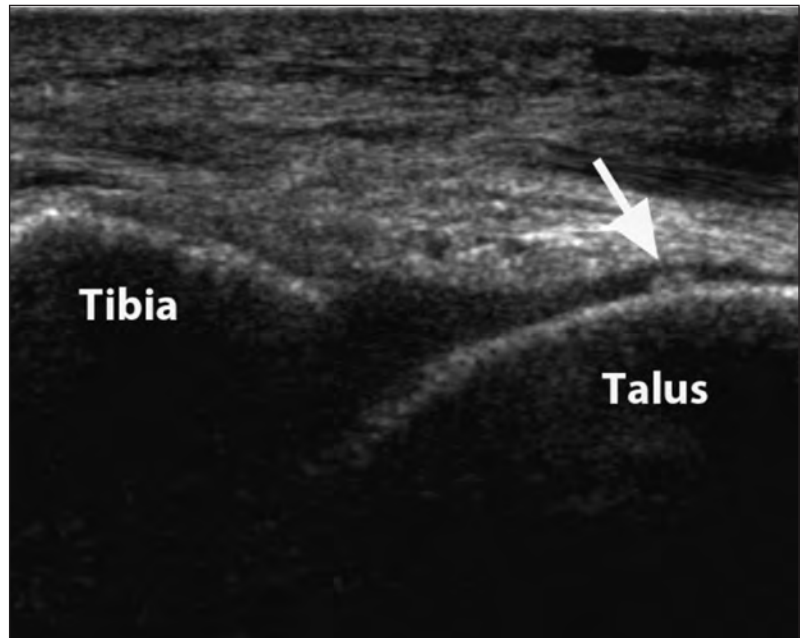


Figure 2. Ultrasound, sagittal view through the tibiotalar joint, showing cartilage calcification (arrow) at the talar dome, diagnostic of chondrocalcinosis

Calcium pyrophosphate dehydrate (CPPD) crystal deposition, and ensuing crystal-induced synovitis, is an important pathologic entity that is part of a spectrum of disease. This includes pseudogout, or acute attacks of CPPD synovitis, chondrocalcinosis, or radiographically evident deposition of CPPD crystals, and CPPD arthropathy, or chronic joint disease that typically accompanies CPPD crystal deposition. This disease process has important epidemiologic implications, as estimates suggest an age-related rise in prevalence of related chondrocalcinosis.¹ CPPD crystal formation is thought to initiate near the surface of chondrocytes and may be related to purely elevated levels of calcium, pyrophosphate, or local cartilage matrix changes that enhance calcium or pyrophosphate levels. Most cases are idiopathic, but some are associated with an underlying disorder. Hemochromatosis, hyperparathyroidism, hypophosphatemia, hypomagnesemia, familial hypocalciuric hypercalcemia, Gitelman's syndrome, gout, and hypothyroidism have been shown to be associated with CPPD. Joint trauma or joint instrumentation is also an important etiology.^{2,3}

Definitive diagnosis of CPPD crystal deposition disease is made by synovial fluid analysis. Microscopy of aspirated fluid will demonstrate the presence of positively birefringent CPPD crystals. CPPD crystal deposits can be imaged by plain film radiography as linear radiodensities in joint cartilage, ligaments and joint capsules.⁴ Ultrasound imaging can also be used to diagnose CPPD deposition disease. CPPD crystals will appear as hyperechoic bands along the cartilage surface or as hyperechoic spots in the fibrocartilage.⁵

There are few cases of CPPD crystal deposition disease associated with severe joint degeneration resembling neuropathic arthropathy and Charcot joint. This rare condition that has been termed "pseudo-neuropathic joint disease." It has been speculated that acute episodes of pseudogout and chondrocalcinosis can precede the development of Charcot arthropathy through cartilaginous microfractures, which results in the shedding of CPPD crystals into the joint cavity and progressive joint destruction.⁶⁻⁸

In patients with acute CPPD crystal arthritis, the CPPD crystals should be removed by arthrocentesis. Intra-articular injection of glucocorticoids is recommended in patients with no more than two involved joints. When more than two joints are involved, administration of oral non-steroidal anti-inflammatory (NSAID) medications is recommended. For patients in whom NSAIDs are contraindicated, colchicine can be used, and in patients for whom NSAIDs and colchicine are contraindicated, systemic glucocorticoids or immunomodulators such as methotrexate can be used. Joint immobilization is the mainstay of therapy for pseudo-neuropathic joint disease in order to prevent the development of microfractures and joint collapse.⁹

Key Points

Pseudo-neuropathic pseudogout is a rare disease process that can be difficult to elucidate. The key to diagnosis is arthrocentesis of the involved joint and the identification of calcium pyrophosphate crystals in the synovial fluid. Ultrasound is a

sensitive and specific technique for identifying chondrocalcinosis in a patient with suspected neuropathic joint disease. The mainstay of treatment is NSAID therapy.

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“Half Dome”

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