A rare presentation of Charcot neuroarthropathy: ipsilateral recurrence in the presence of end-stage renal disease

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MEDICINE & HEALTH SCIENCES

Introduction

Charcot neuroarthropathy (CN) is a rare, catastrophic joint complication that is most often seen in patients with peripheral neuropathy secondary to diabetes mellitus (DM). While the discovery of CN is attributed to French neurologist and pathologist Jean-Martin Charcot in the mid-nineteenth century, the pathogenesis of the disease is still not fully understood. A neurovascular theory describes the source of CN as an increased blood flow to the involved area that initiates bone resorption, later resulting in fractures and deformities. Alternatively, a neuro-traumatic theory states that the affected joints repeatedly undergo trauma that later induces deformities during the healing process (1). It is likely that the cause of CN is a combination of factors, and not one, single source (2).

Acute CN presents as swelling, erythema, and an increased warmth to the foot, specifically a temperature difference of greater than two degrees Celsius compared to the unaffected foot (1, 5). As the disease progresses to chronic CN, the affected foot demonstrates reduced swelling, erythema, and warmth, as well as "consolidation," where the bone demonstrates radiographic healing. There is often associated deformity present (5). One of the most common deformities seen is a collapse of the midfoot, coined "rocker-bottom foot" (3). Current best practice for the management of CN centers around offloading of some variety, whether utilizing a total contact cast (TCC), Charcot Restraint Orthotic Walker (CROW), or other device to limit motion of the affected joints (1).

Patients suffering from renal disease in addition to DM are shown to have a higher incidence of diabetic foot disease, with the three most common pathological findings being ulceration, CN, and vascular compromise of the digits (8). In fact, 30% of patients with CN also present with end-stage renal disease (ESRD), possibly due to similar microvascular complications or the connection between renal alterations of bone structure and mineral metabolism with permissible conditions to trigger CN (9). With this in mind, it is important to remember during diagnosis that multiple pathologies may coexist or occur in succession due to various patient comorbidities (10).

Data on CN recurrence is severely underrepresented in medical literature. A 2013 study by Osterhoff et al. suggests that a contributing factor is the difficulty in differentiating between the re-exacerbation of CN that did not heal properly and recurrence of new CN event after remission (7). Interestingly, it is generally accepted that CN rarely recurs in the ipsilateral limb, while cases of bilateral CN are not considered unusual (6). Very limited instances of multiple CN events occurring on the same limb have been reported in literature, each presenting with few similarities to aid in the connection of these unusual cases.

This case study aims to illustrate a rare presentation and progression of a patient with CN currently undergoing offloading treatment. The objective of this report is to gain a better understanding of the pathogenesis of CN and how comorbidities may affect this debilitating condition. To our knowledge, this case is the only description of an ipsilateral CN incident secondary to uremic neuropathy in the setting of ESRD. In addition, it appears that this is the only reported case of a tertiary ipsilateral CN event.

Case Summary

A 40-year-old male presented to an outpatient foot and ankle clinic with severe pain, redness, and swelling of his right lower extremity. Patient had a history of type 1 DM, peripheral neuropathy, previous right foot ulceration, end-stage renal disease (ESRD) on hemodialysis, hyperuricemia poorly controlled with allopurinol, and non-ischemic dilated cardiomyopathy. Physical examination revealed warm, erythematous, and edematous right foot with pain upon palpation of the midfoot and hindfoot. Radiographs of the right foot were obtained and showed findings consistent with CN of the talonavicular and calcaneocuboid joints (Figures 1a & 1b). CN was described as early stage 1 under the Eichenholtz classification and as type III under the Sander's and Frykberg anatomical classification. A TCC was applied, and patient was followed on a weekly basis. The patient's hemoglobin A1c (HbA1c) was 6.4% at the time of diagnosis, and their blood glucose levels were monitored throughout treatment. At one month follow-up, patient expressed decreased pain and swelling to the area, which was confirmed upon physical exam. Subsequent radiographs were obtained, which illustrated collapse across the midtarsal joints (Figure 2a). Over the next four months, imaging revealed evolution from severe osseous fragmentation to increased radiodensity and sclerosis, suggesting CN progression into the consolidation phase (Figure 2b & 2c). Consistent findings of increased radiodensity to the midfoot, in addition to stable clinical findings, prompted the patient to be transitioned to weightbearing as tolerated in a custom CROW.

After three months of consistent use of his CROW as instructed, the patient presented with new, severe lateral right foot pain. Physical exam revealed increased warmth to the right lower extremity and tenderness upon palpation of his right heel. Imaging revealed the known stable changes to the talonavicular and calcaneocuboid joints, as well as new ipsilateral acute CN of the subtalar joint. This was described as stage 1 under Eichenholtz classification and type IV under Sander's and Frykberg anatomical classification (Figure 3). Patient was then returned to nonweightbearing status in a TCC and continued casting for six months. After being deemed radiographically and clinically stable, he was transitioned to a custom ankle foot orthosis (AFO) with a shoe to accommodate fluctuations in edema secondary to advanced renal and cardiac disease.

Four months later, the patient returned to the clinic with new complaints of acute pain and swelling to his right foot upon standing after a dialysis treatments. Radiographs indicated new changes to the right ankle that were most consistent with CN (Figure 4b & 4c). Patient was once again returned to non-weightbearing status in a TCC and continues to demonstrate improvement clinically and radiographically. Throughout this process, the patient remained afebrile and laboratory values did not suggest an infectious etiology.

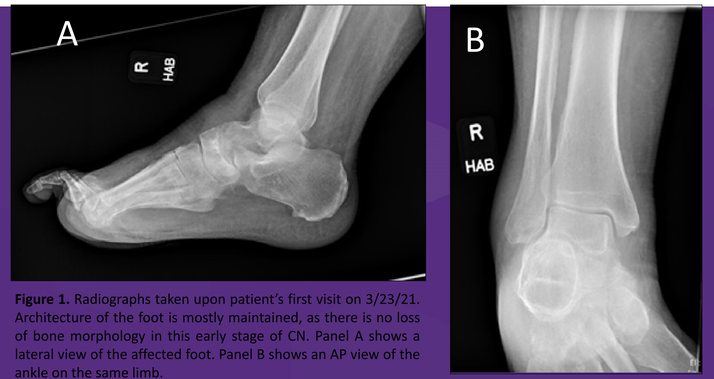


Figure 1. Radiographs taken upon patient's first visit on 3/23/21. Architecture of the foot is mostly maintained, as there is no loss of bone morphology in this early stage of CN. Panel A shows a lateral view of the affected foot. Panel B shows an AP view of the ankle on the same limb.

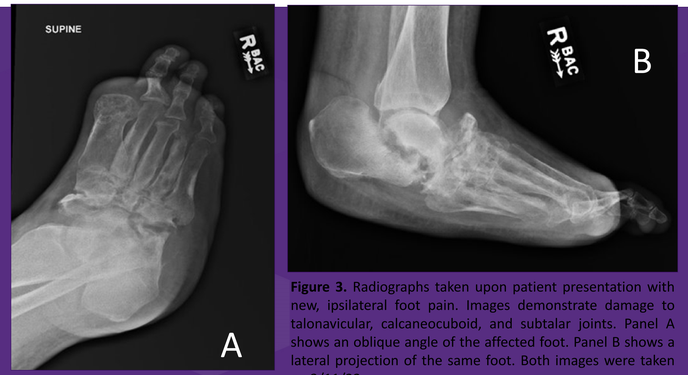
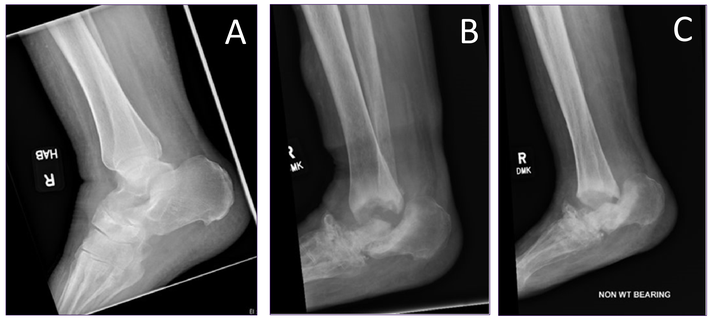


Figure 3. Radiographs taken upon patient presentation with new, ipsilateral foot pain. Images demonstrate damage to talonavicular, calcaneocuboid, and subtalar joints. Panel A shows an oblique angle of the affected foot. Panel B shows a lateral projection of the same foot. Both images were taken on 3/11/22.



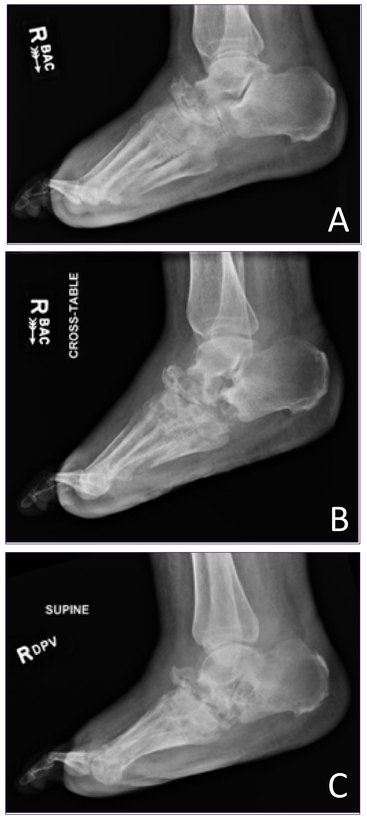


Figure 2. Radiographs taken upon subsequent patient visits, showing further destruction of the midtarsal joints. All images show the affected foot in a lateral projection. Panel A was taken on 5/6/21. Panel B was taken on 7/8/21. Panel C was taken on 9/29/21.

Figure 4. Radiographs of new changes to ankle of affected limb compared to original condition of the foot. All images show the same foot and ankle in a lateral projection. Panel A was taken on 3/23/21. Panel B was taken on 5/11/23. Panel C was taken on 6/15/23.

Discussion

To the best of our knowledge, no publication has discussed short-term ipsilateral secondary CN recurrence while the patient is currently undergoing offloading treatment. A 2013 inquiry by Osterhoff et al., which intended to gauge the rate of CN recurrence after treatment, saw that about 23% of patients in the study had a subsequent episode of CN. Only two of those cases displayed ipsilateral recurrence at a separate joint, only manifesting after the end of initial immobilization or orthotic treatment (7). Alternatively, our patient had CN reactivation after initial immobilization and while offloading in a CROW. Osterhoff et al. also pointed out that the cases of CN recurrence seemed to be most associated with patient obesity and noncompliance, both of which do not apply to our patient (7).

One of the chief complaints of our patient at the onset of both CN reactivations was severe pain in the affected foot, whereas CN often presents without pain (11). There is a strong association between uncontrolled HbA1c, profound peripheral neuropathy, and the development of CN, which explains why most patients present without significant pain. Given the increasingly high prevalence of DM, it is important to perform initial screening for uncontrolled DM in a suspected case of CN (13). Patient with diabetes mellitus and an average HbA1c of 7% were found to be at increased risk for developing CN, while those with an HbA1c of 9% or greater had an incidence of about twice as high (14). Throughout the treatment of our patient's initial and secondary CN episodes, their HbA1C was consistently within target range. Due to the patient's presentation of extreme pain, an HbA1c within goal limits, and history of uricemia secondary to renal dysfunction, we believe a main contributor to our patient's CN is likely impaired uric acid clearance in the setting of ESRD.

Uremic neuropathy is a recognized manifestation in patients undergoing dialysis, specifically those with a severely decreased glomerular filtration rate (GFR) (16). A patient with uremic neuropathy commonly presents with peripheral neuropathy, pain, and paresthesia in the lower extremity, leading to a significantly reduced quality of life (17). One feature of renal failure is the accumulation of uric acid, which is thought to be damaging secondary to precipitation leading to crystal formation and promotion of inflammation. Although uric acid is a dialyzable solute, the clearance of uric acid is only 70-80% on a standard three-times-a-week hemodialysis schedule.

A 2023 case study documented another interesting appearance of CN in a patient with ESRD, but no history of DM prior to their symptoms or during treatment. This female patient presented with classic clinical symptoms of CN, as well as radiographs that were consistent with CN. Aside from one incident of a treatment-induced superficial soft tissue wound, the patient's use of conservative treatment prevented further CN progression. This case supports a possible association between nephropathy alone and the development of CN (15).

It is important to note that previous studies have illustrated improved foot outcomes when foot care programs were instituted within dialysis centers, whereas amputation rate dropped from 50% to 10% when onsite footcare was provided (19, 20). This may be attributed in part due to enhanced collaboration between healthcare teams. Unfortunately, when combined dialysis and podiatry services are not available, it may be difficult for patients undergoing dialysis to access foot and ankle care (21). In summary, an interdisciplinary approach focused on CN education is necessary to improve CN outcomes in these vulnerable patient populations.

Conclusion

In renally-impaired patient populations, early consultation with podiatric care is essential in preventing morbidity associated with foot complications, such as CN. Additional investigation is also needed to examine incidences of ipsilateral secondary CN events and the correlation of renal disease with CN. Understanding the etiology and pathophysiology of CN is critical in recognizing the disease progression and treatment options available to patients.

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