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CLINICAL VIGNETTE

Charcot Neuroarthropathy

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Acute Charcot foot (Charcot neuroarthropathy (CN)) is an often overlooked complication in diabetic patients with neuropathy. The diagnosis is frequently missed or delayed by months to years leading to increased morbidity and mortality in affected patients. In the early stages, patients with CN present with a red, hot, swollen foot and are often misdiagnosed as having cellulitis or gout. Later stages are characterized by joint dislocation and permanent foot deformities. The pathogenesis of CN is thought to involve pain insensitivity, altered blood flow from autonomic dysfunction, and repetitive trauma ultimately leading to joint destruction and deformity. Initial treatment involves prompt recognition and immobilization and bracing to preserve a functioning foot and avoid complications. Physicians must consider the diagnosis of CN in all patients with diabetes and peripheral neuropathy who present with erythema, edema and elevated temperature. Early identification and treatment helps prevent deformity and functional loss of the lower extremity as well as possible subsequent amputation.

Case Report

A 64 year-old woman with poorly controlled type 2 diabetes mellitus, peripheral neuropathy, paroxysmal atrial fibrillation, hypertension, and recurrent urinary tract infections (UTI) complained of having left foot/ankle swelling for a several days. She denied trauma to the left foot. The patient was employed as an attorney and denied illicit drug use. She was already being treated with an oral antibiotic (cefpodoxime) for a recent UTI. Doppler ultrasound of the left leg was negative for deep vein thrombosis. Subsequently, she developed left foot pain, erythema, subjective fever and chills. In addition to cefpodoxime, home medications included repaglinide, levemir insulin, atenolol and hydrochlorothiazide. Vital signs showed temperature 37.2°C, blood pressure 116/65 mmHg, pulse 63 beats per minute, respiration rate 17 breaths per minute with normal oxygen saturation. Physical examination was unremarkable except for her left low extremity. The left leg was edematous to mid shin with taut and shiny skin in addition to erythema on the lateral foot with bruising on the 2nd and 3rd toes. The foot was also slightly warm to touch. There was no ulceration, fluctuance or crepitance. Initial laboratory evaluation showed white blood cell count of 10.4 x $10^3/\mu L$, hemoglobin of 9.8 g/dL, creatinine kinase of 144 U/L, creatinine of 0.9 mg/dL, erythrocyte sedimentation rate of 40 mm/hr and elevated C-reactive protein of 10.7 mg/dL. Initial left foot X-ray showed no evidence of osteomyelitis or foot deformity (**Figure 1A**). The patient was admitted to the hospital with presumed left foot cellulitis and was empirically treated with intravenous daptomycin and piperacillin/tazobactam. Despite antibiotics, the patient had persistent left foot pain and the erythema only slightly improved. On hospital day four, the patient was ambulating and developed acute worsening of the foot pain along with a deformity at the dorsum of the left foot. Repeat left foot X-ray showed multiple subluxations involving the midfoot and tarsometatarsal articulations with small cortical fractures involving the navicular and likely the medial cuneiform bone (**Figure 1B**). Computed tomography (CT) of the left foot showed small bony fragments projected from the navicular bone, intermediate, and lateral cuneiform bones and cuboid bone. The navicular, intermediate and lateral cuneiform bones were subluxed dorsally. These findings were consistent with Charcot foot (**Figure 2**). Podiatry consultation was obtained and patient was placed on strict non-weight bearing of the left foot and was discharged with a controlled ankle motion (CAM) boot and crutches. In follow up, the patient was transitioned to a Charcot restraint orthotic walker (CROW) boot and eventually to diabetic orthotic shoes (**Figure 3**). Surgical options were discussed, but the patient elected to be treated conservatively. A repeat left foot X-ray three years later showed a similar deformity as at the time of diagnosis.

Discussion

CN is a progressive deterioration of the weight-bearing joints, most commonly in the foot or ankle, characterized by painful or painless bone and joint destruction[1]. It occurs most often as a complication of diabetes mellitus and diabetic neuropathy, but other diseases associated with neuropathy (alcohol abuse,

spinal cord lesions, etc.) can also predispose to this condition[2,3]. The first description of "neuropathic arthritis" was recorded in the 1700s as a complication of syphilis[4]. In the mid-1800s, an American physician, John Kearsley Mitchell, reported cases of hot, swollen, and asymmetrical joints in patients with spinal cord injuries[5,6]. In 1868, Jean-Martin Charcot, a French neurologist, identified neuropathic joints with an unusual pattern of destruction in patients with tabes dorsalis caused by syphilis and published his findings[2]. At the Seventh International Medical Congress in London, Sir James Paget recognized the discovery by Charcot as a distinct pathological entity and declared that the disease be known as "Charcot's disease"[7]. However, it was not until 1936, that the link between Charcot arthropathy and diabetes mellitus was recognized[8]. Unfortunately, diagnosis is often delayed or missed as the acute Charcot foot can clinically mimic other conditions such as cellulitis or gout[3,4]. A high index of suspicion is required in all patients with diabetes and neuropathy. Treatment involves immobilization and prompt consultation with orthopedic or podiatric foot specialists to preserve the ability to walk and quality of life[2]. CN severely reduces the quality of life and increases morbidity and mortality in patients with diabetes mellitus and neuropathy.

The pathophysiologic mechanism of Charcot foot has long been debated, but it is thought to begin with peripheral neuropathy[3]. Several theories have been proposed. Of these, the neurotraumatic theory and the neurovascular theory are foremost. The neurotramatic theory points to the loss of pain sensation and proprioception combined with repetitive trauma to the foot (the midfoot most commonly) leading to a complex series of pathological processes culminating in bone and joint destruction and subsequent deformity[1,9,10]. However, the precise role of trauma in CN remains unclear. The Charcot process is known to progress rapidly after trauma in humans and a precipitating minor traumatic event is reported in as many as 50% of patients with Charcot foot[2]. Notably, however, CN sometimes develops in non-weight bearing joints as well. A further complicating factor is that patients with neuropathy often do not recall painless trauma[1,4]. The neurovascular theory proposes that the bony destruction is due to an autonomically stimulated vascular reflex that leads to increased blood flow and bone resorption and osteopenia. Combined with repetitive trauma, this eventually leads to joint and bony destruction[1,10]. It is likely that a number of mechanisms operating simultaneously result in the pathology leading to CN.

While multiple diseases associated with neuropathy can cause CN, diabetes mellitus is the most common cause[3,4]. Most patients with CN have had poorly controlled diabetes mellitus for 15-20 years . It is estimated that ~ 1-7% of diabetics with neuropathy have neuropathic arthropathy, with ~10-30% of these affected patients having bilateral involvement. The distribution of arthropathy is 70% in the midfoot and 15% at the forefoot and midfoot. The tarsometatarsal (Lisfranc's) joint is the most common site for arthropathy[2].

The Eichenholtz classification system has been used to define the four stages of CN (**Table 1**). Each stage is associated by specific characteristics and treatment strategies[10,11]. Stage 0, or the 'inflammation' stage, is the clinical (prefracture) stage when early diagnosis and intervention are critical to prevent long-range sequelae. However, the diagnosis at this stage is commonly missed leading to progression of CN into the active destructive phase[9,12]. Stage 0 is characterized by erythema, edema, and heat but no structural changed. This stage can progress if weight bearing and inflammation persist. Stage 1, or the 'development' stage, is characterized by bone resorption and fragmentation, and joint dislocation leading to an unstable, deformed foot. Stage 2, or the 'coalescence' stage, involves bony consolidation and fusion after bony destruction. Absorption of small bone fragments, joint fusion, and bony sclerosis are seen[2,3]. Stage 3, or the 'reparative' stage (chronic Charcot), is associated with re-stabilization of the foot with progressive fusion of the involved fragments and leads to the return of a stable, although permanently deformed, foot (rocker bottom foot deformity)[2,4,13].

In patients with long-standing diabetes and peripheral neuropathy, a red, hot, swollen foot should raise the suspicion of CN[3,4]. Early recognition and prompt treatment can preserve a functioning foot. Unfortunately, due to the mimicking presentations, many patients with CN are diagnosed initially with cellulitis or gout. The diagnosis of CN is missed initially 25 to 79% of the time and diagnosis is delayed on average up to 29 weeks[12]. Most patients are 50-70 years old and often present 2-3 months after initial symptoms, because pain is often not pronounced in half of patients[3]. The earliest manifestation of CN is typically persistent swelling and discomfort[1]. Approximately 50% of patients with Charcot foot remember a minor traumatic precipitating event. While trauma is not a prerequisite for CN, it can develop very rapidly after minor trauma in patients with diabetes and

neuropathy. A high index of suspicion for acute Charcot foot is needed for any patient with diabetes and neuropathy[2].

On examination during the active stage, the foot is warm, swollen, and tender and can have marked erythema[1]. The differential diagnosis includes cellulitis, osteomyelitis, acute gout, deep vein thrombosis, or neuropathic fracture[3,4,10]. Infection is rare without the presence or history of an open ulceration as most diabetic foot infections began with a direct inoculation through a skin opening. Patients with CN are typically afebrile, have a normal white blood cell count, and often have no skin ulcerations making infection less likely. Ulcers frequently complicate CN, so that even in patients with plantar ulcers, it is critically important to keep the patient non-weight bearing until an acute Charcot process has been ruled out.

A careful medical history is key to the diagnosis, but it is important to remember that many patients with neuropathy and altered pain sensation may be unaware of trauma or injury to the foot. In patients with a plantar ulcer, the physician should determine whether probing to the bone is possible as this is strongly correlated with osteomyelitis. While there are no laboratory criteria for the diagnosis of CN, lab testing can help narrow the differential diagnosis. Leukocytosis, and elevated C-reactive protein and erythrocyte sedimentation rate (ESR) suggest possible infection. Bilateral weight-bearing radiographs should be obtained to determine stability. Even if there is no radiographic evidence of joint dislocation (as in stage 0 disease), CN should still be suspected so that treatment, if indicated, can be started promptly[3]. In the event that the patient is neuropathic and there is no radiographic evidence of osteomyelitis, magnetic resonance imaging (MRI) or a tagged white blood cell scan should be done. MRI can show changes in stage 0 and is extremely sensitive for osteomyelitis, but the presence of osteoarthropathy can lead to false-positive results. MRI has the highest diagnostic accuracy and is increasingly being recommended as the test of choice for diagnosing Charcot neuroarthropathy, especially in the early stages[10,14]. Positron emission tomography (PET) combined with computed tomography (CT) is also gaining support and is very reliable for differentiating CN from osteomyelitis[15]. Despite all these tests, differentiating CN from Charcot with infection remains difficult and bone biopsies may be necessary for a definitive diagnosis. Prompt podiatry consultation is often warranted not only for diagnostic purposes, but also to aide in treatment decisions, casting and close follow-up.

The main goals of treatment include creation and maintenance of a stable foot, wound and bone healing, elimination of infection if present and prevention of deformity[3,10]. For the hospitalist or primary care physician, the most important initial treatment is immediate immobilization and avoidance of weight bearing and the prompt referral to a foot and ankle specialist for further recommendations.[4] Early recognition of the Charcot syndrome and prompt treatment can minimize potential foot deformity, ulceration, and loss of function[2]. Patient and family education regarding compliance are crucial. Most cases of acute Charcot foot can be treated non-surgically with pressure-relieving methods such as total contact casting (TCC)[10]. The goal of TCC is to evenly distribute forces across the plantar surface of the foot. TCC is utilized until the erythema and edema have resolved, the temperature of the foot has normalized, and radiographs show stabilization (generally 8-12 weeks but maybe longer)[16]. Foot ulcers may require surgical debridement and antibiotic therapy prior to the application of TCC. After initial radiographs, surveillance films should be taken at 4-6 weeks intervals. When the active phase of the Charcot process is complete, as evidenced by resolution of swelling and erythema and radiographic stability, the TCC is often converted to a Charcot restraint orthotic walker (CROW) boot for a total of 4-6 months of treatment[16]. Protective footgear with orthotics may also be needed at a later time. Some studies have reported that the use of a bisphosphonate (pamidronate) results in symptomatic relief with decreased erythema, decreased temperature and decreased Charcot activity[1,17]. Surgical treatment is sometimes necessary but is typically reserved for acute fracture or dislocation, severe deformity, or recurrent ulceration[3]. Complications are common and include recurrent ulceration, need for prolonged bracing and even amputation[10].

All physicians should be vigilant and consider the diagnosis of Charcot foot in neuropathic patients who present with foot or ankle erythema, edema, and elevated temperature. Any minor injury in patients with diabetes and neuropathy requires careful observation because of the tendency of the limb to proceed to a Charcot process. Early identification and treatment of the Charcot process helps prevent deformity and decreased function of the lower extremity, as well as possible subsequent amputation. Patients with an established neuropathic foot should

be seen regularly and physicians should provide continuous education about the proper care of the foot and the use of orthotic devices. A multidisciplinary approach with podiatry consultation and co-management is necessary whenever CN is suspected.

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Table 1. **Charcot Foot Classification, Description**[*]

- A. Stage 0 – Clinical, inflammation
  - a. Warm, erythematous, edematous foot
  - b. No structural changes
- B. Stage 1 – Fragmentation, development
  - a. Periarticular fractures, joint dislocation, unstable, deformed foot
  - b. Radiographic changes evident
- C. Stage 2 – Coalescence
  - a. Reabsorption of bone debris
  - b. Joint fusion, bony sclerosis seen
- D. Stage 3 – Reparative, chronic Charcot
  - a. Stable foot with deformities
  - b. Progressive fusion, decreased sclerosis

**adapted from* Sommer TC, Lee TH. Charcot foot: The diagnostic dilemma. American Family Physician. 2001 Nov 1;64(9):1591-8 and Wukich DK, Sung W. Charcot arthropathy of the foot and ankle: Modern concepts and management review. Journal of Diabetes and Its Complications. 2009;23:409-26.

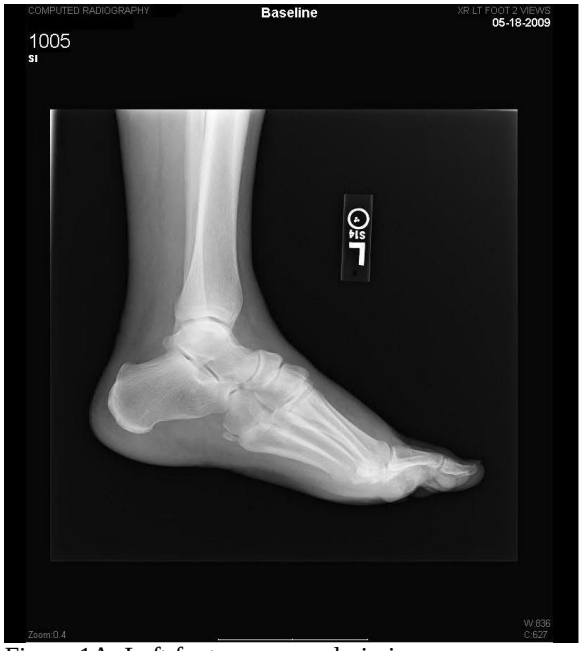

Figure 1A: Left foot x-ray on admission.

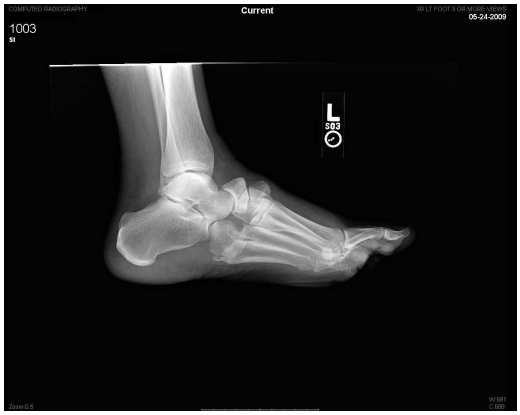

Figure 1B: Left foot x-ray 4 days later showing subluxations at the dorsum of mid foot.

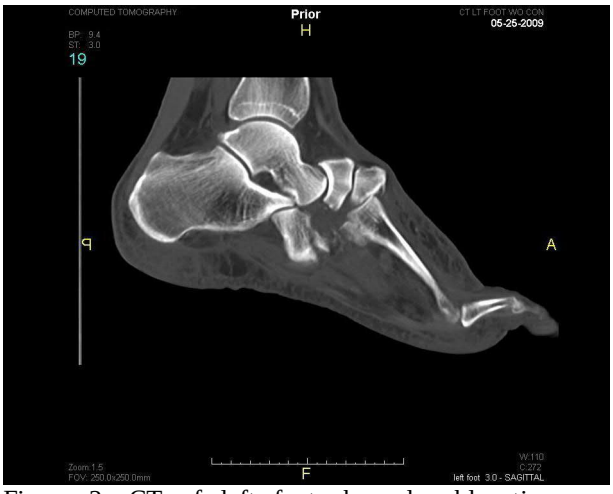

Figure 2: CT of left foot showed subluxations confirming the diagnosis of Charcot foot

Figure 3: Controlled Ankle Motion (CAM) boot (left) and Charcot Restraint Orthotic Walker (CROW) boot (right).