Diabetes mellitus is a leading cause of Charcot neuropathy today. A review of the literature reveals two studies that quote the incidence of from 9%1 of patients with diabetic neuropathy to as high as 12.9%. 2 Although William Musgrave first described the condition in 1703 as an arthritic complication of venereal disease, the theory was advanced by Charcot in 1868 to encompass neuropathic joints in individuals with tabes dorsalis.3 Other conditions reported to be associated with the development of a Charcot joint include alcoholism, leprosy, congenital insensitivity to pain, syringomyelia, poliomyelitis, pernicious anemia, disruption of peripheral nerves (toxic, tumorous, or traumatic), and paraplegia.4 The differential diagnoses include arthritis, cellulitis, deep vein thrombosis, and osteomyelitis. Therefore, it is important for Charcot’s joint to be distinguished from other pathologies, especially osteomyelitis, and to be staged accordingly because of the differences in treatment. An accurate diagnosis is the result of key findings in the patient’s history and a physical examination.5 Charcot’s joint usually presents with a red-hot, swollen foot with reports of minor trauma, such as stubbing one’s toe or no obvious trauma at all (Fig. 1). The individual is usually insensate and may not present with any pain.6 With osteomyelitis, there often is a history of ulceration, trauma, or prior surgery,7 and plain radiographs are helpful but sometimes not reliable during early onset. The triphasic bone scan can be an important imaging modality for determining osteomyelitis.8 However, this modality is sensitive, yet often not specific enough, for differentiating osteolysis secondary to infection or Charcot.9

Osteomyelitis often complicates a diabetic neuropathic foot, leading to amputation, decreased function, and quality of life. Therefore, early detection and treatment are paramount. Furthermore, neuroarthropathic (Charcot) changes in the foot often resemble infection and must be differentiated. Currently, the Tc-99m HMPAO Labeled Leukocytes Scan is considered to be the most reliable noninvasive imaging modality of choice in determining Charcot foot changes versus osteomyelitis. The purpose of this article is to alert the clinician that although the Tc-99m HMPAO Labeled Leukocytes Scan may be the second most reliable test next to bone biopsy for determining osteomyelitis, false positives do occur. (J Am Podiatr Med Assoc 91(7): 365-368, 2001)
sive means of determining osteomyelitis. This scan is performed by extracting the patient’s white blood cells, labeling them with hexamethylpropyleneamine oxime (HMPAO) from venous blood, and reinjecting them back into the patient. Images are then viewed on a large field of a gamma camera using a high-resolution collimator and an energy window similar to that of the triphasic bone scan. The test is considered positive when there is focal bone uptake greater than that of the surrounding soft tissue in the suspected area of osteomyelitis. Theoretically, the white blood cells migrate to the area of infection to aid in the body’s combative response. However, in the case of bone osteolysis secondary to another condition, such as Charcot, false positives may occur. In a study by Blume et al., the investigators found that Tc-99m HMPAO white blood cell accumulation at the site of infection occurred in 18 to 20 cases. The sensitivity of the labeled white blood cell scan for osteomyelitis was 90%, the specificity was 86%, and the specificity for complicated pedal osteomyelitis was 89%. Furthermore, this study included two subjects with Charcot arthropathy who had true negative scans of their feet.

Changes associated with Charcot foot deformity generally consist of three components: autonomic neuropathy, sensory neuropathy, and motor neuropathy. Autonomic neuropathy leads to an increase in peripheral perfusion to the lower extremity, which in turn weakens the osseous structures through the hyperemic process of washing out bone minerals. This can result in susceptibility to fractures. The sensory neuropathy leaves the individual insensate to pain and protective sensation. Unaware of the destructive process occurring, the individual continues with normal weightbearing activities and ambulation as the joints and osseous structures continue to break down. Lastly, motor neuropathy establishes a muscular imbalance leading to faulty biomechanics and deformity. As such, loss of proprioception, protective sensation, combined with the presence of joint effusion, causes ligament laxity and subluxation. In turn, this leads to hypermobility, osteophyte growth, cartilage erosion, bone chips and compression fractures, intra-articular and extra-articular exostoses, and ossification of various ligamentous structures. As with any inflammatory process, regardless of the cause, white blood cell migration to the area aids with repair of bone.

With this process in mind, Charcot has been divided into three stages representing the pathophysiology and treatment interventions popularized by Eichenholtz. The first phase is the acute phase, which is characterized by a red-hot, swollen, insensate, and often painless foot. Radiographically, osteopenia, osteolysis, and joint breakdown may or may not be present. Also, corresponding laboratory values (eg, blood glucose and erythrocyte sedimentation rates) may be elevated. Treatment consists of strict non-weightbearing and compressive or total contact casting. Surgical intervention generally is not advocated at this time, although some surgeons indicate that early surgical intervention is adventitious in preventing deformity. The second phase is the coalescence phase, in which all acute signs with the exception of pedal edema have resolved. Treatment in this phase is geared toward gradual return to weightbearing and prescriptive accommodative shoes. The final phase is the reconstructive quiescence phase, whereby all acute inflammatory processes have subsided and the patient is left with resultant deformity. Conservative treatment during this phase is accommodative footwear. Surgical reconstruction to prevent further breakdown and ulceration is generally recommended to be performed during the reconstructive quiescence phase. The treatment for an osteomyelitic process would be very different, consisting of 6 weeks of intravenous antibiotic therapy and excision of the infected bone to prevent further spreading. Therefore, identification and early diagnosis are essential to protecting the foot and limiting the destructive process in Charcot.

Case Report

A 71-year-old man was admitted to the St Agnes Medical Center in Philadelphia, Pennsylvania, with a chief complaint of a red-hot, swollen left foot with minimal pain of approximately 2 weeks’ duration.
The patient did not recall any specific trauma to the area and was a non-insulin-dependent type 2 diabetic patient of approximately 15 years’ duration. His medical and surgical history consisted of hypertension controlled by medication, surgery on his left foot 15 years ago, and an ulceration under the second metatarsal that had been closed now for 8 months. There were no prior episodes of left or right foot swelling. Physical examination revealed a mildly obese 71-year-old man in no acute distress with palpable pedal pulses bilaterally. He presented with an erythematous, hot, painful, and edematous left foot with absent protective sensation to a Semmes-Weinstein 5.07 monofilament. Also, absent vibratory sensation in all foot joints up to the ankle were noted (Fig. 2). Evidence of a closed ulceration under the second metatarsal on the left foot was also seen (Fig. 3). Pertinent laboratory values were as follows: glucose 224 mg/100mL, white blood cell 6.6/mm³, and sedimentation rate of 45 mm/h. All other values were within normal limits. Radiographically, three views of the left foot were obtained and indicated near-complete destruction of the osseous structure of the midfoot, including the tarsonavicular, cuboid, and cuneiforms. Although present, these osseous structures were severely deformed, demonstrating a mottled sclerotic and lucent density, with ill-defined margins and destruction of the articular surfaces, and increased bone fragmentation. There was diffuse soft-tissue swelling, although without evidence of subcutaneous emphysema. The findings were found to be most consistent with a neuropathic arthropathy (Figs. 4 and 5). A Tc-99m HMPAO scan was then ordered, resulting in asymmetric increased activity involving the left foot and ankle with focal increased activity seen in the left tarsal region. Although there was focal uptake, the radiologist correlated this to Charcot neuroarthropathic joint destruction versus osteomyelitis (Fig. 6). No further tests were ordered and the patient was placed in a nonweightbearing compressive cast and later was discharged to home after a 10-day stay as an inpatient. At the time of discharge, the redness, swelling, and skin temperature had significantly decreased.
Discussion

The purpose of this article is not to discredit the use of the Tc-99m HMPAO Labeled Leukocytes Scan for aiding in the diagnosis of osteomyelitis, but through a clinical application to point out that false positives occur. This is especially true in the presence of Charcot neuroarthropathy. As such, perhaps future studies comparing specificity in the presence of Charcot could help clinicians differentiate and recognize true false positives. To date, no such studies are found in a literature search. Because osteomyelitis and Charcot have very different treatments and outcomes, early detection and diagnosis are essential for maintaining function and quality of life.

References