Pedal Neuroarthropathy in a Nondiabetic Patient as a Result of Long-term Amiodarone Use

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In this article, we describe a case of a man without diabetes with a long history of amiodarone use. He presented with a foot deformity and plantar ulceration. Examination showed him to have a symmetrical peripheral neuropathy and findings consistent with a Charcot foot. Extensive investigations failed to find other causes for his neuropathy, other than his amiodarone use. We believe that this is the first reported case of a neuropathic foot deformity and ulceration occurring with amiodarone use, and we feel that it is important to point out the association of this commonly used antiarrythmic drug with this form of neuropathic osteoarthropathy. Level of Clinical Evidence: 4 (The Journal of Foot & Ankle Surgery 48(3):362–364, 2009)

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Jean-Martin Charcot (1825–1893) first reported neuropathic joint degradation in 1868, and most of the cases that he originally described were caused by syphilis (tabes dorsalis), leprosy, or diabetes mellitus. Since that time, other causes of neuropathic arthropathy have been identified, including chronic alcohol intoxication and spinal cord disorders such as syringomyelia and myelomeningocoele. Worldwide, diabetes and leprosy remain the most common causes of Charcot neuroarthropathy. It is also widely known that the foot, being a weight-bearing structure, is vulnerable to deformation and cutaneous compromise as a result of Charcot neuroarthropathy. In this article, we describe the case of an elderly male patient who developed a Charcot foot secondary to long-term amiodarone therapy.

Case Report

In September of 2008, an 85-year-old man was referred to the orthopedic foot clinic with an ulcer on the plantar aspect of his left midfoot, and deformity consistent with a neuropathic arthropathy, namely Charcot foot. His only past medical history was that of a 20-year history of atrial fibrillation controlled with amiodarone 200 mg administered orally on a daily basis, as well as asthma that was well controlled. He had no previous history of diabetes mellitus, leprosy, syphilis, or spinal cord defects; he did not drink alcohol, and he denied any preceding trauma. Furthermore, he denied any dietary restrictions or exposure to heavy metals or other potential neurotoxins. His only other regular medication was aspirin 75 mg daily, and he inhaled bronchodilators intermittently.

On physical examination, his foot was deformed with a rocker bottom configuration and a superficial (not deep to muscle fascia) plantar ulcer at the apex of the deformity (Figure 1). He had no clinical evidence of cutaneous or mucus membrane involvement consistent with leprosy or syphilis. He displayed a symmetrical, bilateral peripheral neuropathy as evidenced by a diminution in vibration perception threshold on biothesiometry (>30 V), with no sensation in any modality at all to the midshin level. He had no evidence of vascular insufficiency to either lower extremity. Investigations showed he had a normal full blood count, bone metabolic profile, vitamin B_{12}, and erythrocyte sedimentation rate (ESR), and a fasting glucose of 4.5 mmol/L (normal range 3.5–7.8 mmol/L). His immunoglobulin profile was normal, and his rheumatoid factor, autoantibody screen,

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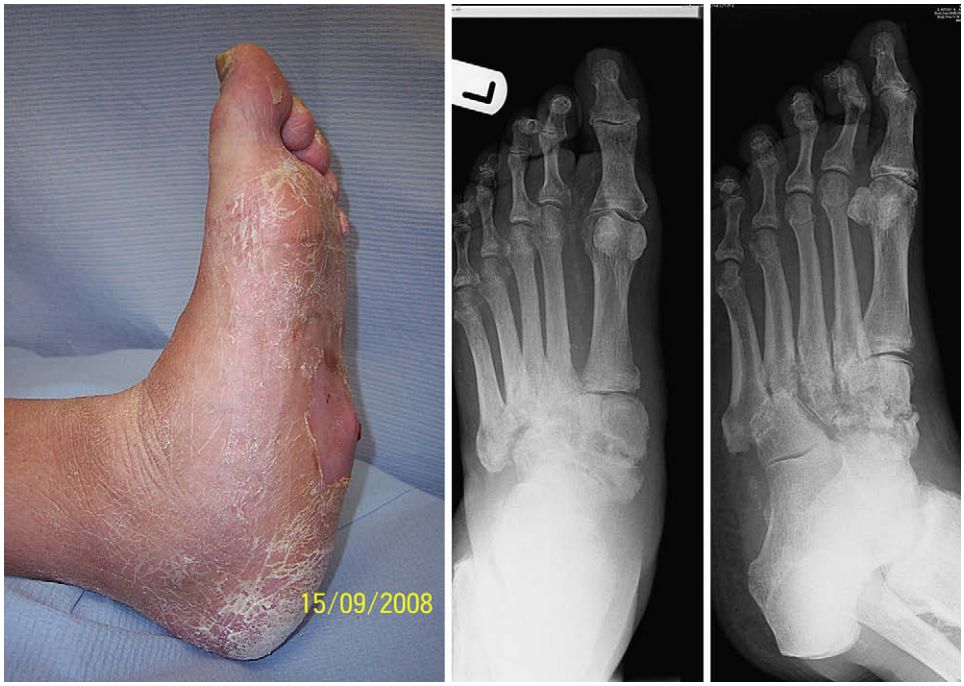

FIGURE 1 View of the left foot displaying plantar convexity with plantar ulceration, and left foot and radiograph consistent with Charcot's deformity showing destruction of the bones of the midfoot.

and anti-neutrophil cytoplasmic antibodies (ANCAs) were negative. His *Treponema pallidum* serology was also negative. His foot radiograph was consistent with that of a neuropathic deformity with destruction and subluxation of the forefoot, Lisfranc joint complex (midfoot), and talonavicular joint (Figure 1). There was no evidence of arterial medial calcific sclerosis on the radiographic images.

Based on the aforementioned clinical, laboratory, and radiographic findings, the diagnosis of a Charcot foot caused by amiodarone-induced peripheral neuropathy was made. Because the plantar ulcer was superficial, we felt that surgical debridement and bone biopsy, as well as magnetic resonance imaging, were not indicated. A swab specimen procured from the base of the plantar ulcer grew *Coliform* sp, and these were felt to be commensals only and were not specifically treated with antibiotics. He was initially treated with off-loading using a full-contact plaster cast and 70 mg of alendronate administered orally on a weekly basis. Because of the therapeutic success in regard to control of the patient's cardiac arrhythmia, no change was made in regard to his use of amiodarone.

After approximately 4 weeks of therapy, follow-up inspection revealed persistence of the plantar ulcer, and surgical debridement with reduction of the bony plantar midfoot protrusion and bone biopsy were undertaken. Bone specimens failed to grow any bacteria, and histopathological inspection of the resected bone and joint tissues was consistent with Charcot neuroarthropathy. Following the surgery, a negative pressure wound dressing was used, and the plantar wound healed within 3 weeks. At the time of the most recent follow-up, approximately 3 months following his initial presentation to our clinic, clinical and radiographic inspection showed a fully intact plantar skin barrier and the joints of the Charcot foot appeared to be consolidating. At that time, moreover, the patient was ambulating full weight bearing on his left neuropathic foot, and he had converted to the regular use of a custom-made shoe to accommodate the bony deformity secondary to the Charcot process and to prevent further ulceration.

Discussion

Peripheral neuropathy is a rare, but well-recognized complication of amiodarone, occurring in up to10% of patients (1). However, after a thorough search of the biomedical databases, including Medline, Embase, and the Cumulative Index of Nursing and Allied Health Literature (CINAHL), to the best of our knowledge, the development of a Charcot foot as a result of amiodarone-induced peripheral neuropathy has not previously been reported. Moreover, the etiopathogenesis of this form of peripheral neuropathy is not yet completely understood. It may be related to the highly lipophilic nature of amiodarone, which leads to the accumulation of intralysosomal inclusions and phospholipid complexes that interfere with cellular membranes, and also causes the development of reactive oxygen species (2). Furthermore, amiodarone-induced peripheral neuropathy has been described as axonal, demyelinating, or a combination of both (3). Many of the reported cases have been a result of prolonged high doses of amiodarone, with symptoms improving upon withdrawal of the drug.

Although we had followed this patient for only just over 3 months at the time that we submitted this article, our primary interest and concern was to present the case to the foot and ankle surgical community because of its link with amiodarone as the likely cause of the peripheral neuropathy and the resultant Charcot foot. We fully realize that most case reports entail a longer period of follow-up; however it was our opinion that the importance of notifying the foot and ankle surgical community of the association between amiodarone and Charcot neuroarthropathy outweighed the need for longer follow-up. This unusual case also highlights the necessity for continued surveillance for the development of peripheral neuropathy in people taking amiodarone, which is a commonly prescribed drug for the treatment of certain types of cardiac dysrhythmia. If peripheral neuropathy is detected in such patients, then appropriate patient education and referral should be made to prevent limb-threatening complications related to the development of a Charcot foot.

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