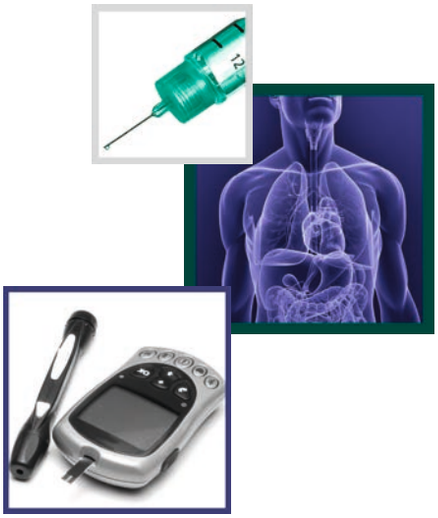

Why is Charcot foot commonly misdiagnosed?

"While the clinical picture in the chronic phase is represented by the complete loss of the foot shape ... in the acute phase the diagnosis is much more difficult because the clinical picture is represented only by an inflammatory condition that involves the whole foot."

Luigi Uccioli*

Charcot neuropathic osteoarthropathy (CN), commonly referred to as Charcot foot, is a condition affecting the bones, joints and soft tissues of the foot and ankle, characterized by inflammation in the earliest phase [1]. This pathological process culminates in bone and joint destruction and subsequent foot deformity, which predisposes to ulceration.

A number of mechanisms operate simultaneously: peripheral sensory and motor neuropathy, biomechanical factors and autonomic neuropathy are all considered to be potential causes of the development of Charcot foot [2]. However, neuropathic osteoarthropathy in its acute phase (acute Charcot foot) is also characterized by uncontrolled inflammation.

It has been suggested that the disorder arises from a sustained and uncontrolled release of proinflammatory cytokines, such as TNF-α and IL-1β, induced by microtrauma; this leads to increased expression of the polypeptide receptor activator of nuclear factor-κB ligand (RANKL) from any of a number of local cell types. RANKL triggers the synthesis of NF-κB, and this in turn stimulates the maturation of osteoclasts from osteoclast precursor cells. Osteoclasts cause progressive bone lysis, leading to further fracture, which in turn potentiates the inflammatory process [3,4]. This has subsequently been shown by an increase in proinflammatory phenotypes of monocytes in those with active Charcot foot when compared with diabetic control subjects [5].

On clinical grounds, Charcot foot is characterized by acute and chronic phases. In acute Charcot neuroarthropathy, the foot is warm, edematous, markedly erythematous, has a temperature difference of >2°C between the affected and nonaffected foot, and can be associated with a history of traumas even if under-reported [6]. There is always some degree of sensory neuropathy, in which reflexes, vibratory sense and proprioception are either diminished or absent. Autonomic neuropathy, which coexists with somatosensory neuropathy, can be clinically appreciated by the presence of anhydrosis with very dry skin. Pain may or may not be present.

The chronic phase is characterized by deformity of the foot, with abnormal pressure on the plantar surface due to the collapse of the plantar arch and the development of a rocker-bottom deformity.

"One of the most difficult tasks in this clinical contest is to differentiate Charcot foot from osteomyelitis of the tarsal bones or the appearance of a osteomyelitis in an already established Charcot foot."

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Continued weight-bearing will cause increasing damage, with progressive destruction of the foot. The skin overlying new bony prominences is associated with callus formation, which are liable to ulceration, especially in the midfoot. A concomitant ulceration will therefore raise the risk of contiguous osteomyelitis. Charcot deformities have been described for all of the foot bones, therefore, an anatomical classification has been proposed: type I: metatarsophalangeal and interphalangeal; type II: tarsometatarsal; type III: tarsal; type IV: subtalar; and type V: calcaneum [7].

While the clinical picture in the chronic phase is represented by the complete loss of the foot shape, and this is characteristic of this disease, in the acute phase the diagnosis is much more difficult because the clinical picture is represented only by an inflammatory condition that involves the whole foot. This is not characteristic of Charcot foot and therefore can lead to misleading diagnoses.

In the acute phase, when Charcot foot's clinical picture is not yet fully established, the bones are still intact when examined using plain x-ray and inflammatory signs such as edema, redness and increased local temperature are the most important aspects (Shibata stage 0) [8]. Another occasion when misleading diagnoses can occur is when a hot swollen foot develops suddenly in an already ulcerated foot. These inflammatory signs may be related to an infection spreading from the ulcer or in a few cases to the development of an acute Charcot foot. Also, in the presence of an already established Charcot foot, if complicated by a plantar ulceration, the appearance of a hot swollen foot may be related to a superimposed infection or to an acute relapse of Charcot foot.

The sudden appearance of a swollen, red, hot foot in an apparently normal subject for no apparent reason is rarely considered to be due to Charcot foot. It is frequently considered to be a clinical picture related to a phlebitis, or to a joint trauma or dislocation, this is also because the plain x-ray is completely normal. On the contrary, the disease is easily suspected if the patient has longstanding diabetes complicated by peripheral neuropathy. When an acute Charcot foot is suspected, the reference diagnostic evaluation that should be performed is an MRI, because conventional radiology in many cases may appear normal. At this stage, MRI shows subchondral bone marrow edema with or without microfracture [9]. There is a concomitant edema and swelling of soft tissues and muscles. Bone marrow edema is typically localized in the subchondral area of the midfoot bones [10]. Bone marrow edema is not a characteristic feature of the acute Charcot foot, and there are many other conditions, such as infectious arthritis, rheumatoid arthritis, gout and osteomyelitis that may have bone marrow edema. Osteomyelitis is one of the most confounding diseases when an acute Charcot foot is suspected. In this case, the clinical history of the patients may help. To have an osteomyelitis it is necessary to have a wound, and therefore the knowledge that a hot swollen foot has never had an ulcer excludes the hypothesis of osteomyelitis. Sometimes Charcot disease in the forefoot may start with tarsal bones fractures that may appear, at the first look, to be secondary to a trauma. A careful clinical evaluation of the history with the lack of a significant trauma together with the specific characteristics of the diabetic patient complicated by peripheral neuropathy, may help in making the diagnosis. Therefore, a foot with swollen, warm, erythematous skin, without a history or presence of ulcer in the neuropathic diabetic patient, is highly suspected to be an acute Charcot. If plain x-ray shows fractures and dislocations, this confirms the suspicion of Charcot foot. If plain x-ray does not show any sign of bone involvement, MRI is the gold standard to confirm or to exclude it.

It is a completely different task to diagnose Charcot foot when a foot ulcer is present. First of all, it is important to consider the localization of the foot ulcer. An ulcer of the forefoot followed by the appearance of a hot swollen foot may lead the clinician to suspect a superimposed infection either of the soft tissues, or the bones, or both, mainly if there is a bone exposed or there is a positive probe-to-bone maneuver. In this condition, the diagnosis of Charcot foot is unlikely. However, a forefoot localization of the Charcot foot may be suspected if the typical x-ray signs appear as demineralization, bone destruction and periosteal reaction, 'pencil and cup' deformity at the metatarso-phalangeal joints or fragmentation of the metatarsal heads.

There is a different line of reasoning when the ulcer is located at the midfoot level. An ulcer at midfoot level may spontaneously appear only if there is a collapse of the plantar arch and the development of a rocker bottom

foot. The midfoot is an area on which low loading forces are applied during walking in normal subjects, therefore a foot ulceration in that area may only be present if there is a foot deformity, such as that of Charcot foot. The picture is different when a hot swollen foot appears after a trauma of the midfoot (i.e., an external body penetrating the deep layers of the foot through the skin). In this situation, an infection of the soft tissues and/or ostemyelitis of the tarsal bone is highly suspicious. A bone culture, a plain x-ray and/or a foot MRI may help in making diagnoses.

Another possibility is that a osteomyelitis of the tarsal bones may complicate a chronic Charcot foot. In this case, the appearance of a hot swollen foot is not related to a relapse of a chronic Charcot foot, but to the appearance of an infection.

One of the most difficult tasks in this clinical contest is to differentiate Charcot foot from osteomyelitis of the tarsal bones or the appearance of a osteomyelitis in an already established Charcot foot. A plain x-ray shows dislocation or fracture in the midfoot and atypical calcaneal fractures. Plain films are useful for anatomical information, but are neither sensitive nor specific for separating Charcot changes from infection [11,12]. While magnetic resonance (MR) is useful for the diagnosis of uncomplicated acute Charcot neuroarthropathy and an MR scan of a Charcot foot is extremely sensitive, with a 100% detection of abnormalities [13], the diagnosis of underlying osteomyelitis can be difficult in chronic Charcot osteoarthropathy with foot ulcers. In this particular condition, MR seems not to be able to distinguish between the marrow edema associated with Charcot and that associated with osteomyelitis. Scintigraphic methods such as combined ^{111}In-leukocyte/bone or leukocyte/marrow scintigraphy are extremely useful in making a differential diagnosis between a Charcot joint with and without osteomyelitis [14–16].

In conclusion, Charcot foot is a clinical condition that is easily detectable in its chronic phase, when the foot has lost its shape and the plain x-rays show a complete alteration of the bone architecture.

On the contrary, it is very difficult to make a diagnosis when the clinical signs are only edema and increased local temperature, and a plain x-ray is completely negative. In this case suspicion may arise from the characteristics of the patient with long-lasting diabetes complicated by peripheral neuropathy. The diagnosis may be made with MR evaluation and the appearance of areas of increased uptake of fludeoxyglucose ^{18}F in discrete areas on the PET/CT scan [17], but finally the confirmation comes from the progressive reduction of the inflammatory signs, such as edema and increased temperature, with the use of a total contact cast, which is the gold standard method to offload the foot when a Charcot foot is suspected.

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