FOOT & ANKLE INTERNATIONAL

DOI: 10.3113/FAI.2007.0952

Current Concepts Review: Charcot Arthropathy of the Foot and Ankle

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INTRODUCTION

Charcot neuroarthropathy can be described as a noninfective, destructive process activated by an isolated or a cumulative neuro-traumatic stimulus that manifests as dislocation, periarticular fracture, or both in patients rendered insensate by peripheral neuropathy.[68] Peripheral neuropathy secondary to diabetes mellitus is the most common etiology of Charcot neuroarthropathy; however, peripheral neuropathy from leprosy, alcoholism, syphilis, syringomyelia, rheumatoid arthritis, multiple sclerosis, and traumatic injury also may be associated with Charcot neuroarthropathy.

Since Jean-Martin Charcot initially published a report describing a hypertrophic destructive "arthritis" that affected the joints of patients with tertiary syphilis in 1868, our collective understanding and capacity to prevent its onset have progressed slowly.[16] The Research Committee of the American Orthopaedic Foot and Ankle Society (AOFAS) has twice rated Charcot foot "neuro-arthropathy" as an important problem confronting orthopaedic foot and ankle specialists.[20,62] Despite the perception among medical and orthopaedic specialists that Charcot neuroarthropathy has a severe detrimental effect on the health-related quality of life for diabetic patients, only a small fraction of clinical research on diabetes-related issues has investigated the morbidity in feet.[17] One hundred patients with Charcot foot arthropathy were followed for 3 years as the target population used in validation of the AOFAS Diabetic Foot Questionnaire. The investigation revealed a significant negative effect on the health-related quality of life in these patients. This negative impact was sustained and did not resolve even if the Charcot event was treated successfully.[19] Similar findings were observed in a small cohort of patients being treated in a specialty diabetic foot clinic, using the Short Musculoskeletal Assessment questionnaire.[56] The goal of this current concepts review is to summarize our current understanding of this process named after the famous French neurologist and to examine the clinical and scientific evidence available to guide the management of this destructive and potentially devastating disorder of the foot and ankle.

BACKGROUND

The epidemiological data for this syndrome are scant and incomplete. A longitudinal observational study reported a 0.3% annual incidence of Charcot neuroarthropathy in 3000 enrolled diabetics.[24] Although this study provides the best available data, inaccuracy or delay in the diagnosis of this syndrome may underestimate the true rate of presentation. Osteopenia, obesity, equinus contracture, peripheral vascular

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Table 1: Level of evidence and grades of recommendation

Level of Evidence
- Level I: high quality prospective randomized clinical trial
- Level II: prospective comparative study
- Level III: retrospective case control study
- Level IV: case series
- Level V: expert opinion

Grades of Recommendation (given to various treatment options based on Level of Evidence supporting that treatment)
- **Grade A** treatment options are supported by strong evidence (consistent with Level I or II studies)
- **Grade B** treatment options are supported by fair evidence (consistent with Level III or IV studies)
- **Grade C** treatment options are supported by either conflicting or poor quality evidence (Level IV studies)
- **Grade I** when insufficient evidence exists to make a recommendation

disease and activity level have been proposed as factors that may endanger a patient with insensate feet. However, only the lack of protective sensation has been identified conclusively as predisposing for the onset of a Charcot event.[6,49] The threshold for the diagnosis of peripheral neuropathy is the inability to perceive 10g of pressure applied to the skin using the Semmes-Weinstein 5.07 monofilament.[6,69,70] With this benchmark in population screening, plantar insensitivity is present in approximately 25% of adult diabetics.[55]

The neurotraumatic and neurovascular theories are two nonexclusive postulates that attempt to explain the pathogenesis of Charcot neuroarthropathy. The neurotraumatic theory hypothesizes trauma, acute, subacute or cumulative-repetitive, as the causative factor in the setting of absent protective sensation. Under these circumstances, the initial traumatic incident activates the process. Continued weight-bearing without the use of defensive strategies such as guarding, offloading, or limitation of activity propels the course and magnifies the intensity of the Charcot event. Eventually, the structural integrity of the extremity is breached because of fracture, dislocation, or both. A reparative process begins either during or after the mechanical failure. Together, these competing processes of destruction and repair create a clinical picture that mimics a hypertrophic nonunion.[30] The neurovascular theory predicates a state of hyperemia generated from an overactive vasomotor-autonomic neuropathy. The increased blood flow accelerates the local bone metabolism, preferentially stimulating the activity of osteoclasts. Excessive resorption of bone ensues, and the resultant focal osteopenia weakens the bone and fosters a mechanically induced deformity.[29,70,71] A recent study analyzing tissue samples from Charcot patients demonstrated an increased osteoclast-to-osteoblast ratio in the presence of multiple cytokines that mediate bone resorption.[8] These results suggest the bone resorption observed during the Charcot process may arise from cytokine-mediated stimulation of osteoclasts and progenitor cells. The authors suggested that regulation of these cytokines may allow for the manipulation of bone turnover and may alter the effects of Charcot neuroarthropathy on bone loss, fracture, and deformity. However, neither theory completely explains this complex phenomenon. It is likely that the true pathogenesis of the Charcot process combines elements from both theories and may include other mechanisms yet to be elucidated.

A concomitant neuropathy of the motor nerves in patients with insensate feet contributes to the Charcot process. Variable denervation of the intrinsic and extrinsic musculature leads to an imbalance between plantarflexors and dorsiflexors of the foot and ankle. This disparity, combined with a contracture of the Achilles tendon, creates a static and dynamic equinus deformity of the ankle. During the terminal stance phase of gait, this deformity generates a pathological bending moment through the midfoot, which may be responsible for collapse of the arch and the development of the rocker-bottom deformity associated with Charcot neuroarthropathy.[5,7,26,37,40,44,50,61,69]

CLASSIFICATION

Eichenholtz characterized the natural history of Charcot neuroarthopathy from the clinical, radiographic, and pathologic data he collected from a consecutive series of patients.[23] He proposed that this process followed a consistent, temporally-related sequence of events that he divided into three stages. Stage I (development-fragmentation) denotes the initiation of the process. Erythema, warmth, and swelling of the extremity herald obvious injury of the bones and joints. Stage II (coalescence) represents a transitional phase when destruction cedes to healing. The deformity ceases to progress markedly, and the three cardinal signs of the first stage resolve. Stage III (reconstruction-consolidation) characterizes the maturation of bony and soft-tissue healing and the deformity consolidates to become fixed and stable. However, it is this resultant deformity that makes the foot susceptible to the development of ulcers, infection, and the need for amputation.

Brodsky[13] introduced an anatomical classification scheme based on the four regions of the foot typically afflicted with Charcot neuroarthropathy. This system is commonly used to classify neuropathic deformities of the foot. A type 1 event involves all or portions of the tarsometatarsal (Lisfranc) joints. This is the most common location for neuroarthropathy of the foot. Injury of the transverse tarsal (Chopart), subtalar, or all three joints of the hindfoot are classified as a type 2 event. Types 3A and 3B comprise injury to the ankle and calcaneal tuberosity, respectively.

Injury of the posterior calcaneus often involves avulsion of the superior tuberosity. Type 3B is the least common Charcot event.

Schon et al.[64,65] developed a classification scheme specific for deformities of the midtarsus that combined anatomic location and severity of the collapse. They divided these Charcot injuries into Lisfranc, naviculocuneiform, perinavicular, and transverse tarsal patterns of deformity. The grade used to designate the severity of a deformity was based on the degree of flattening in the sagittal plane observed on lateral weightbearing radiographs. Stage A deformities did not collapse to the level of the plantar surface of the foot. Stage B deformities collapsed to the plantar surface, making the medial or lateral or both columns coplanar with the plantar surface of the foot. Stage C deformities represent a true rocker-bottom foot with the midtarsus inverted beneath the axis of the forefoot and hindfoot. Schon et al.[64,65] subsequently revised the grading of severity to alpha and beta. The latter grade includes deformity with one or more of the following features: a dislocation, a lateral talar-first metatarsal angle of more than 30 degrees, a lateral fifth metatarsocalcaneal angle of 0 degrees or less, or an anteroposterior talar-first metatarsal angle of more than 35 degrees. However, despite this more detailed scheme, the prognostic value of the Schon classification scheme remains unknown.

CLINICAL PRESENTATION AND DIAGNOSIS

Classically, a patient experiencing an incipient Charcot event presents with painless rubor, warmth, and swelling of the involved joint(s). However, many patients report some degree of pain. Although the extremity appears infected, the patients lack the clinical signs of sepsis, such as fever, leucocytosis, elevated serum glucose, or an increased requirement of insulin to maintain glycemic control. Erythema and swelling of the extremity secondary to neuroarthropathy will rapidly diminish with a brief trial of elevation above heart level. These signs will persist in the setting of infection, whereas patients with neuroarthropathy have no wounds to serve as portals of entry for infection. Patients with infection have punctures, ulcers, or sinus tracks that express pus or seropurulent drainage. Although abscess, osteomyelitis, pyogenic arthritis, and cellulitis may appear to be the obvious diagnosis for a swollen, erythematous extremity, these are unlikely explanations if careful inspection of the affected limb fails to identify a breach in the skin. An infection secondary to hematogenous dissemination is a possible but very rare occurrence. Experience with these precepts will assist in distinguishing a deep-space infection from an infected superficial pressure ulcer in a neuropathic patient.[2,4,6,24,33,59]

The diagnosis of Charcot neuroarthropathy remains clinical. No imaging techniques have been demonstrated to clearly distinguish neuroarthropathy from an evolving deep bone infection. The high-intensity signal observed in the bone and periarticular soft tissues of a patient with Charcot arthropathy overlaps with the appearance of infection. The use of contrast does not clarify the diagnosis, but might assist in identifying an abscess.[10,15]

MANAGEMENT

Early (Stage 1) Neuroarthropathy

Immobilization with a total contact cast has been the prevailing treatment for Eichenholtz stage 1 neuroarthropathy. The affected limb remains casted until it has progressed beyond the fragmentation stage. The resolution of tactile warmth at the site is considered a reliable sign of coalescence and sufficient structural stability to permit transition to appropriate shoes with orthotics or a brace. This approach was based initially on expert opinion (Level V evidence) and has been subsequently supported by several case series (Level IV evidence).[3,35,36,39,47] The prohibition or limitation of weightbearing during total contact casting is thought to prevent the collapse of the intact foot or the progression of an existing deformity and hasten the resolution of stage 1 neuroarthropathy; however, there are no data published to support this claim. If weightbearing is allowed, the use of a rigid rocker sole or a flat or rocker cast shoe in addition to a total contact cast significantly reduces pressure under the midfoot.[18]

Other methods of immobilization have been considered for neuropathic arthropathy. The results of two studies suggest that a prefabricated, pneumatic walking boot may be an alternative to total contact casting.[9,28] In both investigations, the boot demonstrated a capacity comparable to the cast in offloading the forefoot in volunteers with sensate feet. However, these changes in plantar pressure-contact characteristics of the forefoot occurred at the expense of increased loading under the heel. Based on these results, the authors did not recommend their use in patients with plantar ulcerations of the heel.

Clinicians continue to consider other options for immobilization because the use of total contact casting incurs complications in patients with neuropathy. Guyton[27] found a 5.5% incidence of ulceration in 398 total contact casts applied in a specialty orthopaedic clinic for 70 neuropathic patients undergoing serial casting for neuropathy (Level IV evidence). Overall, 30% of the patients developed one ulcer during their course of treatment. A similar study with 82 total contact casts in 13 patients found only nine partial thickness ulcers and four erythematous patches.[72]

Overall, the consistently favorable results from level IV studies constitute fair evidence (Grade B) to support the use of total contact casting in the treatment of stage 1 neuroarthropathy. However, no clinical evidence (Grade I) exists to render a recommendation regarding the weightbearing status during total contact casting or the use of a prefabricated pneumatic walking brace.

Little published data exist regarding the efficacy of operative management of pedal deformity during stage 1 neuropathy. Arthrodesis in situ or combined with realignment theoretically offers the potential to prevent collapse into a rockerbottom deformity, preserve weightbearing capacity, reduce the risk of plantar ulceration, and avoid the need for cumbersome accommodative bracing. One study reported success with debridement, open reduction and internal fixation and autologous bone grafting for the reconstruction of a Charcot event involving the midfoot (level IV evidence).[66] All 14 patients included in the study healed their anatomically reduced reconstructions without any complications. The patients returned to full weightbearing and to wearing regular shoes at an average of 15 and 27 weeks after surgery, respectively. At a mean followup of 41 months, no patient had developed a plantar ulcer and all patients had returned to their preoperative walking capacity. Although this study demonstrated favorable results with early operative intervention on injuries of the Lisfranc complex, no published results exist for the early reconstruction of the hindfoot or ankle. Also, no data comparing the functional outcomes of surgery to casting have been published. Therefore, the quantity of data is insufficient to render a recommendation regarding the operative management of stage 1 neuroarthropathy (Grade I recommendation).

Based on the established paradigm that increased osteoclastic activity weakens the bone in this disease process, adjuvant therapies that inhibit the resorption or facilitate healing of bone may alter the extent and magnitude of the injury to the bones and joints involved in a Charcot event. The parenteral administration of the bisphosphonate pamidronate demonstrated several beneficial effects when compared to placebo in a double-blind, randomized, controlled trial (Level 1 evidence). The use of pamidronate with conventional immobilization and restriction of weightbearing decreased the serum and urinary concentrations of several markers of bone turnover and bone destruction and reduced warmth and pain in the affected foot better than the administration of a saline placebo over the 12-month period of the study.[31] Similar effects on these metabolic and clinical markers were reported in another randomized controlled trial of the treatment of acute Charcot neuropathy with the bisphosphonate, alendronate (Level II evidence).[60] These results constitute strong evidence (Grade A recommendation) to support the use of bisphosphonates in the treatment of early stage Charcot neuroarthropathy; however, neither pamidronate or alendronate has been approved by the United States Food and Drug Administration specifically for the management of treating Charcot arthropathy.

Numerous clinical studies attest to the efficacy of bone growth stimulators in the management of primary and revision arthrodesis of the foot and ankle. Some of these studies included patients with neuropathy undergoing salvage procedures for Charcot deformity. However, no study has examined specifically the efficacy of bone growth stimulators in the treatment of acute Charcot neuroarthropathy. Thus, there is insufficient evidence (Grade I recommendation) to support its use.

Late (Stage 3) Neuroarthropathy

As the involved extremity transitions through the last stage of Charcot arthropathy, the focus of treatment turns to the prevention of limb threatening complications. Neuropathic ulceration of the foot arises from the uneven distribution of compressive and shear forces across the skin. Plantar ulcers occur underneath bony prominences created by collapse of the arch at the apex of each particular deformity. An ulcer typically develops beneath the cuboid after an event that predominantly disrupts the transverse tarsal joints of the midfoot and creates a rockerbottom deformity. Disruption at the tarsometatarsal joints adducts and dorsiflexes the medial longitudinal arch, causing ulceration beneath the medial cuneiform. The treatment of plantar ulceration secondary to a Charcot deformity needs to be determined on a case by case basis. Commercially available depth-inlay shoes with accommodative orthoses molded to match the uneven plantar surface may be used to dissipate the inequalities in pressure that result from less severe deformities. Rockerbottom shoes combined with an ankle foot orthosis (AFO) or Charcot Restraint Orthotic Walker (CROW) may be necessary to manage more severe foot deformities or a Charcot deformity of the ankle. The studies that report the efficacy of therapeutic footwear or bracing define favorable outcomes as the prevention of recurrent ulceration or the preservation of the involved limb. These studies are retrospective case series (Level IV evidence), many with limited-term followup.[6,11,41,45,46,52,54,59] As such, their body of evidence supports a Grade B recommendation for the use of accommodative footwear and bracing for longitudinal management of the extremity in patients with Charcot neuroarthropathy.

The operative management of late stage Charcot deformity offers potential advantages over accommodative footwear; however, significant risks are attendant to these often complex reconstructive procedures. Patients often perceive their therapeutic shoe as a cumbersome impediment to their mobility and its daily use as an intolerable burden to their lifestyle. This perception fosters a reluctance to comply with the treatment plan and compromises the effectiveness of the treatment. Although the accepted indication for reconstruction through realignment and arthrodesis is the persistence of a limb-threatening ulcer despite the use of custom shoes or bracing, the possibility of wearing conventional shoes postoperatively draws both the patient and surgeon towards the option of operative correction of the deformity. However, longstanding diabetic patients with neuropathy frequently have multiple medical problems. Cardiovascular and renal disease combined with morbid obesity render them poor surgical candidates. The extensive dissection and manipulation of the foot and ankle necessary for successful reconstruction challenge these patients' capacity for bone and

soft-tissue healing. Also, as a result of their neuroarthropathy, these patients have severe localized osteopenia at the site of injury, placing them at high risk for loss of fixation and recurrence of the deformity after attempted operative correction.

The reports published for the operative management of late stage Charcot neuroarthropathy are not recent and do not present an easily interpretable body of evidence to judge the utility of realignment and arthrodesis.[12,21,25,51,63] Many of the studies are over 10 years old. The indications for surgery were not clear or uniform among the studies. Some surgeons operated to prevent recurrent ulcerations while others operated to repair severe deformities or simply desired to make the foot "plantigrade." These retrospective case series (Level IV evidence) usually defined success based on the rate of bony union and simple radiographic measures of correction. From these results, it is difficult to assess the impact of the reconstruction on daily function or the health-related quality of life.[12,21,25,51,63] Overall, the results suggest that realignment and arthrodesis improved alignment sufficient to allow the patients to wear custom shoes and may have reduced the recurrence of plantar ulceration. No data exist to directly compare the various methods available to stabilize the reconstruction. Reconstructions with external fixation appear to achieve a lower rate of union with a lower rate of hardware failure than those performed with internal fixation; however, external fixation was used in patients at a higher risk for complications with bone and soft-tissue healing.[25,34,73] The complexity and individuality inherent in each Charcot deformity challenge the capacity of the published research to identify a universally successful solution to this problem. Each deformity demands a carefully considered operative plan, tailor-made to treat the unique nature of the case. With this exacting burden, the amount and quality of the evidence supporting salvage with realignment and arthrodesis by any means is insufficient (Grade I) to support a recommendation for its use in late stage Charcot neuropathic deformities.

Other less invasive and less risky operative options exist for the late-stage Charcot patient with residual deformity with or without ulceration. Exostectomy of plantar bony prominences through limited incisions offers the opportunity to selectively eradicate the deformity contributing to the formation of an ulcer. However, the effectiveness of this approach is unknown as only one study (Level V evidence) published within the last 15 years exists regarding outcomes of plantar exostectomy, for late stage Charcot deformity.[14] Thus, there is insufficient evidence (Grade I recommendation) to support its use.

Under certain circumstances, elective amputation may be a reasonable alternative treatment to accommodative bracing, exostectomy or operative correction. The results of one study (Level IV evidence) suggest that Charcot patients with an abscess and extensive bony and articular destruction may benefit from an elective Syme amputation. The eight patients included in this series did well, demonstrating successful wound healing and weightbearing of the limb. All patients were able to walk without support after their elective amputation. The authors qualified their recommendation for this procedure by stating that a patent posterior tibial artery is essential.[22] Although the authors' experience with elective amputation was favorable, the evidence provided from such a limited number of patients is insufficient (Grade I recommendation) to warrant recommending this approach.

Charcot Neuroarthropathy of the Ankle

The pattern of bony and articular destruction associated with Charcot neuroarthropathy of the ankle often creates a deformity that defies management with orthoses. Use of an AFO or CROW is necessary to contain the talus underneath the distal tibial plafond for weightbearing. However, if destruction progresses and the medial, lateral and posterior malleoli become dissociated from the tibial metadiaphysis, the ability to stabilize the joint becomes unachievable and amputation becomes inevitable. For this reason, early ankle, tibiotalocalcaneal, or tibiocalcaneal arthrodesis may be considered before weightbearing function of the ankle is irrevocably lost. Biomechanical data from one study suggest that fixation with a retrograde, statically locked intramedullary nail may provide the most stable construct.[43] However, this technique requires medial translation of the talus for proper insertion of the implant. This maneuver places the hindfoot in varus relative to the ankle, locking the transverse tarsal joint and creating a rigid foot. Another potential problem is a stress fracture of the tibial diaphysis proximal to the tip of the nail which is known to occur after successful arthrodesis.[38,39,53,67,72] Recent biomechanical studies suggest that this complication can be avoided by the use of a longer intramedullary nail that extends to the proximal tibial metaphysis.[48] Although a popular technique in the management of neuroarthropathy of the ankle, the efficacy of ankle-hindfoot arthrodesis with an intramedullary nail is uncertain.[1,32,42,57,58] The results of several case series (Level IV evidence) suggest that containment with or without successful union may be achieved in most patients. However, data assessing the functional capacity after surgery are scant. These results would constitute inadequate evidence (Grade I) to support the use of retrograde intramedullary nailing for neuropathic deformities of the ankle. Similarly, the evidence is insufficient (Grade I) to support a recommendation for the stabilization of these ankle deformities with plates, screws, ring fixators, or combinations of these techniques.

SUMMARY

Virtually all of the clinical studies referenced in this review are retrospective case series. The evidence compiled from these studies resists the formulation of constructive comparisons and generalizations because of the individuality, heterogeneity, and complexity of this population and their orthopaedic conditions. Each of the investigators had

his own perception of the problem and had a different appreciation of what would constitute a favorable outcome. We are rapidly gaining an understanding of this complex metabolic disease and how it impacts the quality of life, often leading to lower extremity amputation or death from sepsis. Going forward, we are faced with challenges in further understanding Charcot neuroarthropathy in this era of evidence-based medicine. What we seem to understand to date includes the following:

1. Charcot neuroarthropathy is a non-infective, destructive process occurring in patients rendered insensate by peripheral neuropathy.
2. Repetitive trauma from standing and walking provides a neurotraumatic stimulus that leads to dislocation, periarticular fracture, or both within the foot.
3. The joints most frequently affected by Charcot arthropathy in the order of frequency are (1) the tarsometatarsal joints, (2) the transverse tarsal joint, and (3) the ankle joint.
4. The Charcot arthropathy process can take up to 2 years to run its course. An early Charcot arthopathy is characterized by swelling, warmth, and erythema. This stage is sometimes confused with osteomyelitis of the foot; however, it can be differentiated on clinical grounds by the absence of wound breakdown (portal of entry) and the failure to manifest clinical and laboratory signs of a significant infection.
5. There is evidence to support a Grade B recommendation for the use of total contact casting in the treatment of early Charcot arthropathy. It is unclear whether prefabricated walking devices yield equivalent results.
6. Late stage Charcot arthropathy is characterized by symptoms related to any resulting foot deformity. The most common and worrisome of these is a plantar ulceration secondary to a rocker bottom foot deformity.
7. There is Grade B evidence to support the use of nonoperative treatment of deformities associated with late stage Charcot arthropathy; however, patients likely need to be assessed on a case by case basis to optimize management. Nonoperative treatment may include commercially available depth-inlay shoes with accommodative orthoses or rocker-bottom shoes combined with an AFO or CROW.
8. Surgery may be indicated in the treatment of Charcot neuroarthropathy. The most common indications for operative intervention are a persistent plantar ulceration that cannot be managed nonoperatively and an unstable Charcot ankle arthropathy. The type of operative intervention needs to be determined on a case by case basis.

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