DOI: https://doi.org/10.30795/jfootankle.2021.v15.1241

Special Article

Charcot arthropathy of the foot and ankle: an update

João Marcos Nunes Montechi[1], Weslen Luiz Pinto de Barros[1], Rodrigo Sousa Macedo[1], Rafael Barban Sposeto[1], Alexandre Leme Godoy-Santos[1], Tulio Diniz Fernandes[1]

1. Lab. Prof. Manlio Mario Marco Napoli, Instituto de Ortopedia, Hospital das Clinicas, Faculdade de Medicina, Universidade de São Paulo, São Paulo, SP, Brazil.

Abstract

Objective: To critically evaluate the current literature on the etiopathogenesis of Charcot neuroarthropathy, its diagnostic methods and therapeutic management.

Methods: We searched for studies that related Charcot arthropathy with a location in the foot and ankle in the PUBMED and MEDLINE databases.

Results: A total of 52 studies were used for this analysis.

Conclusion: Charcot neuroarthropathy is a serious disease with significant potential to impact patient quality of life. Although its pathogenesis still raises much controversy, neuropathy seems to have a central role, leading to a trauma, injury, and inflammation cycle.

Level of Evidence V; Therapeutic Studies; Expert Opinion.

Keywords: Charcot; Neuroarthropathy; Diabetes mellitus; Ankle; Foot Diseases.

Introduction

Charcot neuroarthropathy (CN) is a rare but serious complication of peripheral neuropathy and is also known as Charcot osteo-neuroarthropathy[1]. It is a disabling osteoarticular pathology that causes weakening of the musculoskeletal system, progressing to fracture and destruction of the joint under stress. The foot and ankle are the most often affected segments[2]. However, there are reports of the involvement of several body segments, such as the knees, spine, shoulders, hips, and wrists[3].

Several neurological conditions, many of which are affected by sensitive neuropathy, are associated with CN, such as tertiary syphilis, meningomyelocele, syringomyelia, poliomyelitis, Charcot-Marie-Tooth disease, alcoholic peripheral neuropathy, and Hansen's disease. Currently, diabetes mellitus (DM) has become the most common etiology of CN[1,3-5].

In 1968, Jean-Martin Charcot described osteoarticular changes in patients with tabes dorsalis. Despite the pathology having his name, he recognized he was not the first to describe such changes[5]. JK Mitchel, in 1831, and William Musgrave, although with controversy, had already described cases of osteoarticular destruction associated with neurological dysfunction[1,5]. However, only in 1936 did Jordan[6] publish the first work associating CN with DM[7,8].

Despite the high worldwide prevalence of DM, CN is underdiagnosed; this is due, in part, to the difficulty and delay in diagnosis, resulting from the lack of clinical and radiological criteria, especially considering an initial approach by non-specialists[1,7,9,10]. The annual incidence is estimated to vary from 0.1% to 29% and the prevalence, between 0.08% to 13%[2,9]. CN usually appears asymmetrically in the fifth or sixth decades of life, usually 10 years after DM onset[11]. The proportion of men and women with CN is similar, with some studies showing greater involvement in male patients[9,11].

CN is considered a risk factor for lower limb amputation in diabetic patients, reaching rates of up to 67%[2]. When associated with ulcers, this prevalence increases considerably, as does mortality, with almost half of these patients undergoing at least one foot surgery[7,12].

As well as other chronic changes that are part of the DM, CN is also a complication of its progression, being one of the concerns of the diabetic foot syndrome. Therefore, these comorbidities should always be carefully screened by a multidisciplinary team, as their early detection and management are essential[11,13].

Study performed at the Lab. Prof. Manlio Mario Marco Napoli, Instituto de Ortopedia, Hospital das Clinicas, Faculdade de Medicina, Universidade de Sao Paulo, Sao Paulo, SP, Brazil.

Correspondence: João Marcos Nunes Montechi. 333 Dr. Ovídio Pires de Campos, St, Cerqueira César, São Paulo, SP, Brazil, **Zip Code:** 05403-010. **Email:** jmontechi@gmail.com. **Conflicts of interest:** None. **Source of funding:** none. **Date received:** March 15, 2021. **Date accepted:** March 19, 2021. **Online:** April 30, 2021

How to cite this article: Montechi JMN, Barros WLP, Macedo RS, Sposeto RB, Godoy-Santos, AL, Fernandes TD. Charcot arthropathy of the foot and ankle: an update. J Foot Ankle. 2021;15(1):83-91.

Methods

Through a research of the PUBMED and MEDLINE platforms, studies published between 1936 and 2021 were retrieved. Descriptors used in the research were "Charcot neuroarthropathy" and "ankle and foot", as described in table 1. Case-control, cohort, and experimental studies, as well as case reports, systematic reviews, and meta-analyses were included.

All studies relating Charcot arthropathy to a location in the foot and ankle were included. Studies unrelated to the involvement of the pathology in this region were excluded. The analyzed results included epidemiology data, pathophysiology, classification, diagnostic tests, conservative and surgical treatments, and complications; these were retrieved from 52 studies, classified as shown in table 2.

Pathophysiology

The exact mechanism of CN is not yet established[14]. Nevertheless, this understanding is evolving rapidly. Several theories have been postulated and it is currently accepted that the pathophysiology is multifactorial and theories that were previously antagonistic now complement each other[3].

Neurovascular theory

This French theory, supported by Charcot and Mitchel[3,5,15], considers that a vascular reflex secondary to an autonomous neurological dysregulation (sympathectomy) would increase bone blood flow (arteriovenous shunts) and arterial perfusion, causing greater bone resorption (osteopenia) due to osteoclastic activity and resulting in destructive changes and pathological fractures and dislocations[2,15].

Table 1. Keywords used for researching the PUBMED and MEDLINE databases.

Main keywords used in our literature search on the PUBMED and MEDLINE databases			
Neuropathy	Charcot	Ankle	Foot
Subtitles used for research in Literature search on PUBMED and MEDLINE			
Imaging exams	Pathophysiology	Diagnosis	Diabetic Foot
Diabetic neuropathy/ complications	Diabetic neuropathy/ treatment	Quality of life	Bone metabolism
Surgeries	Treatment	Diabetes	Therapies under study

Table 2. Types of studies and numbers of cases retrieved from the databases.

Review/Meta-analysis	24
Case series	5 (Total cases: 131)
Cohort	9 (Total cases: 10 491)
Case control	5 (Total cases: 345)
Case reports	2 (Total cases: 4)
Guidelines	1
Technique/Biomechanics	4
Randomized clinical trial	2 (Total cases: 60)
Total selected studies	52

Neurotraumatic theory

The German theory, proposed by Volkman and Virchow, suggests that repetitive mechanical microtrauma or even acute trauma of insensitive joints causes progressive bone destruction, with joint deformity and incongruity[2,3,15].

Inflammatory theory

Current evidence directly linking osteopenia to diabetic neuropathy vary[15]. However, it has been shown that bone mineral density is diminished in the acute phase of foot involvement by CN, and this fragility can predispose to fracture–dislocations[15–17].

The receptor activator of nuclear factor-kB (RANK) is located on the surface of osteoclast progenitor cells and regulates their differentiation. The RANK ligand (RANK-L) is a molecule produced by osteoblasts and bone marrow stromal cells that binds to its specific RANK receptor. This ligation promotes osteoclast differentiation, activation, and survival (osteoclastogenesis), as well as bone resorption. On the other hand, osteoprotegerin (OPG) is a cytokine produced by activated osteoblasts that antagonizes the binding of RANK-L to RANK in the osteoclast membrane, limiting excess osteoclastogenesis and osteolysis. Therefore, regulation of the RANKL/OPG ratio is one of the mechanisms of bone metabolism control, with an impact on bone density[14,18,19] (Figure 1).

Jeffcoate et al.[20] suggested that the RANK/RANKL/OPG signaling pathway, responsible for balancing bone metabolism, has implications in the development of an acute CN event. They considered, along with other authors[21,22], that in this phase of CN there is an accentuated inflammatory response to trauma, increasing the expression of pro-inflammatory cytokines such as TNF-α, IL-6, and IL-1β and the number and local function of osteoclasts, activated by RANK-L and with insufficient OPG to neutralize them; this potentializes local inflammation, resorption, bone fragility, and bone destruction[3,8,15,18–20]. Jansen et al.[23] showed this increase in the acute phase of NC, but not in the chronic phase; it may even be a potential marker of Charcot activity[15].

These theories can be interpreted in a complementary fashion, and some authors consider 2 factors to be essential in the pathophysiology of NC: neuropathy and inflammation[2,20]. In summary, it is as if the exacerbated post-traumatic inflammatory response in a patient with CN increased RANK-L expression by increasing pro-inflammatory cytokines, resulting in clinical signs of inflammation and stimulating osteoclastogenesis and osteolysis. In individuals without a neuropathy, this process is limited by immobilization in response to the pain caused by local inflammation. However, when the sensation of pain is reduced due to a sensory neuropathy, there is no protective suppression, allowing the continuation of the mechanical injury and inflammatory process, which in turn leads to bone fragility and fractures. The result is the establishment of a vicious cycle of inflammation and structural damage to the foot[15,20] (Figure 2).

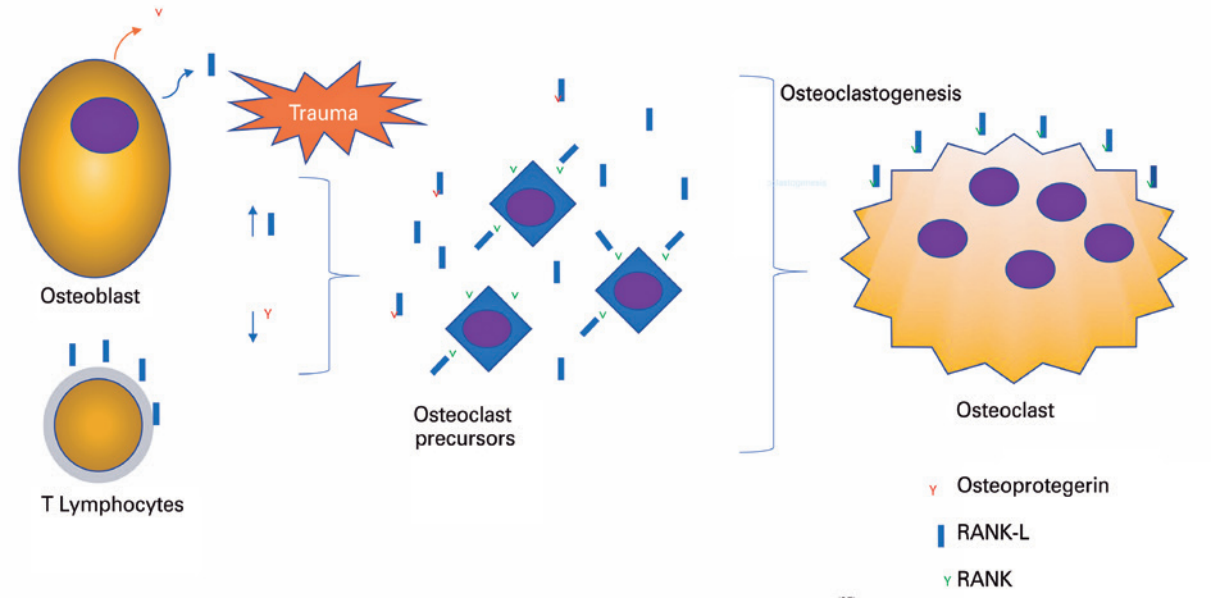

Figure 1. Schematic representation of the RANK/RANK-L/OPG signaling pathway in CN. Adapted from Molines et al.[27] and Ndip et al.[19]. RANK: receptor activator of nuclear factor-kB; L: ligand.

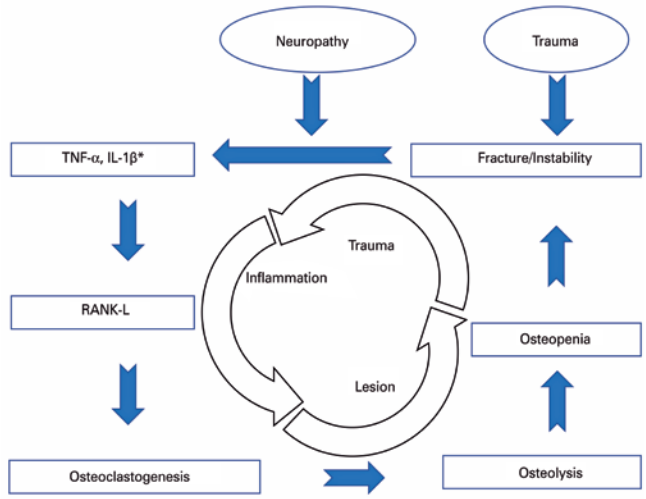

Figure 2. Schematic representation of the inflammatory theory in the development of the acute Charcot foot.
Adapted from Molines et al.[27] and Jeffcoates et al.[20].

The hyperglycemic state in diabetic patients has been shown to increase the levels of advanced glycation end products that when associated with inflammation, denature and weaken tendons and ligaments, further increasing instability and corroborating the vicious cycle[2].

Classification

One of the most well-known and used classifications is that of Eichenholtz, described in 1966 and modified in 1990[1,24,25]. CN staging, according to this classification, considers clinical and radiographic criteria, and describes the natural history of the disease in four stages. It has been used as an aid, although controversial, for deciding the best surgical moment[15] (Table 3).

The inflammatory process is evident in the initial stages (0 and 1), and some authors consider it as acute CN[2,15,26]. In these phases, the inflammatory process is exacerbated due to the loss of protective innervation and perpetuation of microtrauma, progressing to a vicious cycle of trauma – injury – inflammation. There is an increase in inflammatory cytokines and, consequently, in the osteoclastic activity that weakens the bone. Chronic CN is recognized when a reduction of inflammatory activity is observed and the patient presents changes in radiographic images due to the collapse or destruction of the joint (classically represented as a "rocker bottom deformity"[15,26]); it is described by Eichenholtz as stages 2 and 3.

In association with the abnormal mechanics of the foot, the formation of these bone deformities causes changes in areas of plantar pressure during gait, resulting in tissue damage and ulceration. The midfoot is a common area of collapse as it is subjected to substantial forces during the transfer of weight from the hindfoot to the forefoot[2,11]. This way, some authors classify CN in the foot and ankle according to the anatomical location of involvement. Brodsky and Rouse, in 1993[1], described one of these classifications and the prevalence of each

Table 3. Eichenholtz classification modified by Shibata et al.[24], Yu et al.[25], Botek et al.[15], and Dodd et al.[2].

Stage	Image	Physical examination
0 – Inflammatory	X-ray: - Normal findings MRI: - Signal change in bone marrow and subchondral bone (edema) Nuclear: - Positive scintigraphy PET-CT: - Positive	- Hyperemia and edema. - >2°C difference between members - Neuropathy
1 – Development	X-ray: - Osteopenia - Subchondral bone fragmentation - Fractures - Joint incongruity - Loose bodies	- Edema - Hyperemia - Local heat - Neuropathy
2 - Coalescence	X-Ray: - Bone formation at fracture sites - Resorption of bone fragments - Beginning of the fusion process of the affected joints MRI: - Reduction of bone edema Nuclear: - Reduced uptake	- Decreased signs of inflammation from previous phases
3 – Remodeling	X-ray: - Bone consolidation - Sclerosis - Arthritis - Bone deformities	- Great decrease or absence of phlogistic signs - Varied degrees of deformity and stability

type. The most affected site, the midfoot (with 60% prevalence), is classified as type 1. In type 2 it occurs in the hindfoot, the second most affected site. Type 3 is subdivided into 3A when it affects the tibiotalar joint and 3B when it affects the calcaneus tuberosity, which is the least frequently affected site.

Diagnosis

Identifying CN can be as challenging as its etiopathogenesis, resulting in high rates of late and even incorrect diagnoses that can lead to gross deformities, ulceration, and amputation of the foot[3,7]. CN should always be considered in a patient with diabetes who presents with edema, hyperemia, heat, and sometimes pain in the foot or ankle, depending on the degree of neuropathy[2,26].

Investigating the presence of inflammatory diseases, such as gout, and infection, such as cellulite and osteomyelitis, helps in the differential diagnosis[2,3]. These pathologies can even coexist, being extremely important a search for ulcers, secretion, and direct contact of the bone with the external environment[2,27].

Infrared dermal thermometry, when compared to the contralateral side, can present a difference of more than 2°C and be used with confidence[28,29]. The presence of neuropathy is one of the pillars for diagnosis, and the Semmes-Weinstein 10g monofilament and the 128 Hz tuning fork should be used; in general, proprioception and reflexes are reduced or absent[30]. If sensory neuropathy is absent, some authors question the diagnosis of NC[2].

Vascular conditions must be assessed; pulses are generally present and even increased, and some authors consider their absence to be a protective factor for CN[20]. Determining the time of onset of signs and symptoms is important, as the inflammatory phase can last for up to 18 weeks[31].

The similarity with the onset of several pathologies that have different treatments makes laboratory investigations a routine. However, we must consider that even though they assist with many diagnoses, these tests can be negative in patients with DM, even in the presence of infection. An association between CN and infection exists and should be considered[27].

So far, there is no imaging technique that is specific and sensitive enough to detect CN, especially in the acute phase (stage 0). Radiography, a cheap and widely available examination, cannot distinguish it from other differential diagnoses, being not enough sensitive and specific. Even so, it should be the first examination to be requested with front, lateral, and

oblique views of the feet and front, lateral, and mortise of the ankle, preferably in a weight-bearing modality. Radiographic images provide important information on anatomy and bone alignment, and one should always look for signs of fractures, dislocations, consolidations, and eventual radiological signs of osteomyelitis. However, our findings usually follows what was described by Eichenholtz[11,32].

Magnetic resonance imaging (MRI) is particularly useful in the early stages of NC, detecting subtle changes in face of a normal radiograph, and is considered the imaging exam of choice at this stage as it has good diagnostic accuracy[15,25,27].

When there is a suspicion of infection associated with CN, we can resort to nuclear imaging studies, seeking early diagnosis and treatment guidance. Scintigraphy with marked leukocytes (Indium-111) has excellent diagnostic capabilities for musculoskeletal infection; however, these scintigraphic methods have poor spatial resolution and lack anatomical details[27,33].

Positron emission tomography (PET-CT) with fluorodeoxyglucose, which measures the increase in the intracellular glucose metabolism, has shown promise in diagnosing NC, particularly with regard to its negative predictive value[2]. It offers excellent sensitivity and specificity for the diagnosis of osteomyelitis in the diabetic foot and is able to distinguish CN from osteomyelitis better than MRI with the advantage of having less image artifacts in the presence of synthesis material[2,15].

Despite the good specificity and sensitivity of PET-CT, its use is still limited when compared to MRI and leukocyte scintigraphy. MRI has a slightly lower sensitivity and specificity than PET-CT and an excellent spatial resolution, identifying the extent of the involved area and assisting in surgical planning[27,34].

Regardless of the diagnostic method, the most important aspect is the recognition of the pathology, mainly by the non-specialist, by performing a good anamnesis and physical examination. Therefore, in the presence of a patient with a hot and swollen limb associated with sensory neuropathy, the diagnosis of CN should be considered.

Treatment

The treatment is eminently multidisciplinary, with medical, nursing, and physiotherapy professionals working to control comorbidities and promote dressing changes and rehabilitation[31,32,35].

Orthopedic goal of CN treatment is to obtain and maintain a stable, plantigrade foot with satisfactory alignment, allowing weight-bearing, use of shoes or orthoses, performing of daily activities, and avoiding ulcerations and amputations[15,32,36,37].

In general, treatment is based on the evolutionary stage of the disease, and early diagnosis and interventions are essential to prevent progression to deformities that require more complex and costly treatments.

Conservative treatment

Treatment in the early or inflammatory stages (0, 1, and 2) consists of immobilization, protection, and offloading, leading to a reduction in the inflammatory stimulus and better pain control while preventing the progression of deformities[38,39].

The main measures in this phase consist of removing or reducing the load with full contact plaster casts or removable orthoses[2,15,40,41]. This type of treatment with load protection can be extended from months to more than a year, which decreases patient compliance, especially considering those who are not allowed to weight-bearing[39,41]. Some authors have demonstrated that full load release with these devices is safe and also effective in preventing progression of the deformity and reducing acute symptoms[40,41].

Treatment is continued until there are signs of bone consolidation (which can take much longer than in patients without diabetes) and reduced inflammation. Objective parameters include a temperature difference of less than 2°C between limbs and a reduction of hyperemia[2,29,31,39], but there is scarce evidence in the literature to support their use[3]. PET/CT seems to offer a more objective assessment to quantify the inflammatory process, showing its persistence for a much longer time even after its clinical resolution, which could lead to early withdrawal of immobilization and recurrence[2,15].

Drug therapies are focused on anti-osteoporotic drugs, mainly bisphosphonates, and appear to have benefits even though studies present little evidence[3,32]. Calcitonin has also been tested in association with calcium supplementation for its regulatory effect on bone turnover[15]. Other studies have demonstrated benefits of anti-RANK-L and teriparatide antibodies[15]. Despite satisfactory results, there is a lack of better evidence in the literature regarding their benefits in faster the healing process and to provide satisfactory clinical results[3,15].

There is a considerable recurrence rate after treatment, which ranges from 7.1% to 33% in an average time of 27 months; obesity (body mass index [BMI] >30) and non-adherence are the main risk factors[39]. Saltzman also demonstrated that non-surgical treatment is associated with a prolonged immobilization time, with a 23% risk of immobilization for more than 18 months, an amputation rate of 2.7%, and a 49% risk of recurrent ulcerations[42].

Surgical treatment

Surgical treatment is classically reserved for later stages of the disease (stage 3), although some authors have proposed approaches in earlier stages[43]. Surgical indications include gross deformities that do not allow the use of orthoses, joint instabilities, recurrent ulcerations, infection, chronic pain, and some cases of acute fractures. The goal is to obtain a stable, plantigrade and functional foot that allows weight bearing[2,15,31,35,39].

Despite being well described in the literature, the considerable recurrence rate (7.1% to 33%[39]) associated with a prolonged restriction time imposed by the conservative treatment, while not always providing the desired results[37], has led to a trend towards an earlier surgical approach to stabilize these feet[15].

There are several types of surgical treatments, from soft tissue surgical procedures and simple exostectomy to complex internal fixations (plates, screws, intramedullary nails) and external fixators[37,39].

The treatment method is guided by the location of the disease, the degree of bone deformity, soft tissue conditions, presence of associated osteomyelitis, and surgeon's expertise. Challenges encountered by the surgeon include large bone defects, osteopenic bone, chronic deformities, fibrosis close to the neuro-vascular bundles, and less potential for healing[15,39].

Lowery et al.[43], in a review of more than 1000 cases of Charcot, observed that the most surgically approached location is midfoot, followed by the ankle. Exostectomy and arthrodesis have a Grade C recommendation; lengthening of the posterior chain has a grade B recommendation; and there is no conclusive evidence on the superiority of fixation techniques. Schneekloth et al.[12] found that the hindfoot was the most surgically approached site.

It is important to remember that patients with Charcot have diabetes in advanced stages associated with other comorbidities that may hinder their post-surgical rehabilitation, also influencing in the extension of the proposed surgery[2].

Rettedal et al.[44] proposed one of the currently available preoperative prognostic scores for predicting the outcome of Charcot reconstruction. It evaluates age, BMI, the presence of wounds or osteomyelitis, anatomical location, disease activity, and glycated hemoglobin levels, totalizing 10 points. Patients who scores more than 4 points would have higher chances of having a poor outcome, with reasonable sensitivity and statistical specificity.

Lengthening of the posterior chain

Shortening of the posterior chain, evidenced by an inability to dorsiflex the ankle beyond neutral or objectively less than 10° being clinically assessed with the Silfverskiold test, has a direct correlation with the increase in plantar pressure[35,43,45]. DM itself seems to act in the pathophysiology of this issue, with structural changes to the Achilles tendon that predispose to its shortening[45].

This increase in plantar pressure raises the risk of ulcers in patients with neuropathy[45]. Surgical lengthening of the posterior chain leads to a reduction of stress in the joints of the midfoot and forefoot, enhancing the healing of ulcers. This procedure is indicated in cases of recurrent ulcerations in the forefoot associated with equinus[15,37,39].

Lengthening is generally used as an adjunct treatment, associated with other procedures, and is performed by stretching one of the portions of the sural triceps. Several techniques have been described for this procedure, such as the release of fascia of the medial head of the gastrocnemius, total tenotomy of the calcaneus tendon, and percutaneous releases[45] (Figure 3).

Exostectomy

Exostectomy is a procedure for removing bone prominences that may be symptomatic, leading to recurrent ulcerations or problems with shoe adaptation; it is only performed on stable feet.[2,15,31].

It can be done indirectly, through accessory pathways and minimizing the risk of spreading the infection, or directly through the ulcer, with primary or delayed closure. Exostectomy can be associated with other procedures, such as Achilles tendon lengthening[15,35].

One of the possible complications of this procedure is the instability of the midfoot in aggressive resections[31]. It is contraindicated in case of peripheral arterial insufficiency, acute infection, unstable midfoot, and in the inflammatory stages of arthropathy[15] (Figure 4).

Arthrodesis

The main objective of arthrodesis is to restore, through surgery, the alignment and stabilization of the foot[31,35].

Dodd et al.[2], in a literature review, found mean fusion indices of 84% (50–100%). The mean non-union rate was 13.6% (0–38%). Amputations below the knee were observed in up to 5.8% of the cases. Wound complications and postoperative infections were commonly found. Shazadeh Safavi et al.[46] found consolidation rates of 91% and amputation rates of 6%.

This procedure involves the removal of non-viable or infected bone, correction of the deformity, and stabilization. Correction can be performed in 1 or more instances, depending on soft tissue injury, infection, and the degree of deformity[31].

Sammarco et al.[36], in an attempt to increase local stability and decrease the chance of failure regularly found in common fixations due to poor bone quality and poor local biology, defined the concept of superconstructs. These involve extending fusions beyond the injury area and including

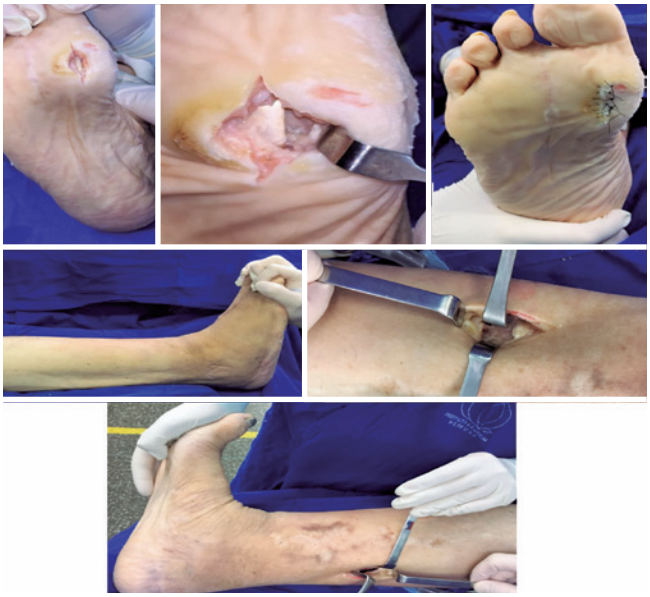

Figure 3. Patient with a plantar ulcer under the head of the first metatarsal and signs of chronic osteomyelitis in the sesamoid. Surgical debridement of the ulcer was performed with resection of the sesamoid and lengthening of the posterior chain to reduce plantar pressure in the forefoot.

non-diseased joints to increase fixation; bone resection allowing the reduction of the deformity without tension in the soft parts; and using the strongest fixation that can be tolerated by the soft parts in a position that optimizes local mechanics. Examples of constructs that fit this concept include plantar plating, locked plating, and axial screw fixation[36] (Figure 5).

Plantar plates and axial screws

Plantar plates offer mechanical superiority because they are positioned on the tension side of the fusion and can be extended up to the metatarsals and into the cortical bone, allowing better fixation[36,43]. The use of locked plates can add even more rigidity and stability to this type of fixation[36,47].

Garchar et al.[48] described a series of cases in which 96% consolidation was achieved, and a return to walking was reached in around 12 weeks.

Axial screws involve fixation of the fusion with longer and larger caliber screws, in which the distal portion is intramedullary in the metatarsals; it can be performed in a minimally invasive, anterograde, or retrograde manner[15,36].

As advantages of this technique, the position of passage of the screws helps reduce the deformity, while pre-fixation with a cannulated guide wire allows the surgeon to check the position before final synthesis. Compression is achieved only by tightening the screw, and the intraosseous position reduces the risk of exposure[36].

Pope et al.[47], in a biomechanical comparison between plantar plates and axial screws, found no differences between rigidity and load until failure, with the plantar plate forming a more rigid construct in the first tarso-metatarsal joint. Simonik et al.[49] also found no statistical difference between the stiffness of the 2 constructs, although the axial screws supported more load until failure.

A major disadvantage of plantar plates is the extensive mobilization/dissection of soft tissues for fixation.

External fixation

External fixation provides a less invasive form of stabilization than internal syntheses, avoiding a direct approach to sites of intense contamination, with soft tissue injury or poor bone stock; it also allows gradual correction and can tolerate weight bearing[2,15,31,50]. It manages to correct the deformity, simultaneously providing stability and compression. External fixators can be used as primary stabilizers or even to increase the stability of another construct[50]. Their use is proposed even in cases of severe infection as an alternative to amputation[51].

External fixation can even be used in a 2-time procedure, where the first stage comprises the correction of the deformity performed with a computer-aided hexapod external fixator, allowing a more anatomical correction and without much pressure on soft parts; later, in the second procedure, stabilization is achieved with internal synthesis[37].

Amputation

With the improved perioperative management of patients with Charcot, along with better surgical techniques, wound management, and understanding of the disease pathophysiology, amputation numbers have decreased; it is currently

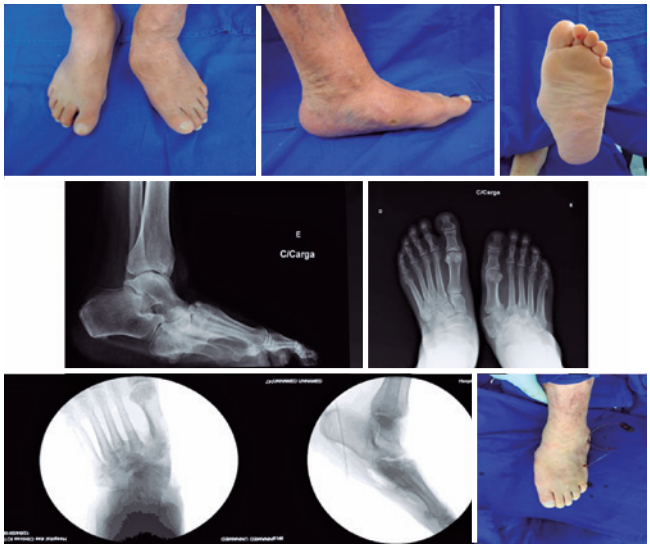

Figure 4. Patient with midfoot Charcot, rocker bottom deformity, and pre-ulcerative lesions on medial and plantar exostoses. The foot was stable upon clinical examination. Exostectomies of medial and plantar prominences were performed, leading to reduced pressure on soft tissues.

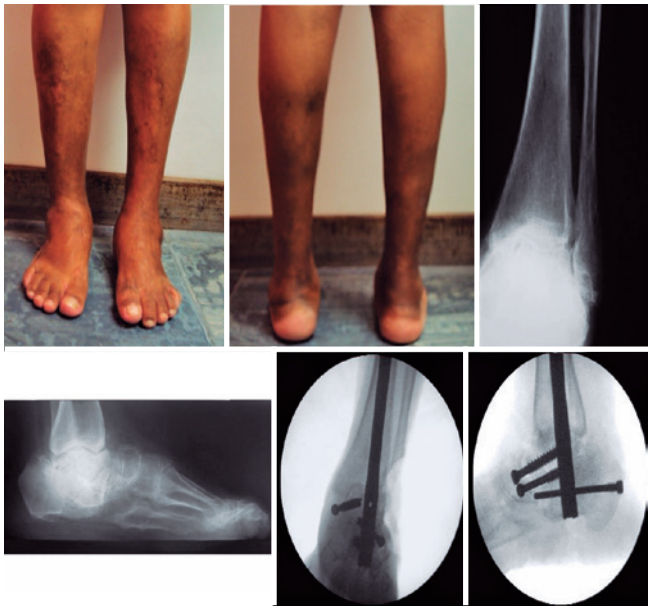

Figure 5. Patient with Charcot neuroarthropathy affecting the hindfoot. The treatment option was surgical correction of the deformity and stabilization with a panarthrodesis; fixation was done with an intramedullary nail and screws.

reserved as a salvage procedure when reconstruction is not possible or active infections pose a risk to the patient's life[31].

Indications for amputation would be refractory infections with multi-resistant bacteria and non-functional limbs that have already undergone several surgical approaches[32,35]. Studies show rates that can range from 5.8% to 8.9% of all cases[2,12].

Amputations are associated with higher energy expenditure, increased chances of contralateral amputation, and a worsening quality of life. More proximal amputations tend to have worse clinical results and poorer outcomes for the patient[52].

Conclusion

CN, commonly associated with DM, is a serious disease that can have great morbidity, impacting the patient's quality of life and ability to move. Despite research efforts, its complex pathophysiology is not yet fully understood, being related to neuropathy and resulting in a cycle of trauma – injury – inflammation. Its evolution seems to occur in phases, based on which treatment strategies are designed. In the early inflammatory stages, the focus is on the use of orthoses and devices that reduce stress on the region. The role of transmitters and inflammatory markers in pathogenesis and the potential use of medications or immunobiologicals that modulate this response are currently in vogue, leading to better results without surgical approaches. Surgical treatment is reserved for cases of complications and refractoriness to conservative treatment. Regardless of the method of choice, the objective is to obtain a stable plantigrade foot, without ulcerations or infections, that allows the patient to perform his or her daily activities.

Authors' contributions: Each author contributed individually and significantly to the development of this article: JMNM *(https://orcid.org/0000-0002-3274-6603) Wrote the paper, interpreted the results of the study; WLPB *(https://orcid.org/0000-0002-7957-0123) Wrote the paper, interpreted the results of the study; RSM *(https://orcid.org/0000-0002-5025-4338) Participated in the reviewing process, approved the final version; RBS *(https://orcid.org/0000-0003-1085-0917) Data collection, participated in the reviewing process, approved the final version; ALGS *(https://orcid.org/0000-0002-6672-1869) Data collection, participated in the reviewing process, approved the final version; TDF *(https://orcid.org/0000-0002-9687-7143) Participated in the reviewing process, approved the final version. All authors read and approved the final manuscript. *ORCID (Open Researcher and Contributor ID).

References

1. Crim BE, Lowery NJ, Wukich DK. Internal fixation techniques for midfoot Charcot neuroarthropathy in patients with diabetes. Clin Podiatr Med Surg. 2011;28(4):673-85.
2. Dodd A, Daniels TR. Charcot neuroarthropathy of the foot and ankle. J Bone Joint Surg Am. 2018;100(8):696-711.
3. Dardari D. An overview of Charcot's neuroarthropathy. J Clin Transl Endocrinol. 2020;22:100239.
4. Singh D, Gray J, Laura M, Reilly MM. Charcot neuroarthropathy in patients with Charcot Marie Tooth Disease. Foot Ankle Surg. 2020:S1268-7731(20)30250-2.
5. Gupta R. A short history of neuropathic arthropathy. Clin Orthop Relat Res. 1993;(296):43-9.
6. Jordan WR. Neuritic manifestations in diabetes mellitus. Arch Intern Med. 1936;57(2):307-66.
7. Chaudhary S, Bhansali A, Rastogi A. Mortality in Asian Indians with Charcot's neuroarthropathy: a nested cohort prospective study. Acta Diabetol. 2019;56(12):1259-64.
8. Johnson-Lynn SE, McCaskie AW, Coll AP, Robinson AHN. Neuroarthropathy in diabetes: pathogenesis of Charcot arthropathy. Bone Joint Res. 2018;7(5):373-8.
9. Frykberg RG, Belczyk R. Epidemiology of the Charcot foot. Clin Podiatr Med Surg. 2008;25(1):17-28.
10. Schmidt BM, Holmes CM. Updates on diabetic foot and Charcot osteopathic Arthropathy. Curr Diab Rep. 2018;18(10):74.
11. O'Loughlin A, Kellegher E, McCusker C, Canavan R. Diabetic Charcot neuroarthropathy: prevalence, demographics and outcome in a regional referral centre. Ir J Med Sci. 2017;186(1):151-6.
12. Schneekloth BJ, Lowery NJ, Wukich DK. Charcot neuroarthropathy in patients with diabetes: an updated systematic review of surgical management. J Foot Ankle Surg. 2016;55(3):586-90.
13. Labovitz JM, Shofler DW, Ragothaman KK. The impact of comorbidities on inpatient Charcot neuroarthropathy cost and utilization. J Diabetes Complications. 2016;30(4):710-5.
14. Yates TH, Cooperman SR, Shofler D, Agrawal DK. Current concepts underlying the pathophysiology of acute Charcot neuroarthropathy in the diabetic foot and ankle. Expert Rev Clin Immunol. 2020;16(8):839-45.
15. Botek G, Figas S, Narra S. Charcot neuroarthropathy advances: understanding pathogenesis and medical and surgical management. Clin Podiatr Med Surg. 2019;36(4):663-684.
16. Petrova NL, Foster AV, Edmonds ME. Calcaneal bone mineral density in patients with Charcot neuropathic osteoarthropathy: differences between Type 1 and Type 2 diabetes. Diabet Med. 2005;22(6):756-61.
17. Barwick AL, de Jonge XA, Tessier JW, Ho A, Chuter VH. The effect of diabetic neuropathy on foot bones: a systematic review and meta-analysis. Diabet Med. 2014;31(2):136-47.
18. Jansen RB, Svendsen OL. A review of bone metabolism and developments in medical treatment of the diabetic Charcot foot. J Diabetes Complications. 2018;32(7):708-12.
19. Ndip A, Williams A, Jude EB, Serracino-Inglott F, Richardson S, Smyth JV, et al. The RANKL/RANK/OPG signaling pathway mediates medial arterial calcification in diabetic Charcot neuroarthropathy. Diabetes. 2011;60(8):2187-96.
20. Jeffcoate WJ, Game F, Cavanagh PR. The role of proinflammatory cytokines in the cause of neuropathic osteoarthropathy (acute Charcot foot) in diabetes. Lancet. 2005;366(9502):2058-61.
21. Pasquier J, Spurgeon M, Bradic M, Thomas B, Robay A, Chidiac O, et al. Whole-methylome analysis of circulating monocytes in acute diabetic Charcot foot reveals differentially methylated genes involved in the formation of osteoclasts. Epigenomics. 2019;11(3):281-96.

22. Pasquier J, Thomas B, Hoarau-Véchot J, Odeh T, Robay A, Chidiac O, et al. Circulating microparticles in acute diabetic Charcot foot exhibit a high content of inflammatory cytokines, and support monocyte-to-osteoclast cell induction. Sci Rep. 2017;7(1):16450.
23. Jansen RB, Christensen TM, Bülow J, Rørdam L, Holstein PE, Jørgensen NR, et al. Bone mineral density and markers of bone turnover and inflammation in diabetes patients with or without a Charcot foot: an 8.5-year prospective case-control study. J Diabetes Complications. 2018;32(2):164-70.
24. Shibata T, Tada K, Hashizume C. The results of arthrodesis of the ankle for leprotic neuroarthropathy. J Bone Joint Surg Am. 1990;72(5):749-56.
25. Yu GV, Hudson JR. Evaluation and treatment of stage 0 Charcot's neuroarthropathy of the foot and ankle. J Am Podiatr Med Assoc. 2002;92(4):210-20.
26. Molines L, Darmon P, Raccah D. Charcot's foot: newest findings on its pathophysiology, diagnosis and treatment. Diabetes Metab. 2010;36(4):251-5.
27. Heidari N, Oh I, Li Y, Vris A, Kwok I, Charalambous A, et al. What Is the Best Method to Differentiate Acute Charcot Foot From Acute Infection? Foot Ankle Int. 2019;40(1 suppl):39S-42S.
28. Dallimore SM, Puli N, Kim D, Kaminski MR. Infrared dermal thermometry is highly reliable in the assessment of patients with Charcot neuroarthropathy. J Foot Ankle Res. 2020;13(1):56.
29. Moura-Neto A, Fernandes TD, Zantut-Wittmann DE, Trevisan RO, Sakaki MH, Santos AL, et al. Charcot foot: skin temperature as a good clinical parameter for predicting disease outcome. Diabetes Res Clin Pract. 2012;96(2):e11-4.
30. Schaper NC, van Netten JJ, Apelqvist J, Bus SA, Hinchliffe RJ, Lipsky BA; IWGDF Editorial Board. Practical Guidelines on the prevention and management of diabetic foot disease (IWGDF 2019 update). Diabetes Metab Res Rev. 2020;36 Suppl 1:e3266.
31. Idusuyi OB. Surgical management of Charcot neuroarthropathy. Prosthet Orthot Int. 2015;39(1):61-72.
32. Pitocco D, Scavone G, Di Leo M, Vitiello R, Rizzi A, Tartaglione L, et al. Charcot neuroarthropathy: from the laboratory to the bedside. Curr Diabetes Rev. 2019;16(1):62-72.
33. Palestro CJ, Mehta HH, Patel M, Freeman SJ, Harrington WN, Tomas MB, et al. Marrow versus infection in the Charcot joint: indium-111 leukocyte and technetium-99m sulfur colloid scintigraphy. J Nucl Med. 1998;39(2):346-50.
34. Höpfner S, Krolak C, Kessler S, Tiling R, Brinkbäumer K, Hahn K, et al. Preoperative imaging of Charcot neuroarthropathy in diabetic patients: comparison of ring PET, hybrid PET, and magnetic resonance imaging. Foot Ankle Int. 2004;25(12):890-5.
35. Galli M, Scavone G, Vitiello R, Flex A, Caputo S, Pitocco D. Surgical treatment for chronic Charcot neuroarthropathy. Foot (Edinb). 2018;36:59-66.
36. Sammarco VJ. Superconstructs in the treatment of Charcot foot deformity: plantar plating, locked plating, and axial screw fixation. Foot Ankle Clin. 2009;14(3):393-407.
37. LaPorta GA, D'Andelet A. Lengthen, alignment, and beam technique for midfoot Charcot neuroarthropathy. Clin Podiatr Med Surg. 2018;35(4):497-507.
38. Vopat ML, Nentwig MJ, Chong ACM, Agan JL, Shields NN, Yang SY. Initial diagnosis and management for acute Charcot neuroarthropathy. Kans J Med. 2018;11(4):114-9.
39. Blume PA, Sumpio B, Schmidt B, Donegan R. Charcot neuroarthropathy of the foot and ankle: diagnosis and management strategies. Clin Podiatr Med Surg. 2014;31(1):151-72.
40. Parisi MC, Godoy-Santos AL, Ortiz RT, Sposeto RB, Sakaki MH, Nery M, et al. Radiographic and functional results in the treatment of early stages of Charcot neuroarthropathy with a walker boot and immediate weight bearing. Diabet Foot Ankle. 2013;4.
41. Pinzur MS, Lio T, Posner M. Treatment of Eichenholtz stage I Charcot foot arthropathy with a weightbearing total contact cast. Foot Ankle Int. 2006;27(5):324-9.
42. Saltzman CL, Hagy ML, Zimmerman B, Estin M, Cooper R. How effective is intensive nonoperative initial treatment of patients with diabetes and Charcot arthropathy of the feet? Clin Orthop Relat Res. 2005;(435):185-90.
43. Lowery NJ, Woods JB, Armstrong DG, Wukich DK. Surgical management of Charcot neuroarthropathy of the foot and ankle: a systematic review. Foot Ankle Int. 2012;33(2):113-21.
44. Rettedal D, Parker A, Popchak A, Burns PR. Prognostic scoring system for patients undergoing reconstructive foot and ankle surgery for Charcot neuroarthropathy: the Charcot reconstruction preoperative prognostic Score. J Foot Ankle Surg. 2018;57(3):451-5.
45. Ramanujam CL, Zgonis T. Surgical correction of the Achilles tendon for diabetic foot ulcerations and Charcot neuroarthropathy. Clin Podiatr Med Surg. 2017;34(2):275-80.
46. Shazadeh Safavi P, Jupiter DC, Panchbhavi V. A Systematic review of current surgical interventions for Charcot neuroarthropathy of the midfoot. J Foot Ankle Surg. 2017;56(6):1249-52.
47. Pope EJ, Takemoto RC, Kummer FJ, Mroczek KJ. Midfoot fusion: a biomechanical comparison of plantar planting vs intramedullary screws. Foot Ankle Int. 2013;34(3):409-13.
48. Garchar D, DiDomenico LA, Klaue K. Reconstruction of lisfranc joint dislocations secondary to Charcot neuroarthropathy using a plantar plate. J Foot Ankle Surg. 2013;52(3):295-7.
49. Simonik MM, Wilczek J, LaPorta G, Willing R. Biomechanical comparison of intramedullary beaming and plantar plating methods for stabilizing the medial column of the foot: an in vitro study. J Foot Ankle Surg. 2018;57(6):1073-9.
50. Scott RT, DeCarbo WT, Hyer CF. Osteotomies for the management of Charcot neuroarthropathy of the foot and ankle. Clin Podiatr Med Surg. 2015;32(3):405-18.
51. Dalla Paola L, Brocco E, Ceccacci T, Ninkovic S, Sorgentone S, Marinescu MG, et al. Limb salvage in Charcot foot and ankle osteomyelitis: combined use single stage/double stage of arthrodesis and external fixation. Foot Ankle Int. 2009;30(11):1065-70.
52. Evans KK, Attinger CE, Al-Attar A, Salgado C, Chu CK, Mardini S, et al. The importance of limb preservation in the diabetic population. J Diabetes Complications. 2011;25(4):227-31.

JOURNAL OF THE
Foot & Ankle