Recent Modalities in Management of CHARCOT JOINT in Diabetic Foot

A systematic Review

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List of Abbreviations

Abb.	Full term
ACA	*Acute charcot arthropathy*
CROW	*Charcot restraint orthotic walker*
EBG	*Electric bone growth*
ESR	*Erythrocyte sedimentation rate*
OM	*Osteomyelitis*
PPWB	*Prefabricated pneumatic walking brace*
SWM	*Semmes Weinstein monofilament*
TCC	*Total contact cast*
VPT	*The vibration perception threshold meter*

INTRODUCTION AND RATIONALE

Neuropathic arthropathy, also referred to as Charcot arthropathy which was named after the French neurologist Jean-Martin Charcot (1825-1893), is a progressive, denervation-induced degeneration of the foot and ankle joints. Considering devastating outcomes, such as eventual deformity which is almost always inevitable when untreated, the etiology and pathophysiology of this insidious disorder is vigorously studied in the literature as one of the core topics. A significant amount of content is amassing in the literature about this topic and this may be a sign of unclarity about the pathophysiology of Charcot arthropathy. Although numerous factors have been attributed as a contributor, the big picture is still not fully revealed ***(Kaynak et al.,. 2013)***.

Charcot arthropathy or neuroarthropathy is a fracture and dislocation process of the foot and ankle that occurs in patients with sensory and autonomic neuropathy. Fracture is often associated with unrecognized injury or minor trauma that might otherwise appear innocuous***(Sidawy et al., 2018)***.

Historically, syphilis and leprosy were the most common causes of CN; however, diabetes mellitus (DM) has emerged as the most common cause of CN over the past several decades ***(Shen and Wukich, 2013)***.

With the increased number of diabetics worldwide and the increased incidence of morbid obesity in more prosperous cultures, there has become an increased awareness of Charcot arthropathy of the foot and ankle. Outcome studies would suggest that patients with deformity associated with Charcot Foot arthropathy have impaired health related quality of life. This awareness has led reconstructive-minded foot and ankle surgeons to develop surgical strategies to treat these acquired deformities ***(Shen and Wukich, 2013)***.

The American Diabetes Association estimates that 25 million people in the United States, or 7.8% of the population have diabetes mellitus. thus, The incidence of Charcot arthropathy appears to be relatively common, perhaps affecting some 8.5 per 1000 people with diabetes per year ***(Lowery et al., 2012)***.

It affects both type 1 and type 2 diabetes. Recently, a relative preponderance of type 1 diabetes has been noted, and the odds ratio for a patient with type 1 diabetes to develop CN is 3.9 times greater than that of the odds ratio for a patient with type 2 diabetes. It is associated with significant morbidity, and patients often report a reduced quality of life ***(Balducci et al., 2014).***

Primary risk factors for this potentially limb-threatening deformity are the presence of dense peripheral sensory neuropathy, normal circulation, and history of preceding trauma (often minor in nature). Trauma is not limited to injuries such as

sprains or contusions. Foot deformities, prior amputations, joint infections, or surgical trauma may result in sufficient stress that can lead to Charcot joint disease ***(Frykberg et al., 2006)***.

Charcot neuroarthropathy has been recognized for more than 130 years, and remains a major cause of morbidity in diabetic patients. It is a progressive condition of the musculoskeletal system, characterized by joint dislocations, pathological fractures, and debilitating deformities commonly affecting the neuropathic lower extremity. In the United States, many surgical limb salvage procedures for the Charcot foot deformity are performed annually. These procedures range from simple exostectomy to full reconstructions with metatarsal and tarsal osteotomy, arthrodesis, internal and external fixation, free flaps, and, finally, amputation ***(Pinzur and Schiff, 2017)***.

As we will see there are different surgical & non-surgical methods of treatment, However, few studies elaborated best methods as regards patient satisfaction and improved quality of life. And there is no clear guideline for choose the best method of treatment.

Aim of the Work

The aim of this study is to make a systemic review on the results of different methods of treatment of CN, review the indications of surgical intervention, and correlate patient satisfaction with the outcome of different limb salvage procedures. This review will include studies published from 1995 to 2017.

PATHOPHYSIOLOGY OF CHARCOT ARTHROPATHY

Almost all affected individuals have a dense sensory peripheral neuropathy. The neuropathy is most commonly associated with diabetes, but may also be associated with leprosy, alcoholism, tabes dorsalis (syphilis), syringomyelia, peripheral nerve injuries, or congenital absence of sensation**.** Usually the larger joints of lower extremity are involved in syphilis, and the larger joints of the upper extremity are involved in syringomyelia**.** In contrast, diabetes related Charcot arthropathy primarily affects the foot and ankle ***(*Galhoum and M.Abd-Ella, 2016).**

Pathogenetic knowledge has focused on purely mechanical theories for some time. Two theories, initially thought to be competing concepts, are now considered to be overlapping to varying degrees.

On one hand, the neurotraumatic theory, noted that the common thread of pathogenesis included continual injuries from minor trauma or isolated major trauma to neuropathic joints. There are many authors who believed that charcot arthropathy may be triggered in diabetic patients by some type of joint trauma, and they are supported by the identification of the lack of protective sensation as a predisposing factor to the disease ***(Gupta, 1993)(*Kaynak et al., 2013*).***

On the other hand, the neurovascular theory is based on the presence of vasomotor neuropathy in individuals with sensory neuropathy and intact blood flow. The vasomotor neuropathy produces arterio venous shunting, leading to bone resorption and mechanical weakening ***(Edelman et al., 1987)(Sun PC et al., 2013).***

The autonomic neuropathy leads to a hyperemic state, with an increase in blood flow to the lower limbs due to the development of arteriovenous shunts. The hyperemia appears to cause osteopenia, bone resorption and bone weakening. Ultimately, it is on this weakened foot that, either spontaneously or due to minor trauma, microfractures and dislocations occur ***(Jeffcoate et al., 2005)***.

Although both these theories are attractive, they are not able to explain some of the typical features of acute CNO and, in particular, why the condition is unilateral while neuropathy is most often bilateral, why CNO is so infrequent while neuropathy is a common complication of diabetes, and what is the link with the inflammatory reaction that is initially observed.

However, a currently recognized novel theory is able to answer all of these questions. It is a more 'inflammatory' than 'mechanical' theory that also includes the idea of a triggering factor, most often a minor trauma that goes unnoticed because of the sensory neuropathy, but also sometimes a previous ulcer infection or foot surgery. The common link between these factors is local inflammation **(Baumhauer JF et al., 2006),**

these factors are also all associated with the release of proinflammatory cytokines such as interleukin (IL)-1β and tumour necrosis factor (TNF)-alpha, which are known mediators of bone resorption via excess osteoclastic activity ***(Petrova et al., 2007)(P Wojdasiewicz et al., 2014).***

Interestingly, however, a dissociation between the local inflammatory response related to the increased proinflammatory cytokine secretion and lack of systemic inflammatory response has been found in patients with acute CNO ***(Jeffcoate, 2004).*** In such patients, these cytokines lead to an increased expression of the receptor activator of nuclear factor-kB (RANK) ligand. The RANK ligand (RANK-L) is located in the cell membranes of osteoblasts and bone-marrow stromal cells, and belongs to the TNF super family. Its receptor (RANK) is expressed in the membrane of pre osteoclasts and other cells of this membrane lineage, and belongs to the TNF-receptor superfamily. The involvement of the RANK/RANK-L signaling pathway in the pathogenesis of acute CNO was first hypothesized by Jeffcoate in 2004, who observed RANK-L overexpression in a variety of degenerative bone diseases, including rheumatoid arthritis, psoriatic arthritis, postmenopausal or glucocorticoid-induced osteoporosis and multiple myeloma ***(Jeffcoate, 2008).***

RANK-L stimulates the expression of nuclear factor (NF)-kB, a transcription factor that, in turn, induces the maturation of precursor cells into mature osteoclasts. At the same time, NF-kB induces the increased expression of the glycoprotein

osteoprotegerin (OPG), which acts as a decoy receptor for RANK-L to effectively neutralize its effect and so avoid excess osteolysis (Fig. 1). Different regulatory mech- anisms of the RANK/RANK-L/OPG system are involved in bone remodelling, including other cytokines, growth factors and hormones that variably increase (TNF-α, glucocorticoids, parathyroid hormone) or suppress (sex steroids, calcitonin, calcitonin gene-related peptide, leptin) the expression of RANK-L and, thus, stimulate or inhibit bone turnover ***(Boyle et al., 2003).***

Atraumatic triggering factor causes the release of inflammatory cytokines that increase the expression of RANK-L, thereby resulting in clinical signs of inflammation, osteoclast matura- tion and activation, and osteolysis. Physiologically, this process is limited by immobilization in response to the pain caused by local inflammation. However, when pain perception is reduced due to sensory neuropathy, there is no protective suppression, thereby allowing the inflammatory process to continue which, in turn, ultimately leads to osteolysis and bone breakdown. The result is the establishment of a vicious circle of inflammation and worsening structural damage to the foot (Fig. 2) ***(Molines et al., 2010).***

In practice, this indicates that it is essential that clinicians make the diagnosis of acute CNO early as possible to avoid its progression to the chronic, stable stage, with bony deformity and the classic 'rocker-bottom' appearance if the midfoot is involved. At this stage, the bony plantar prominence becomes a site of abnormally high pressure that particularly exposes the