Charcot foot: why have we not made progress?

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Charcot neuroarthropathy (CN) is a rare disease (Centers for Disease Control and Prevention [CDC], 2017) affecting less than 40,000 patients in the United States each year. The prevalence is estimated to be 0.1%–0.9% (Stuck et al, 2008; Sohn et al, 2009; Rogers and Frykberg, 2013). The significant deformity and classic rocker-bottom foot makes late-stage CN extremely recognisable but unfortunately, the early signs are missed. Risk factors for CN include diabetes mellitus (DM) greater than 10 years, elevated haemoglobin A1c, trauma and obesity (Stuck et al, 2008). CN is an independent risk factor for lower-extremity amputations (Sohn et al, 2009; Rogers and Frykberg, 2013).

Primary emphasis for CN has been on treatment and not on early diagnosis and wide spread knowledge and dissemination. Modalities included in the standard of care are regular application of total contact casting until a stable braceable or shod condition is attained. Medical management also focuses intervention to regulate bone turnover. However, if medical and non-surgical approaches fail, surgical reconstruction would be entertained with an ultimate goal to create and maintain a plantigrade foot. In spite of improvement in treatment and management, little emphasis has been placed on diagnosing the disease despite supporting evidence that early diagnosis improves patient outcomes (Koeck et al, 2009).

The aetiology of CN is truly unknown. Although, it is accepted that small fibre peripheral neuropathy precedes the disease. A conceptual model proposed by Koeck et al (2009) describes important components of CN, which include peripheral neuropathy, excessive or repetitive micro trauma, increased vascularity and a general pro-inflammatory response leading to excess bony turnover and weakening of bone. The study demonstrated the joint synovium in patients with CN lacks adequate sympathetic control compared to the control sample of patients with osteoarthritic joints. This ultimately leads to joint destruction.

Munson et al (2014) used a big data approach to identify 710 associations of different conditions with CN. In addition, Munson et al (2014) discovered that 111 of these medical conditions have direct temporal associations with the development of CN. Not unsurprisingly, the strongest associations to develop CN occurred when those patients had endocrine disorders, namely DM, and neurotrophic disorders, which lead to local sensory loss and selective sympathetic denervation. Thus, any patient with endocrine disorders should ultimately be suspect to the possibility of a CN event.

Furthermore, an early diagnosis of CN will yield better patient outcomes and, as such, all clinicians that are routinely performing diabetic foot screenings should have a high clinical index of suspicion for patients presenting with neuropathy, and/or an erythematous, with calor, oedematous foot in the presence of a normal X-ray. This may represent Stage 0 CN (Chantelau and Grützner, 2014) (*Table 1*). A clinician's high index of suspicion will only be triggered by first adding CN, in particular, stage 0 CN, to the short list of differential diagnosis. Recent literature suggests that 67% of primary care doctors and internal medicine specialists have little or no knowledge of CN (Schmidt et al, 2017). A differential diagnosis list should include: infection or osteomyelitis (especially if skin breakdown is noted), fracture, deep vein thrombosis, gout, trauma, ankle sprain. Consideration for stage 0 CN should increase when the patient has no apparent skin breakdown, an erythematous, hot, and oedematous foot, with or without a history of trauma.

CN most commonly affects the mid foot joints (tarsometatarsal and midtarsal) (Sanders, 1991; Sella and Barrette, 1999) and there is no single laboratory or imaging test to confirm diagnosis. For example, there is a strong relationship between duration of DM, elevated haemoglobin A1c (HbA_{1c}), and

Table 2. Chantelau and Grützner MRI Classification of the Charcot foot. Adapted from Chanetelau and Grützner (2014) classification and diagnosis of Charcot neuroarthropathy.

	Low severity (without cortical fracture)	High severity (with cortical fracture)	
Active Arthropathy	Mild inflammation/oedema No skeletal deformity X-ray is otherwise normal MRI: abnormal with oedema, **microfractures** and bone bruise	Severe oedema/inflammation Severe Skeletal deformity Microfractures on X-ray MRI: abnormal with oedema, **macrofractures** and bone bruise	
Inactive Arthropathy	No inflammation No skeletal deformity X-ray is otherwise normal MRI: **No significant oedema**	No inflammation Skeletal deformity X-ray with past macrofractures MRI: no significant oedema	
Combined clinical symptoms, advanced imaging and histopathology classification			
	Clinical signs and symptoms	**CT and MRI features**	**Histopathology**
Active stage, grade 0	Mild inflammation but no gross deformity	Obligatory: diffuse BMO and STO (Kiuru Grade I–III) No cortical disruption Facultative: subchondral trabecular microfractures (bone bruise); ligament damage	Lamellar bone with active surface. Remodelling of trabeculae associated with microfractures Marrow space replaced by loose spindle cells
Active stage, grade 1	Severe inflammation with gross deformity, increased by unprotected walking	Obligatory: fracture(s) with cortical disruption, BMO and STO (Kiuru grade IV) Facultative: osteoarthritis, cysts, cartilage damage, osteochondrosis, joint effusion, fluid collection, bone erosion/necrosis, bone lysis, debris, bone destruction, joint luxation/subluxation, ligament damage, tenosynovitis, bone dislocation	Increased vascularity of the marrow space, active remodelling of woven bone. Compatible with response to (impaction) fracture Osteonecrosis. Thickened synovium, fragmented cartilage and subchondral bone, invasion of inflammatory cells and vascular elements
Inactive stage, grade 0	No inflammation, no gross deformity.	No abnormal imaging, or minimal residual BMO; subchondral sclerosis, bone cysts, osteoarthrosis, ligament damage	Sclerosis of bone characterised by broad lamellar trabeculae with collagenous replacement and a low vascularity of the marrow space
Inactive stage, grade 1	No inflammation; persistent gross deformity and possible ankylosis	Residual BMO, cortical callus (Kiuru grade IV); joint effusion, subchondral cysts, joint destruction, joint dislocation, fibrosis, osteophyte formation, bone remodelling, cartilage damage, ligament damage, bone sclerosis, ankylosis, pseudoarthrosis	Woven bone, immature and structurally disorganised, fibrosis

development of CN. However, while elevated HbA$_{1c}$ is helpful in diagnosis and management of DM, it is not a direct cause of CN (CDC, 2017) and other aetiologic factors may cause CN. Some laboratory values like complete blood count and inflammatory markers (C-reactive protein and erythrocyte sedimentation rate) can be assistive in management of infection in patients with CN but do not diagnose CN itself. Other laboratory values, such as vitamin D levels, are not definitively related to a CN event and are not helpful in diagnosis (Greenhagen et al, 2019). Due to the lack of laboratory tests to complement diagnosis, it is even more important for providers to have a high index of suspicion of CN based on clinical presentation.

Providers frequently suspect CN in a rocker-bottom foot with substantial deformity and acute fractures. While this late stage is easy to diagnose, it is the most difficult to treat. Early in the condition, an insensate patient will present with pain in their foot and notice increased oedema and erythema because of the acute inflammatory response. The foot will be clinically warm to touch and recent literature suggests that normative pedal temperatures in patients with diabetic peripheral neuropathy are approximately 29.21°C (~83°F) in the midfoot (Schmidt et al, 2019). Early in the condition, a lack of a foot deformity is expected and only after the damage is done will deformity present. Perhaps increasing awareness will allow for individuals with this condition to receive earlier access to care possibly in the 'prodromal stage'. We have failed to achieve real progress in the treatment of CN because resources have focused on treatment modalities when CN has progressed to later stages. These strategies are certainly useful for limb salvage but by the time of late-stage presentation, the patient has already amassed significant risk for morbidity and mortality (McEwan et al, 2016).

Earlier suspicion of stage 0 CN by providers allows for seamless treatment of the condition, even when gross deformity is not (yet) present. This includes immediate immobilisation in an irremovable walker or plaster cast, and a rapid referral to a foot specialist. This sequence of treatment should be considered standard of care and our goal should be for all patients suspected of having CN, to be treated the same initially, and without delay. This 'knee-jerk' reaction can prevent sequela and mortality associated with the disease. Currently, education models focus on patients and their presentations and not necessarily the providers. It begs the question: "Why do providers ask a vulnerable and insensate population to screen themselves, recognise their problem, and present in a timely manner when we have not shown mastery in this area?" Acting in a preventative manner and educating ourselves can mitigate many of the effects of misdiagnosis or delayed care.

Therefore, the best treatment strategy for CN should be its identification and our focus should be on the prevention of its progression to an unstable foot deformity predisposing patients to ulcerations, infections, and amputations. As providers, our lack of education surrounding this subject is causing us to miss the best opportunity to have a profound impact on our patient's lives. Education and our own self-assessment should guide us to improve our awareness of the condition, our diagnostic accuracy and knowledge. As a result of this paradigmatic shift, we believe that placing a greater emphasis on education providers about CN would save limbs and lives. ∎

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