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Charcot neuroarthropathy in diabetes mellitus

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Abstract

Charcot neuroarthropathy has been recognised for over 130 years and yet it remains a major cause of morbidity for patients with diabetes mellitus and a continuing challenge for physicians. It is rare but it seems to be increasing in prevalence and this provides hope that with larger studies it will soon be possible to clarify the natural history and optimal treatment regimens. The underlying cause is thought to be trauma in a neuropathic foot that leads to a complex series of pathological processes culminating in bone and joint destruction and subsequent deformity. The acute reaction is often misdiagnosed and many patients present late with established deformity. Even when the diagnosis is considered at an early stage there are no definitive criteria or tests to confirm charcot neuroarthropathy and a high index of suspicion is necessary in any diabetic patient with a swollen warm foot in the presence of somatic or autonomic neuropathy. Treatment has traditionally involved the use of various methods to avoid weight bearing but recent work has begun to suggest that bisphosphonates might be able to arrest the acute process. In the long term, treatment involves a multidisciplinary approach aimed at providing appropriate footwear to reduce plantar pressures and avoid foot ulceration; in some circumstances this involves surgical correction of deformities before adequate footwear can be supplied. Further studies of the emerging treatments for Charcot neuroarthropathy are needed to provide long-term outcome data on morbidity and deformity. [Diabetologia (2002) 45:1085–1096]

Keywords Charcot, neuroarthropathy, diabetic foot, neuropathy, Charcot joint, foot deformity, diabetic foot ulcer, diabetic osteoarthropathy, Charcot arthropathy, diabetic neuropathy.

Charcot neuroarthropathy (CN) is a chronic and progressive disease of bone and joints, characterised by painful or painless bone and joint destruction in limbs that have lost sensory innervation [1]. Affected joints exhibit synovitis, instability, subluxation, and destruction [2]. Although not often recalled, trauma is thought to be an important initiating factor. Despite awareness of the condition for more than 130 years, our knowledge about CN remains limited. The main cause of CN in the developed world is now diabetic polyneuropathy [3] with the joints of foot being most commonly affected [4].

The true prevalence of CN in patients with diabetes mellitus is not known but it is likely that many cases are undiagnosed due to a lack of recognition of the typical acute presentation and the often asymptomatic nature of the condition. In patients with established CN, foot ulceration secondary to deformity is the most common presenting feature and therapeutic efforts tend to be concentrated on healing ulcers rather than

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Abbreviations: CN, Charcot neuroarthropathy; CT, computerised tomography; In-WBC, labelled white cell scans; IP, interphalangeal; MR, magnetic resonance; MTP, metatarso-phalangeal; STIR, short-tau inversion-recovery; Tc MDP, Technetium 99m methylene diphosphonate; TMT, tarso-metatarsal.

arresting the disease process. In recent years there has been increasing interest in the management of the diabetic foot [5] not least because of the massive health economic consequences of foot ulcers [6]. Multidisciplinary foot clinics have been established in many centres and have co-ordinated the management of CN [6, 7]. New imaging techniques and treatment modalities are also increasingly being used for the diagnosis and management of CN [8].

The relative rarity of CN has hampered attempts to study the condition. There is a paucity of good quality, controlled studies of the natural history of CN or of the effects of the different treatments. Fortunately this situation is now being remedied and the approach to treatment is becoming more evidence-based. There have been a few publications regarding CN [9, 10, 11] and in this article we review new developments in this condition.

History

Jean-Martin Charcot, a French neurologist, described the condition in 1868 [12], although similar reports had been made earlier. J.K. Mitchell from Philadelphia had described twelve cases of "arthritis" in 1831 related to spinal cord lesions [13], and two years later reported 35 more patients with similar pathologies [14]. Charcot duly acknowledged Mitchell's earlier reports [15]. However, there is considerable controversy as to whether Mitchell's reports were truly due to neuropathic arthritis [16, 17]. Even a century before Mitchell's description, W. Musgrave from Exeter had described a case of neuropathic arthritis in a luetic patient who later died of a "convulsion" [18]. In his work, "Antiquitates Britanno-Belgicae", Musgrave devoted four volumes to "arthritis" and pointed out the need to recognise that arthritis could be secondary to other diseases [18]. In 1882, the 'Rapport du Congres' published in London, named these distinct pathological changes as 'Charcot's joint'. Since then case reports of CN in association with neurological disorders other than tabes dorsalis have been made and in 1936 Jordan made the first report of CN in diabetes mellitus [19]. Several neurological conditions such as spina bifida, meningomyelocele, cerebral palsy, syringomyelia have been associated with the development of CN [20, 21]. However, in endemic areas leprosy is the most common cause [22] followed closely by alcohol abuse [23].

Epidemiology

There are no population based epidemiological studies of CN. The reported incidence and prevalence of CN varies between 0.1% to 0.4% of diabetic populations [24, 25, 26, 27]. In one of the largest series published, 101 cases were found among 68000 consecutive diabetic patients between 1947 and 1970, giving an incidence of 1:680 [24]. In 1947, 17 cases of CN were found in a study of 20000 consecutive diabetic patients at the Joslin Clinic in Boston giving an incidence of 1 in 1100 [25]. A more recent survey found an incidence of 1 in 333 [26] supporting the notion that CN is becoming more common. Similarly, in a series of 1001 diabetic patients screened at a Liverpool hospital, the prevalence of CN was found to be 0.4%, although 17.8% had neuropathy [27]. In another survey radiographic evidence of lower limb bone and joint changes were found in 29% of 333 diabetic patients with peripheral neuropathy [28]. However, in a more recent study of foot radiographs of 456 diabetic patients, CN changes were seen in only 1.4% [29]. As there are no agreed clinical or radiological diagnostic criteria for CN, it is likely that cases are misdiagnosed or missed.

The majority of patients with CN present between the fifth and sixth decades [24, 25, 28, 30] and most will have had diabetes mellitus for at least 10 years [24, 25, 28, 30]. Recent observation has shown CN to be associated with premature mortality [31]. There is no particular sex preponderance and it could be bilateral. Although CN was bilateral in only 9% [32], others have reported a higher level of bilateral involvement, even up to in 75% of cases [33]. Similarly, another study found bilateral changes when the feet were examined by computerised tomography (CT) in 75% of 22 patients [34]. As in other centres, we have observed an increase in the incidence of CN in the diabetes mellitus clinic [4]. This could be due in part to increasing awareness of the condition amongst physicians caring for people with diabetes mellitus. With greater attention being given to the care of patients with the diabetic-foot and management strategies involving a multidisciplinary approach, the numbers of hospital admissions and lower limb amputations have decreased [35, 36]. In addition, the current practice of treating patients with foot ulcers in out-patient foot clinics, rather than as in-patients has resulted in earlier mobilisation and weight bearing. All these factors could have contributed to the increased prevalence of CN.

Anatomical classification

Charcot neuroarthropathy in diabetes almost exclusively affects the foot although other sites including the wrist [37, 38], knee [39], hip [40] and spine [41] have been reported. In the foot, CN can be classified into five different types depending on the joints involved [42] (Fig. 1). Type I CN involves metatarsophalangeal (MTP) and interphalangeal (IP) joints [43]. The involvement of MTP joints is not commonly reported as the external deformity and its consequences

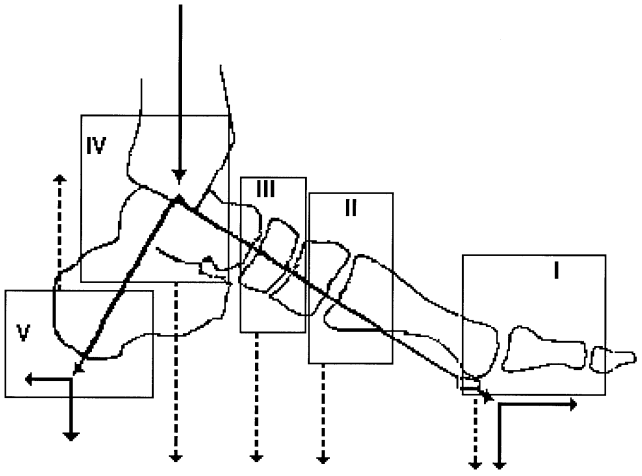

Fig. 1 Schematic diagram of affection of different joint in Charcot neuroarthropathy. The *bold arrows* show the normal weight distribution in feet. *Dotted arrows* show weight distribution in the different types (I–V) of Charcot neuroarthropathy (CN). Type I CN involves metatarso-phalangeal and interphalangeal joints; Type II CN involves tarso-metatarsal joints, Type III CN involves tarsal joints, Type IV involves the sub-talar joints and Type V, the calcaneum

are minimal but it is thought to be one of the more commonly involved joints [44]. Type II CN involves tarso-metatarsal (TMT) joints, Type III CN involves tarsal joints, Type IV involves the sub-talar joints and Type V, the calcaneum. A separate system of classification [45] divides CN into fore-foot CN, involving IP and MTP joints, mid-foot CN involving TMT and tarsal joints, and hind-foot CN, which includes lesions in the ankle joint and calcaneum. The most common clinical presentation is that of mid-foot CN [46], mainly of the Type II variety. The classifications have some clinical importance as forefoot CN has a good prognosis whereas hind-foot CN is rare and carries a poor prognosis due to the effects of weight distribution during walking (Fig. 1).

Pathogenesis

The pathogenic mechanisms of CN have been the subject of a long debate and there are a number of competing theories that are not necessarily mutually exclusive. A major difficulty in this area is in differentiating whether abnormalities, such as the increased lower limb blood flow, are a cause or consequence of CN.

Neuro-vascular theory. Mitchell and Charcot favoured the so called ‘neuro-vascular theory’ which suggests that an increase in the blood supply to bone due to damage to ‘trophic nerves’ causes bone resorption and weakening, ultimately resulting in fractures and deformities. It is now clear that these ‘trophic nerves’ are autonomic nerves. There is now little doubt that diabetic neuropathy leads to an increase in the blood flow to the lower limbs [47]. Few studies have compared the blood flow in the feet of CN with that of peripheral diabetic neuropathy without CN. The vasomotor regulation of blood flow to the lower limb skin is preserved in CN [48]; however, others have shown that there is no difference in the microcirculation between them [49]. Raised venous pressure was observed in the foot in both groups compared with control subjects [50]. The clinical findings of a warm foot with dilated veins suggests that there is arteriovenous shunting in CN [51] and it is notable that peripheral arterial disease seems to be protective against the development of CN [52].

Neuro-traumatic theory. Volkman and Virchow proposed the so-called ‘neuro-traumatic theory’ which suggests that the insensate joints undergo repetitive trauma resulting in fractures, which are complicated with deformity during healing. In 1917, Eloesser [53] conducted his famous experiments on cats. The dorsal roots of the spinal cord of 42 cats were ligated on one side and the animals observed for 3 years, during which time the majority developed CN. He also subjected 3 cats to iatrogenic joint damage and these animals developed typical changes of CN within 3 weeks. As the physical properties of bones including the “breaking strength” were not changed, he concluded that trauma was very important in the genesis of CN [53]. Dogs with hind-limb deafferentiation by L4–S1 dorsal root ganglionectomy developed severe degenerative changes on transection of the anterior cruciate ligament of the knee [54]. This shows that neuropathy and trauma interact in the genesis of CN. More recently, a rat model of CN has been developed in which the typical features of CN are produced with the injection of immunotoxins to the joints to cause selective destruction of sensory innervation [55].

The precise role of trauma in the genesis of CN is not clear. Charcot neuroarthropathy is recognised to progress very rapidly in humans after trauma [40, 56, 57, 58]. However, the observation that CN can develop in non-weight bearing upper limb joints whereby there is very little trauma [59, 60] suggests that trauma might not be a necessary prerequisite. Unfortunately, this is a rather difficult area, as neuropathic patients often do not recall painless trauma.

Bone pathology. There is an association between diabetes mellitus and osteoporosis that could contribute to the development of CN [61]. Patients with CN were shown to have reduced bone density in the lower limbs in comparison to neuropathic control subjects [62]. Studies using bone markers to assess bone formation and resorption have indicated that there is an increase in osteoclastic activity in comparison with osteoblastic activity in acute and chronic CN [10, 63]. This is thought to lead to osteopenia, which can then

predispose to fracture even with minimal trauma [64]. In addition, the loss of peripheral pain sensation means that protective mechanisms are lost and joint immobilisation, which is essential for proper healing of the bone injury, might not occur. This can result in non-union of fractures and pseudo-arthrosis, often with the formation of osteophytes [4]. The end result is a gross disorganisation of bone architecture in established CN.

Atypical neuropathy? It is not entirely clear why only a small proportion of patients with neuropathy develop CN. Trauma is likely to play an important part but some authorities have suggested that people with CN have a different variant of neuropathy from the usual distal chronic sensorimotor neuropathy. In one study, patients with CN were found to have preserved perception of warmth, but had complete loss of peripheral cold perception [65]. This contrasted with patients with foot ulceration, who had severe impairment of both warm and cold sensory thresholds [65]. Light touch perception was also preserved in CN but vibration perception at the big toe and cardiovascular autonomic function tests were abnormal in both groups [65]. In a more recent study, there was no difference in sensory impairment between the two groups but CN patients showed evidence of reduced bone density in their lower limbs with a relatively preserved bone density in the spine [62].

Non-enzymatic glycation. In diabetes mellitus there is non-enzymatic glycation of various proteins, including collagen. Electron microscopy of the Achilles tendon has shown that there is increased packing density of collagen fibrils, a decrease in fibrillar diameter and abnormal fibril morphology [66]. These changes can lead to shortening of tendons [66]. Some authors have suggested that the abnormal collagen in these patients could make joints susceptible to wear and tear and predispose to the development of CN [66, 67].

Increased plantar pressure. Plantar pressures were found to be higher in patients who developed acute CN compared with patients with distal sensorimotor neuropathy or neuropathic ulceration [68]. They found that plantar pressures are increased in the MTP joints (fore foot) although CN affected mid-foot joints and postulated that the forefoot might have acted as a lever causing collapse of the midfoot [68]. Thus, the imbalance in pressure distribution associated with motor and sensory neuropathy could be involved in the genesis of CN.

Summary of pathogenesis. A synthesis of the various pathogenic mechanisms involved in CN is emerging. The classic debate between the 'neuro-traumatic' and 'neuro-vascular' theories is rapidly becoming redundant and a number of simultaneously operating mechanisms are likely to work in concert resulting in CN (Fig. 2). The CN process is probably triggered in the majority of patients by trauma [69], which may or may not be remembered. This seems to trigger an abnormal vascular reflex with an increase in bone blood flow [57] due to autonomic dysfunction, perhaps in an analogous manner to the process which is seen in reflex sympathetic dystrophy [70]. Abnormal healing processes occur with a predominance of osteoclastic action on a background of reduced bone strength [63]. Abnormal weight-bearing, due to an imbalance between flexors and extensors of the feet as a consequence of sensorimotor neuropathy, can lead to further bone damage progressing rapidly through an acute phase which is rapidly transformed into a deformed foot. In some cases this process takes only a few weeks (Fig. 3A, B).

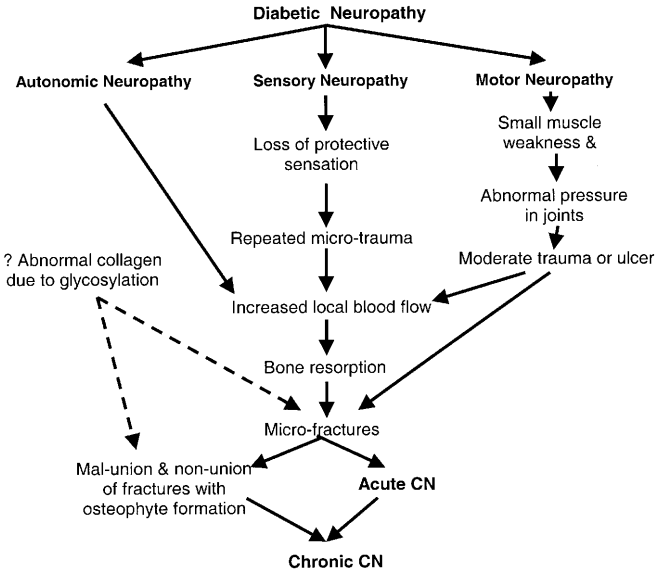

Fig. 2 Schematic diagram of potential pathological pathways to the development of Charcot neuroarthropathy (CN). Both neuropathy and increased blood flow appear to be important, and the abnormality of collagen structure could be involved

Clinical features

The earliest manifestation of CN is persistent swelling (oedema) with some discomfort which is the main reason for which medical treatment is sought [4]. Charcot neuroarthropathy can present as an acute or chronic condition and clinical features depend on the nature of the presentation. There is a considerable overlap in these phases and it can present to clinicians in many disciplines.

Acute presentation. In acute CN, there is usually moderate pain and oedematous swelling although the foot might be completely insensate. There could be a history of trauma although this is possibly under-reported

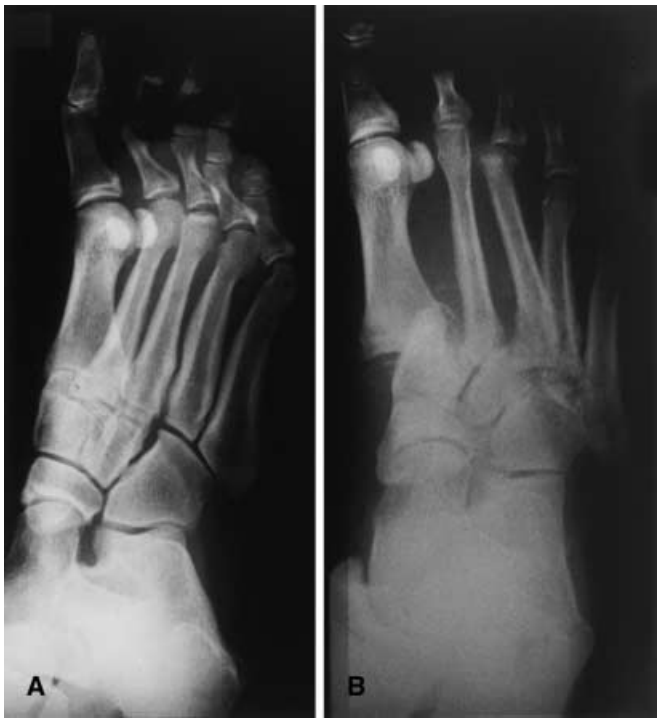

Fig. 3 **A** X ray of the foot showing minor flattening of the third metatarsal head; the rest of foot is normal. **B** 4 months later, there is complete disorganisation of the tarso-metatarsal joints with dislocation and bony debris present. The third metatarso-phalyngeal joint is also disorganised

due to the lack of associated pain. A study showed that 73% of patients did not recall any precipitating event, 22% recalled a specific traumatic episode within one month before the onset of symptoms and 4% of patients with CN had recent foot surgery [32].

On examination, the foot is warm, swollen, and tender and can be markedly erythematous. At this stage the differential diagnosis includes cellulitis, acute gout, deep vein thrombosis and osteomyelitis [24] and it can be a considerable challenge to make an accurate diagnosis. The exclusion of cellulitis or osteomyelitis is particularly important if foot ulceration is also present. Unfortunately, due to the rarity of CN, the initial diagnosis is often missed leading to a delay in recognition of CN and consequent late deformity. The progression from acute to chronic phase can be rapid with considerable irreversible damage occurring within 6 months or less (Fig. 3A, B).

Chronic presentation. Chronic CN is characterised by established deformity. Mid-foot CN, which is the most commonly observed CN, causes the arch to collapse resulting in a rocker-bottom deformity of the foot [46]. There is usually abnormal pressure on the weight bearing sites on the plantar surface [71, 72] with associated callus formation, which predisposes to ulceration.

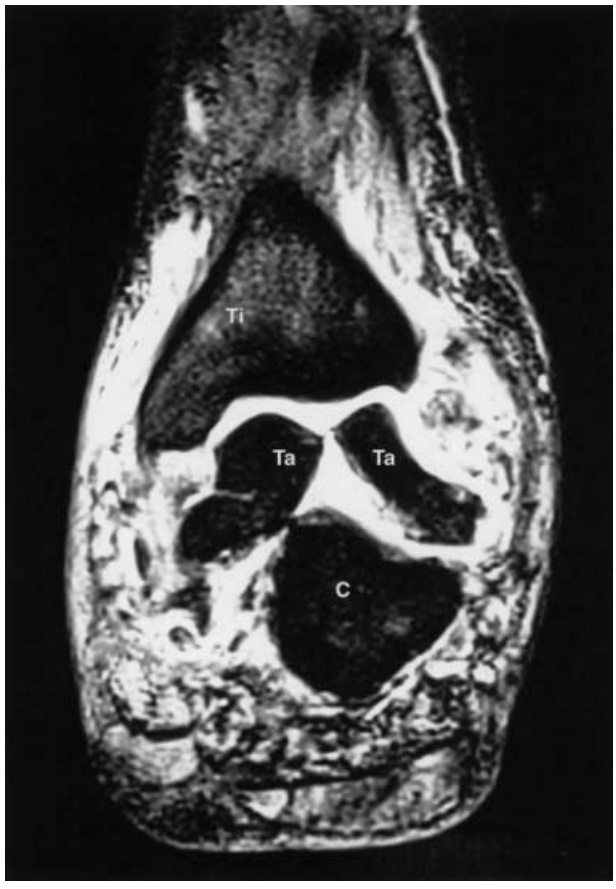

Fig. 4 Coronal gradient echo T2 image showing calcaneus (C) displaced upwards through split talus (Ta). *Ti*, Tibia

Investigations

The diagnosis of CN remains primarily clinical, particularly in the early stages, and the purpose of investigations is to distinguish CN from other conditions that cause pain and swelling of the foot, such as osteomyelitis, inflammatory arthritis, cellulitis, trauma, deep vein thrombosis or gout [4]. In chronic CN with foot ulcers, accurate diagnosis of underlying osteomyelitis can be difficult but is clearly important in the management of patient care.

Plain x-ray. Plain films are cheap and are useful for anatomical information but are neither sensitive nor specific for separating CN changes from infection [73]. The forefoot can show demineralisation, bone destruction and periosteal reaction, typically the triad of uncomplicated osteomyelitis but in the context of diabetes could be atrophic neuropathy and fracture without infection [45, 74]. Severe changes can develop in this form of CN with ‘pencil and cup’ deformity at the MTP joints or fragmentation of the metatarsal heads [75]. In the mid foot, Lisfranc fracture or dislocation develops after initial joint swelling and ligamentous laxity. Eburnation and bony fragmentation occurs at the disorganised TMT joints and there is col-

lapse of the longitudinal arch. All these changes can occur very rapidly with a normal x-ray deteriorating to grossly abnormal within a few weeks (Fig. 3A, B). The five D's summarise the situation: joint distension, dislocation, debris, disorganisation and increased density. In the hind foot, talocalcaneal dislocation with talar collapse can occur with the calcaneus driving up through the talus (Fig. 4). Atypical calcaneal fractures can occur. Distal fibular fractures and instability of the talus within the ankle mortise are less common. With such severe changes associated osteomyelitis can not be distinguished [76].

Radionuclide (isotope) imaging. Radionuclide imaging can be a useful investigative tool in some instances. A number of isotope imaging techniques have been used in CN. The three-phase bone scan using technetium (Tc-MDP) will be positive in all three phases and merely reflects the increased turnover of bone in CN. It is a very sensitive test but non-discriminatory. A four phased boned scan with delayed image acquisition at 24 h, is more specific for detecting woven bone but conditions such as fractures, tumours and severe degenerative changes will give false positive results [76]. Hence in clinical practice the delayed image is rarely useful. Labelled white cell scans (In-WBC) show increased activity at the site of infection and do not usually accumulate where there is new bone formation occurring without infection being present [76]. Therefore, a combination of three phase TcMDP and In-WBC scans, which has a sensitivity and specificity of 80 to 90%, is valuable for diagnosis if there is a penetrating ulcer underneath the deformity [76]. However in the presence of a recent onset, rapidly advancing CN, In-WBC scan can be falsely positive without infection being present. This is due to localisation of labelled WBC at acute fracture sites that are not visible on plain films [77]. This can be differentiated by complementary marrow scanning using Tc-nanocolloid along side In-WBC scans [78]. If both of these scans are congruent; i.e. both positives in the same area, then there is no infection and the appearances are due to CN [76, 77]. This is probably more specific than magnetic resonance imaging (MR) in determining whether there is infection in a CN joint. Some authorities have criticised In-WBC scanning as it shows poor definition, involves handling of blood products and complicated labelling processes, and takes a longer time. Specific Tc-monoclonal antibodies which are easier to label, and bind with antigens on the leucocyte, give comparable results within 2 h and have better resolution and could therefore be preferable [76].

Computerised tomography (CT) and magnetic resonance (MR) imaging. Computerised tomography scanning can detect the presence of sequestra, cortical destruction, periosteal reaction and intraosseous gas, which might not be detected on MR imaging. However, MR is superior for soft tissue imaging and gives exquisite anatomical detail [8, 77, 79, 80, 81] and has largely superceded CT.

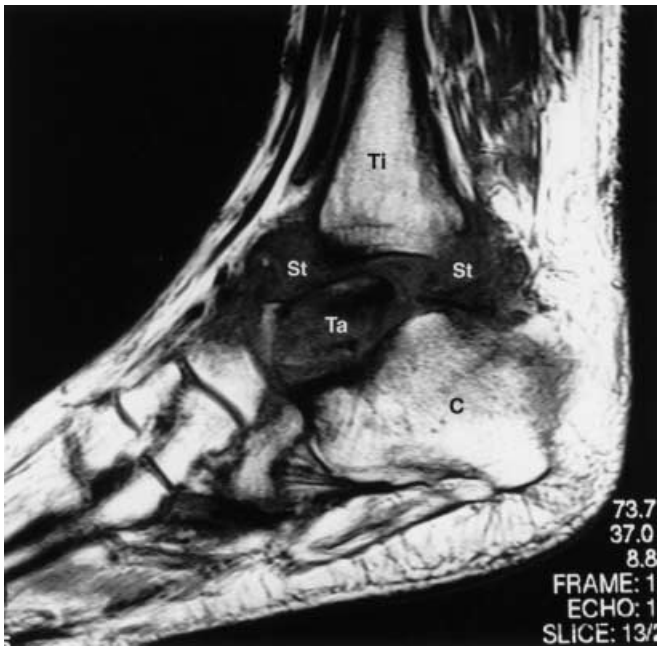

Fig. 5 Sagittal spin echo T1 image showing loss of marrow signal in the destroyed talus (Ta) with patchy low signal in the distal tibia (Ti) and calcaneus (C) signifying oedema in the adjacent bones. There is also low signal in the soft tissues (St) in this region consistent with oedema. The T2 image (not shown) showed high signal in the talar region and in the adjacent bones. This appearance can be found in either acute Charcot neuroarthropathy or osteomyelitis

Magnetic resonance scan of foot is extremely sensitive [82], having a 100% detection of abnormalities and thus the most sensitive modality discussed so far. It also has a specificity rate of 80% for osteomyelitis and has a good negative predictability when there are equivocal radiographs or bone scans [83]. Routine sequences include a T1spin echo, T2 fast spin echo and either a short-tau inversion-recovery (STIR) or T2 fat suppressed sequence, usually in at least two planes [84]. In established CN there is a low TI signal from the joint and a low T2 signal from the marrow. However, if there is rapid onset CN with marked bone turnover and oedema, then the T2 signal could be high, thus mimicking osteomyelitis. Other conditions such as osteonecrosis and recent surgery can also give this picture [73], and the signal could remain high for 3 to 6 months after surgery. Differentiation between CN and infected joint can be difficult, as there is a considerable overlap of signal intensity from the marrow for both infection and oedema (Fig. 5). The greater the signal from the marrow on T2 weighted images, the more likely the bone is to be infected. When the signal equals that of adjacent joint effusion, it is almost certainly infection, providing there are compara-

ble changes on T1 weighted images. This correlation of preoperative MR signal to the resected specimens has been shown [73, 83]. Gadolinium treatment does not add to the differentiation of oedema and infections and is therefore not routinely given [83]. Thus unlike isotope scanning, MR imaging gives better anatomical definition and is therefore useful for preoperative assessment and to monitor the progression of disease.

Other investigations. The differentiation between CN and peripheral neuropathy can also be made by measuring laser doppler blood flow in skin during warming, where an increase flow is observed in CN but not in neuropathy [85]. Occasionally, increased C-reactive protein can be seen in CN [86]. Leucocyte count, erythrocyte sedimentation rate and C-reactive protein concentrations can also be raised if there is an associated infection. Markers of bone turn over including bone alkaline phosphatase, telopeptide have been shown to be increased in CN [9, 10]. There is very little data on synovial fluid in CN but a case report has described the presence of a few white cells with pyrophosphate crystals [86]. Other studies have shown high concentrations of hyaluronan but these are also seen in osteoarthritis [87]. There has also been a report of dense collagenous material without any evidence of inflammation on bone biopsy [41].

Summary of investigations. The diagnosis of CN can be very difficult and the differentiation of infection from rapid onset CN remains a considerable problem in a small proportion of cases. There is no definite confirmatory test but the appropriate use of different isotope scans and MR imaging can help diagnose CN as well as monitor the progression of disease and response to treatment. Combined isotope scanning can provide a more accurate diagnosis in the future [88]. The radiological investigations should be carried out in close liaison with a radiologist who should be fully aware of the limitation of each imaging modality.

Management

There have been various treatment regimens advocated by several authorities [89, 90] with no single regimen emerging as the most effective. This is largely due to the paucity of randomised, double-blind, controlled trials looking into the most efficacious way of treating CN. The fact that CN is not a common condition and the difficulty in accurately measuring the efficacy of therapy has hampered progress in this area. Specific treatments are outlined below but it is important to provide comprehensive foot education for patients and their doctors or caretakers to prevent or limit new problems from occurring, and to ensure that attention is sought promptly [91]. It is also important to recognise that patients with CN have a range of other complications of diabetes mellitus and therefore need to be managed in a holistic manner by a multidisciplinary team.

Acute CN. The aims of treatment are to arrest the acute process to prevent the development of permanent deformity and to relieve pain [92]. Disease activity can be monitored by clinical assessment (skin temperature [93], erythema and swelling), pain scores, isotopic bone scanning and serial radiography. In experimental settings bone markers are useful in monitoring disease activity [9].

Reduction of weight-bearing. Strategies to prevent the affected limb from weight bearing have been the mainstay of the management of acute CN. In 1905, Henderson recognised that a better outcome with regard to joint deformity resulted from the use of crutches and bed rest [94]. In 1931, Steindler demonstrated that conservative treatment with proper alignment, supporting leg braces or casting along with physiotherapy was the treatment of choice [95]. In diabetic patients with ankle joint CN, treatment with a non-weight-bearing protective device produced better limb survival than was seen in those who were allowed to bear their weight [33]. Thus current opinion favours non-weight-bearing but not necessarily total immobilisation as this has its attendant risks. This is often achieved using plaster casting [93]. A recent study reported that, on average, 18 weeks of non-weight bearing is required [32] for the acute phase to subside. Another study found that ambulation in a total-contact cast resulted in a mean healing time of 86 days, with the most rapid healing occurring in forefoot CN rather than CN at other parts in the foot [96]. It is often very difficult for the patients to accept prolonged use of a cast as they can be relatively asymptomatic and thus appropriate explanation of its value could be required.

Many studies have shown the benefit of specialised footwear in acute CN. After immobilisation in a plaster cast, different types of footwear, such as Charcot restrain-orthotic-walker [11, 97, 98] and patellar tendon-bearing braces [99, 100] have been used. Total contact bivalve ankle-foot orthoses have also been used successfully [101]. Recently pneumatic walking braces have been introduced as specialised footwear for the treatment of foot and ankle conditions. They reduce weight bearing to a similar degree as plaster casting [102]. Although there is no published data on its efficacy in the treatment of acute CN, several centres including ours have found this treatment effective and patient friendly. The device allows early mobilisation with relative joint immobility and reduced weight bearing. It is comfortable to use, lightweight and can be removed at night. Clearly, long-term outcome data are required to fully evaluate the role of the pneumatic boot in the management of CN. One poten-

tial hazard of pneumatic compression boots is that they can compromise blood supply to the foot in the presence of occult arterial disease [103] but this is an unlikely scenario in CN.

Bisphosphonates. The bisphosphonate, pamidronate was used in the treatment of six patients with acute CN which decreased the local temperature and pain [104] although there was no follow-up data on the degree of deformity. Another similar study showed decrease in peak cutaneous blood flow in response to warming, suggesting anti-inflammatory action of pamidronate infusion [105]. A case report of a non-diabetic CN patient also reported success in the use of pamidronate [106]. More recently, a 12-month, double-blind, randomised and controlled study of a single, 90 mg pamidronate infusion in 39 patients with active CN has been published [9]. Markers of bone turnover and skin temperature were high at baseline and decreased in both treated and control subjects, although to a greater degree in the treated patients. However, some have suggested that a response could have been seen with higher doses of pamidronate or with a more potent bisphosphonate. We have anecdotal experience of marked symptomatic relief in patients with acute CN treated with two infusions of 90 mg of pamidronate.

Other treatments. Low intensity ultrasound has been tried in CN as an adjunct to conventional treatment and was reported to be useful [107]. Similarly, magnetic fields have been used to stimulate bone growth in the acute phase [108] and electrostimulation has been reported to be helpful in a small group of patients [109]. Non-steroidal anti-inflammatory drugs have been prescribed to control pain [110] but there is no evidence as to their effect on the progression of the disease. There is very limited experience with regard to surgery in the management of acute CN. A recent study has reported an uncontrolled series of 14 patients with acute CN who had arthrodesis at an early stage [111] but as the patients also received casting and prolonged reduction in weight bearing, it was difficult to assess the merits of this approach.

Chronic CN. The goals of treating the chronic phase of CN are to reduce plantar pressures, preserve skin integrity and provide a stable foot. The presence of CN increases the relative risk of foot ulceration 3.5-fold [112] and prevention of foot ulceration is therefore a major objective in chronic CN.

Pedorthotic treatment. Involvement of the pedorthotist who has an understanding of foot biomechanics [113] and orthoses [114] is vital. Most patients require adaptation of footwear to accommodate their deformity in addition to total contact insoles [115]. Stabilisation of the foot and modification of weight-bearing by the use of rocker soles may help to solve the problem of recurrent ulceration. It is very important for shoes to be checked regularly and to account for changes in the shape of the foot as well as shoe wear out.

Surgery. Surgical correction of deformities has been used with variable results in chronic CN. Techniques such as arthrodesis [82, 116], exostectomies [117], reconstruction [118, 119, 120] and Achilles tendon lengthening [121] have been carried out. In one of the largest series, 221 cases of CN were reported, whereby surgical arthrodesis was indicated in two-thirds of the hind foot in CN patients, whereas only one-third of the mid-tarsal joint CN required surgery [123]. Similarly, 29 patients were reported with CN treated with open reduction and arthrodesis of various joints of the foot and ankle [121]. The main indications for surgery were marked instability or a fixed deformity. Joint fusion developed in 19 patients at an average of five months post-operatively while 10 patients developed a pseudoarthrosis [121]. At follow-up, after an average of 42 months, one patient died, one patient had a below-knee amputation and of the remaining 27 patients, only one had recurrent ulceration [121]. There are no long-term data available on other case reports of surgical treatment. Potential risks of surgery include long-term worsening of the condition [124], possible non-union, infection, as well as the general risks of surgery and anaesthesia. In addition, surgery can precipitate acute CN in the contralateral limb. We do not advocate routine surgery in the diabetic foot to correct deformities. However, in appropriate cases a simple procedure, such as excision of abnormally weight-bearing bone [117, 125] can allow the use of appropriate footwear and reduce the chance of further foot ulceration.

Conclusion

Charcot neuroarthropathy is becoming increasingly common in the diabetic foot clinic. Specialists involved in the care of patients with diabetes mellitus should be vigilant and consider acute CN in any patient with the combination of a warm, red joint and underlying neuropathy. The mainstay of diagnosis remains clinical but magnetic resonance imaging and newer forms of isotope bone scanning are proving to be important tools for the early diagnosis of CN. Very early treatment can potentially prevent limb-threatening deformity so prompt investigation and treatment is essential. Reduction in weight-bearing, for example by immobilisation in a plaster cast, has been accepted as a standard treatment but the efficacy of other treatments needs to be established in prospective, controlled studies which will probably need to be multicentred to recruit sufficient subjects. The use of drugs such as the bisphosphonates holds much promise as an

adjunct to traditional treatment. As CN is an uncommon condition, we suggest referring patients to a specialised, multidisciplinary clinic to concentrate expertise and to facilitate further studies. Agreed criteria for the diagnosis of CN would help in allowing comparison of different treatments. Chronic CN with deformity requires specialist assessment and review by a pedorthotist to allow appropriate footwear to be supplied [126]. In some cases, such as in recurrent ulceration due to deformity, surgery can be indicated to correct deformity [127, 128] and allow the use of appropriate footwear. Finally, although progress in our knowledge of the pathogenesis and treatment of CN has been hampered due to paucity of cases, hopefully, the increasing use of computer registers for diabetic patients will identify sufficient numbers to conduct randomised, controlled trials to address this issue.

Sources. We searched Medline for articles published in peer-reviewed journals from 1966 to 2001. We used search terms 'Charcot', 'Charcot's', 'neurogenic', 'diabetic neuropathy', 'arthropathy', 'arthritis', 'neuroarthropathy', 'osteoarthropathy', 'osteoarthritis', 'diabetic feet', 'diabetic foot', 'foot lesion' and 'foot ulcer' both as 'heading search' and 'word search'. The search results were refined using 'AND' as combination tool. In addition we also looked for further relevant references from retrieved articles.

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