A retrospective case study of Charcot osteoarthropathy

Mike Masding, Michelle Spruce, David Coppini

Article points

1. Charcot osteoarthropathy is an important complication because it is associated with significant morbidity and mortality.
2. People with Charcot foot had a longer duration of diabetes than people without the condition.
3. As only a small sub-group of people with established neuropathy go on to develop Charcot foot, other determining factors seem to trigger its onset.
4. A reduced blood flow to the lower extremities may have a protective role against the development of Charcot foot.

Key words

- Charcot osteoarthropathy
- Risk factors
- Diabetic neuropathy
- Glycaemic control

Mike Masding and David Coppini are Consultant Diabetologists, Michelle Spruce is a Research Podiatrist. All are based at Poole Hospital, Dorset.

It is difficult to predict who will develop Charcot osteoarthropathy (Charcot foot), mainly due its poorly understood aetiology. Although Charcot foot is often difficult to diagnose in its early stages, recent studies suggest that early pharmacological treatment to inhibit osteoclast activity may alter the natural history of Charcot foot (Jude et al, 2001; Pitocco et al, 2005; Tan et al, 2005). If those at risk of developing Charcot foot could be identified, treatment could be instigated at the first suspicion of a neuropathic joint developing, thus reducing morbidity and mortality. In this study, the authors investigated the metabolic and clinical characteristics of a small cohort of people with Charcot foot and compared them with people with diabetes both with and without significant sensory neuropathy. The main aim was to identify risk markers for the development of Charcot foot.

Charcot osteoarthropathy (Charcot foot) is defined by painful or relatively painless bone and joint deformity in limbs that have lost sensory innervation (Edmonds, 1999). It is a disabling complication of diabetes with a reported prevalence of approximately 0.2% in people with diabetes (Jeffcoate et al, 2000). It is an important complication because it is associated with significant morbidity and mortality (Rajbhandari et al, 2002). While distal sensory neuropathy seems to be an important and relatively common prerequisite, reasons for the development of Charcot foot in only a small subgroup of the diabetes population are unknown. Postulated mechanisms include an increased pedal blood flow, abnormal bone metabolism and repeated subclinical trauma (Rajbhandari et al, 2002). More recent literature also suggests a role for proinflammatory cytokines in the pathogenesis of Charcot foot (Jeffcoate et al, 2005).

Methods

Ethical approval was obtained from the Local Research Ethics Committee and all individuals gave consent for their data to be used in the study. Data on those who had been identified as having Charcot foot during 2001 (n = 15) were retrieved from Poole Hospital diabetes database.

The definition of Charcot foot for the purpose

of this study was based on an established disorganised foot architecture, following a non-infective acute inflammatory phase (Buttke, 2006). All those recruited to the study had quiescent Charcot foot of variable duration (2–10 years). The clinical diagnosis at the acute inflammatory stage in our clinics is supported by means of dermal infrared thermometry (Dermatemp Infrared Thermographic Sensor, Exergen, US). A ≥3°C temperature elevation at two or more sites (dorsal third metatarsal base, dorsal base third toe, lateral styloid process, dorsal mid-foot, medial navicular, medial and lateral malleolus or subtaler joint) when compared to the opposite foot supports a diagnosis of Charcot foot (Armstrong and Lavery, 1997).

Two comparison groups were assembled. First, people with existing or a history of non-Charcot diabetic foot problems were identified from the dedicated hospital diabetes foot clinic (n = 163). Most attendees of such clinics will have neuro-ischaemic diabetic foot ulcers. Second, people with diabetes without any documented foot complications were recruited via a random selection of individuals who had attended the hospital general diabetes clinic in 2001 (n = 400).

The following parameters on all individuals during 2002 were obtained from the database: age; sex; duration of diabetes; BMI; systolic blood pressure; HbA_{1c} (based on a single measurement in 2002); lipid profile; cardiovascular (CV) risk score (calculated via a computer programme based on the Joint British Societies' Risk table [British Cardiac Society et al, 1998]); and the presence or absence of diabetic retinopathy.

The retrospective search of the database did not allow a distinction between type 1 and type 2 diabetes, but did allow categorisation between those on insulin therapy (n = 309), those on lifestyle intervention alone (n = 13) or those on oral hypoglycaemic agents (n = 256).

The presence of peripheral vascular disease (PVD) was defined by the absence of both dorsalis pedus and anterior tibial foot pulses in either foot. Foot sensation was assessed by measuring vibration perception threshold (VPT) using a neurothesiometer on the plantar surface of the hallux. The average of the right and left VPT measurements were calculated and used for the analysis.

In order to test the hypothesis that changes in HbA_{1c} and VPT may be greater in individuals with Charcot foot than in those without, retrospective longitudinal data were retrieved for every year between 1999 and 2002. Data were only included for those individuals with a complete data set. Data beyond the 4 year scope of the study could have been used in an attempt to recruit more people with Charcot foot, but missing variables limited the search.

Statistical analysis

The data was analysed using SPSS v10.0 (Chicago, Illinois). For the cross-sectional data from 2001, differences between quantitative variables were measured using ANOVA with post-hoc Tukey's tests for differences between groups for normally distributed data (age, diabetes duration, HbA_{1c}, lipids, systolic blood pressure, VPT, CV risk score), while non-parametric data (triglycerides and creatinine) were log-transformed so that ANOVA could be used. The difference in the presence of PVD and diabetic retinopathy between groups was measured using Chi-squared tests.

For the longitudinal data analysis, only data sets with all measurements of HbA_{1c} and VPT between 1999 and 2002 were included. HbA_{1c} and VPT data were analysed using repeated measures ANOVA, with post-hoc Tukey's tests for differences between groups.

Results

Cross-sectional data

Results of the cross-sectional analysis for patient characteristics and risk factors are shown in *Table 1*. Those with Charcot foot had significantly longer mean duration of diabetes and higher mean HbA_{1c} level than people without Charcot foot ($P<0.001$ for all comparisons). In addition, people with foot problems had, as may be expected, higher mean VPT measurements than the diabetic population without foot problems. Although PVD was less prevalent in the Charcot foot group than the group with non-Charcot diabetic foot complications, there was no significant difference in prevalence between the Charcot foot group and people with diabetes without foot complications (13 % versus 6 %, respectively; $P=0.34$). Fewer people recruited from the foot clinic were on insulin therapy when compared to the other two groups: 20% versus 66% and 73%; $P<0.001$. Lipid levels were similar in people with Charcot foot and other foot complications with both being significantly higher than people without diabetic foot complications. Similarly, mean systolic blood pressure was higher in the groups with foot complications than in the one without ($P<0.05$).

Retrospective longitudinal data

Complete sets of HbA_{1c} results were obtained for 13 of the 15 people with Charcot foot, 108 of the 163 with non-Charcot diabetic foot complications and 308 of the 400 who had no foot complications. There were no significant differences in mean HbA_{1c} between groups over the period 1999–2002 (*Figure 1*). Overall, mean HbA_{1c} fell over time ($P=0.004$), with a significant interaction between time and subject group ($P=0.029$), suggesting differences between groups in the rate of reduction in HbA_{1c}. A significant difference in the rate of reduction of HbA_{1c} was only seen between the group with non-Charcot foot complications and the group without foot complications ($P=0.01$).

Complete sets of VPT data were obtained for 12 of the 15 people with

Charcot foot, 71 of the people with non-Charcot foot complications and 291 of the people with diabetes but without foot complications. VPT measurements between 1999 and 2002 are shown in *Figure 2*. In the entire cohort, VPT increased significantly between 1999 and 2002 (P<0.001), with a significant interaction between time and subject group (P=0.005). This suggests differences between groups in the rate of VPT increase. The only statistically significant difference observed between groups in rate of VPT change was between the group with non-Charcot foot complications and the group without foot complications (P=0.006).

Discussion

The results show that people with Charcot foot have a longer duration of diabetes than those without Charcot foot. This is generally observed with the microvascular complications of diabetes (Jarrett and Keen, 1979), suggesting that concomitant microvascular disease may contribute to the development of Charcot foot.

In the original cross-sectional study, Charcot foot and people with non-Charcot diabetic foot problems, unsurprisingly, had higher VPTs than those attending the routine diabetes clinic deemed to be without diabetic foot complications, indicating more severe sensory neuropathy. As only a small sub-group of people with established neuropathy go on to develop Charcot foot, other determining factors seem to trigger its onset.

The diagnosis of neuropathy was based on VPTs alone and people with isolated small fibre neuropathy may have been overlooked. However, VPT is a robust and validated measurement for large-scale screening and monitoring of diabetic neuropathy (Coppini et al, 2001). Age can influence VPT, reducing its reliability for diagnosing neuropathy in older individuals; thus other tests should be used in older people. Young et al (1995) have also previously shown a global impairment of neurological function with autonomic involvement in people with Charcot foot.

This study suggests that other factors such as a normal blood supply to the feet may also have a contributory role in the development of Charcot foot. The prevalence of PVD was significantly higher in the group with non-Charcot foot problems than in the Charcot foot group, although both had elevated VPT, indicating that the development of Charcot foot in people with neuropathy is extremely unlikely to occur in the dysvascular foot. It also seems very unlikely to see Charcot foot in people with a history of PVD in everyday clinical practice. Contrarily, Charcot foot patients may indeed develop PVD at a later stage. This is in keeping with previous reports on the onset of Charcot foot following revascularisation procedures in people with diabetes plus PVD (Shapiro et al, 2005) and with the severe hyperaemia that occurs in the early stages of Charcot foot (Jeffcoate et al, 2000).

A reduced blood flow to the lower extremities may have a protective role against the development of Charcot foot, raising some debate about the indications for revascularisation in the absence of significant ischaemia (such as ulceration or gangrene). These findings add to evidence collected by Shapiro et al (2005) that suggests that the loss of peripheral

Table 1. Patient characteristics in 2002 results stated as mean ± SD unless stated otherwise.

	Charcot foot (n = 15)	Non-Charcot foot complications (n = 163)	No diabetic foot complications (n = 400)	*P*
Age range (years)	54–77	58–84	48–62	<0.001
Male	12 (80 %)	105 (59 %)	229 (57 %)	0.05
Mean BMI (kg/m^2)	29.9 ± 4.1	31.1 ± 19.5	28.3 ± 5.9	<0.001
Mean diabetes duration (years)	26.5 ± 15.0 [a,b]	14.8 ± 11.5	16.1 ± 11.1	<0.001
Number on insulin (%)	11 (73 %)	32 (20 %) [c]	266 (66 %)	<0.001
Mean HbA_{1c} (%)	9.1 ± 1.6 [a,b]	8.1 ± 1.4	8.8 ± 1.4	<0.001
% with proliferative DR	20	16	21	0.27
Mean creatinine (µmol/l)	133 ± 128	118 ± 67 [d]	96 ± 42	<0.001
Mean VPT (V)	31.5 ± 12.6 [e]	31.7 ± 13.3 [e]	14.5 ± 11.3	<0.001
Number with PVD (%)	2 (13 %)	66 (40 %) [f]	23 (6 %)	<0.001

Superscript denotes statistically significant differences between individual patient groups:
a = P<0.05 for the Charcot foot group versus the non-Charcot foot complications group.
b = P<0.05 for Charcot foot group versus people without diabetic foot complications.
c = P<0.001 for the non-Charcot foot complications group versus both Charcot foot group and people without diabetic foot complications.
d = P<0.001 for the non-Charcot foot complications group versus people without diabetic foot complications.
e = P<0.001 for both Charcot foot group the non-Charcot foot complications group versus people without diabetic foot complications.
f = P=0.05 for the non-Charcot foot complications group versus the Charcot foot group and P<0.001 for foot clinic patients versus people without diabetic foot complications.

blood flow and vasomotion often seen in neuropathy may protect against Charcot foot by preventing bone resorption. The diagnosis of PVD was a clinical one, based on palpability of foot pulses. Although peripheral neuropathy tends to reduce their sensitivity and specificity, foot pulses are a recognised useful and sensitive screening tool for vascular status in people with and without diabetes (Williams et al, 2005).

In the cross-sectional part of the study, the Charcot foot group had higher HbA_{1c} levels than the other groups. When assessing the rate of change of HbA_{1c} between 1999 and 2002, the only statistically significant differences were between those with non-Charcot foot complication and those without any foot complications. As seen in *Figure 1*, HbA_{1c} in people with Charcot foot is also notably and persistently higher than in those without the condition.

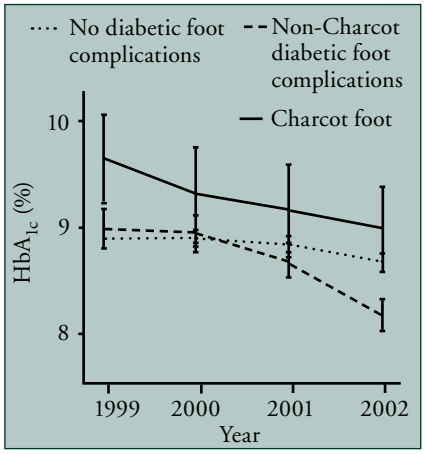

Figure 1. Change in HbA_{1c} between 1999 and 2002.

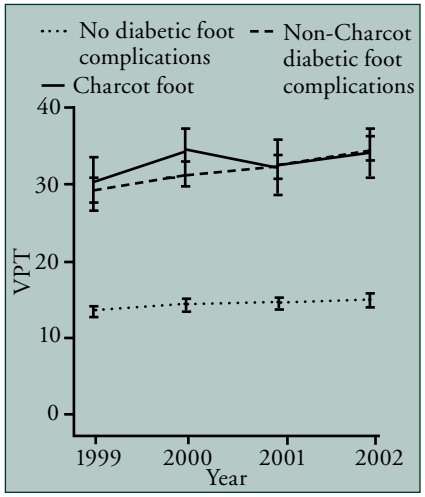

Figure 2. Change in VPT between 1999 and 2002.

Limitations

The lack of statistical significance may be related to the small number of people with Charcot foot in this study and a larger population study would have included more patients with Charcot foot, improving statistical power. However, the prevalence of Charcot foot in our study is comparable to that in other papers (Rajbhandari et al, 2002). This study is dependent on the quality of entered information, which may contain errors. The control groups consisted of people attending the hospital foot and routine diabetes clinics, and most people attending the foot clinic have foot ulceration, usually of neuro-ischaemic origin, although some individuals may have purely ischaemic foot ulcers. Likewise, some of those attending the routine diabetes clinic may have had neuropathy. Hospital clinic attendees tend to have poorer glycaemic control and more complications than those being managed in primary care (Goyder et al, 1998) thus, there may be an underestimation of the difference in metabolic and clinical characteristics between Charcot foot patients and the general population with diabetes. Although a prospective study may be more accurate than the observational longitudinal data used, it would be difficult to obtain large enough numbers to carry this out.

Conclusion

Glycaemic control, peripheral sensory neuropathy and a good blood supply seem to have a role in the pathogenesis of Charcot foot. Further appropriate intervention studies may help address the impact of these clinical and biochemical risk factors on the development of Charcot foot. ■

Acknowledgements

We would like to acknowledge the hard work of Mr Phil Wallace in retrieving the data and Professor Peter Thomas of the Dorset Research and Development Support Unit for his invaluable statistical advice. The cross-sectional data was presented in poster form at the Diabetes UK Annual Professional Conference, 2003.

Armstrong DG, Lavery LA (1997) Monitoring healing of acute Charcot's arthropathy with infrared dermal thermometry. *Journal of Rehabilitation Research and Development* **34**: 317–21

British Cardiac Society, et al (1998) Joint British recommendations on prevention of coronary heart disease in clinical practice. *Heart* **80** Suppl 2: S1–29

Buttke J (2006) Identifying the Charcot foot. *Advances in Skin & Wound Care* **19**: 189–90

Coppini DV, Wellmer A, Weng C et al (2001). The natural history of diabetic peripheral neuropathy determined by a 12 year prospective study using vibration perception thresholds. *Journal of Clinical Neuroscience* **8**: 520–4

Edmonds, ME (1999). Progress in care of the diabetic foot. *Lancet* **354**: 270–2

Goyder EC, McNally PG, Drucquer M et al (1998) Shifting of care for diabetes from secondary to primary care, 1990-5: review of general practices. *BMJ* **316**: 1505–6

Jarrett RJ, Keen H (1979) The WHO multinational study of vascular disease in diabetes: 3. Microvascular disease. *Diabetes Care* **2**: 196–201

Jeffcoate WJ, Lima J, Nobrega L (2000). The Charcot foot. *Diabetic Medicine* **17**: 253–8

Jeffcoate WJ, Game F, Cavanagh PR (2005). The role of proinflammatory cytokines in the cause of neuropathic osteoarthropathy in diabetes. *Lancet* **366:** 2058–61

Jude EB, Selby PL, Burgess L et al (2001) Bisphosphonates in the treatment of Charcot neuroarthropathy: a double-blind randomized controlled trial. *Diabetologia* 44: 2032–7

Pitocco D, Ruotolo V, Caputo S et al (2005). Six-Month Treatment with Alendronate in Acute Charcot Neuroarthropathy: a randomized controlled trial. *Diabetes Care* **28**: 1214–5

Rajbhandari SM, Jenkins RC, Davies C, Tesfaye S (2002) Charcot neuroarthropathy in diabetes mellitus. *Diabetologia* **45**: 1085–96

Shapiro SA, Stansberry KB, Hill MA et al (1998) Normal blood flow response and vasomotion in the diabetic Charcot foot. *Journal of Diabetes and its Complications* **12**: 147–53

Tan AL, Greenstein A, Jarrett SJ, McGonagle D (2005) Acute Neuropathic Joint Disease: a medical emergency? *Diabetes Care* **28**: 2962–4

Williams TD, Harding KG, Price P (2005) An evaluation of the efficacy of methods used in screening for lowe-limb arterial disease in diabetes. *Diabetes Care* **28**: 2206–10

Young MJ, Marshall A, Adams JE (1995) Osteopenia, neurological dysfunction, and the development of Charcot neuroathropathy. *Diabetes Care* **18**: 34–8