Pattern of diabetic neuropathic arthropathy associated with the peripheral bone mineral density

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The relationship between the bone mineral density (BMD) and Charcot arthropathy is unclear. Prospectively, 55 consecutive diabetic patients presenting with a Charcot arthropathy of the foot or ankle were classified as having a fracture, dislocation, or a combination fracture-dislocation pattern of initial destruction. In these groups we used dual-energy x-ray absorptiometry to compare the peripheral bone of the affected and unaffected limbs. The clinical data relating to diabetes and related major comorbidities and the site of the arthropathy (ankle, hindfoot, midfoot, forefoot) were also compared. There were 23 patients with a fracture pattern, 23 with a dislocation pattern, and nine with a combination.

The age-adjusted odds ratio for developing a Charcot joint with a fracture pattern as opposed to a dislocation pattern in patients with osteopenia was 9.5 (95% confidence interval 2.4 to 37.4; p = 0.0014). Groups also differed as to the site of the arthropathy. Fracture patterns predominated at the ankle and forefoot whereas dislocations did so in the midfoot. Diabetic Charcot arthropathy of the foot and ankle differs according to the pattern of the initial destruction. The fracture pattern is associated with peripheral deficiency of BMD. The dislocation pattern is associated with a normal BMD.

Diabetic neuropathic arthropathy is a destructive process of the bony components of a denervated joint. Although it was initially associated with tertiary syphilis, now diabetes is now the main cause of neuroarthropathy in the developed world. Charcot arthropathy has been estimated to affect at least 1 in 680 diabetics and may occur in up to 29% of diabetics with peripheral neuropathy. Its incidence is suspected to be rising with the increasing prevalence of diabetes.

Regional osteopenia is considered to be a classic finding of Charcot arthropathy. A few small studies have shown that patients have reduced bone mineral density (BMD) in their ipsilateral and contralateral peripheral skeleton. Whether peripheral deficiency of BMD is a risk factor for the development of Charcot neuroarthropathy, results from changes, or occurs with changes from a common aetiology is as yet unknown.

Clinically, good results with bracing or early surgery have been reported for Charcot arthropathy in the midfoot, but not in the ankle. The cause for the discrepancy is unknown. Recognising that Charcot arthropathy at the ankle often appeared to result from fracture, whereas neuroarthropathy of the midfoot typically had an associated dislocation, we hypothesised that Charcot changes may be subclassified by the initial pattern of injury, and further that a fracture pattern may be associated with a deficient peripheral BMD.

Patients and Methods

Patients newly diagnosed as having Charcot arthropathy of the foot and ankle and having current pharmacological therapy for diabetes were eligible for enrolment in the study. Charcot arthropathy was defined as a clinically inflamed, erythematous, or swollen foot or ankle with radiological correlation of destruction of the bone and joint, fragmentation or remodelling. Patients newly presenting with already advanced Charcot changes, were not excluded. They were excluded if they had systemic inflammation, fever, an elevated ESR or level of C-reactive protein, or osteomyelitis. Informed consent was given by each patient.

We recorded age, gender, the type and duration of the diabetes, the method of glycaemic control, the duration of Charcot symptoms and the presence of retinopathy, nephropathy, and neuropathy. We defined the neuropathy as loss of light touch sensation or proprioception of the involved foot. Nephropathy included a
documented history of proteinuria (not microalbuminuria), dialysis or renal transplantation. Retinopathy was determined from the patient’s notes and review of ophthalmological records.

**Radiography.** At presentation, weight-bearing (when possible) radiographs were obtained for each patient. Evolving neuroarthropathy was followed by serial radiography. Previous radiographs were also reviewed when available.

The earliest available radiographs were used to group patients by the initial pattern of destruction: fracture, dislocation or combined fracture-dislocation. To be classified as a fracture, bony injury alone should be present (Fig. 1) but the joint should be intact without evidence of subluxation or dislocation. To be classified as a dislocation, separation of the joint surfaces only should be seen without evidence of bony injury (Fig. 2). The presence of small flecks of avulsion fragments was acceptable for inclusion within this group. If dislocation with more substantial associated bony injury was present the patient was placed in the combined fracture-dislocation group (Fig. 3).

The Charcot process was also clarified in relation to four sites: the ankle, including the talar dome; the hindfoot, consisting of the calcaneum, the subtalar, talonavicular, and calcaneocuboid joints; the midfoot, distal to the talonavicular and calcaneocuboid joints and proximal to the proximal metadiaphysis of the metatarsals; and the forefoot which included more distal regions (Fig. 4).

The Eichenholtz classification was also recorded from radiographs at presentation (Table I).18

The inter- and intra-observer reliability of each of these measurements was examined. Two authors (CLS and SAH) first reviewed 20 radiographs and reached a consensus
opinion on each. Next, radiographs from 20 other patients were scored by each independently. One author then repeated the scoring on a separate day. Weighted kappa values were calculated for the inter- and intraobserver reliability of each assessment (Table II). There was substantial reliability for all three.

**Measurement of peripheral BMD.** Dual-energy x-ray absorptiometry (DXA) was performed on all patients. The contralateral femoral neck was scanned unless the patient had bilateral Charcot changes (possibly confounding disuse osteopenia), or the radiologist thought that obesity would hinder the accuracy of DXA at the femoral neck. For these exceptions, the distal radius was scanned. A single machine (Hologic QDR 4500A, Hologic Inc, Bedford, Massachusetts), with interscan variability under 1%, was used for all scans. The BMD (g/cm²), the t-score (SD from site- and gender-matched healthy young adult means, and the z-score (SDs from age-, site-, and gender-matched means) were recorded.

**Statistical analysis.** The three groups were compared regarding the t-scores, age, and the duration of diabetes and of Charcot disease using one-way ANOVA followed by Tukey’s test ($\alpha = 0.05$). Gender, the type of diabetes, the presence of diabetic comorbidities, and the site of neuroarthropathy were compared using Fisher’s exact test. Multiple logistic regression analysis evaluated gender, age, and the osteopenic score as predictors of the neuropathic pattern. To achieve 80% power to detect a relative risk of 8 (with $\alpha = 0.05$) so that WHO criteria for osteopenia would be associated with fracture as opposed to the dislocation...
pattern, 20 patients were needed for each of these two groups.

Secondary analysis to determine if t-score variance was associated with other variables used the Pearson correlation coefficient for continuous variables and the t-test for categorical variables. Further analyses, stratified for the type of diabetes, were performed for all variables with p < 0.2 on the initial secondary analysis, to test for differing trends between the two types of diabetes.

**Results**

Between June 1999 and March 2001, 55 patients with 61 involved feet or ankles (six bilateral) consented to be included in the study. Twenty-three had the fracture pattern, 23 the dislocation pattern, and nine the combined fracture-dislocation pattern. The groups did not differ with regard to gender, the duration of diabetes, the use of insulin, the presence of retinopathy or nephropathy, the duration of Charcot symptoms, or the Eichenholtz stage (Table III). There was a trend towards significance for differences between the fracture and dislocation groups for the type of diabetes, the presence of neuropathy and age.

**Site of Charcot arthropathy.** The site of neuroarthropathy differed significantly between the fracture and dislocation groups. Overall, Charcot changes were found in 12 ankles (19%), 17 hindfeet (28%), 30 midfeet (50%), and two forefeet (3%). All patients with changes in the ankle and forefoot were in the fracture group (Fig. 5). The midfoot primarily contributed to dislocations. The hindfoot was affected in all three groups.

**Peripheral BMD.** The fracture group had significantly lower t-scores than the dislocation group (p = 0.0011; Fig. 6). Sixteen fracture-pattern patients (74%) had t-scores of less than -1.0, the threshold for osteopenia according to the WHO criteria. Twenty-three of these (39% of the entire fracture-pattern group) had t-scores below -2.5, the WHO threshold for osteoporosis. Only four patients with dislocation had t-scores below the threshold for osteopenia.

The age-adjusted odds ratio of a patient with osteopenia according to the WHO criteria having a fracture rather than a dislocation was 9.5 (95% confidence interval (CI) 2.4 to 37.4; p = 0.0014).

The fracture-pattern group also had a significantly lower mean z-score than the dislocation group (p = 0.0009).

**Secondary analysis.** Among all the groups together, the t-score was not significantly related to gender (p = 0.51), the presence of nephropathy (p = 0.27) or neuropathy (p = 0.76), the duration of symptoms of Charcot arthropathy (p = 0.55), or the Eichenholtz stage (p = 0.95). Insignificant trends towards correlation were noted between the t-score and the duration of diabetes (p = 0.08), the use of
The pattern of Charcot arthropathy does not result from the fracture pattern of Charcot arthropathy. Osteoporosis was found only in patients with osteoporosis because they grouped all three patterns of Charcot arthropathy. A number of known risk factors for osteopenia were highlighted, including type-I diabetes, microangiopathy, hypothyroidism, abuse of alcohol, anorexia nervosa, and end-stage renal disease. Osteopenia from these and other causes, as measured by peripheral DXA, is a predictor of the risk for fracture, which is measurable after fracture has occurred. The evidence for this association is strongest in women. These data suggest that it also predicts the Charcot pattern in patients who will eventually develop neuroarthropathy. This is important because, as distinct from a possible but yet unproven regional osteopenia from neuroarthropathy, our study identifies a possibly modifiable systemic risk factor for developing the fracture pattern and general arthropathy around the ankle.

In conclusion, an identifiable subgroup of diabetic patients with Charcot arthropathy have an initial fracture pattern of destruction. They most commonly present with difficulties at the ankle and have marked peripheral BMD deficiency, which may adversely affect treatment. Further study to determine the treatment of osteopenia as a risk factor for this pattern of Charcot arthropathy in diabetes may advance preventative measures for these often devastating problems.

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References