Midfoot and Hindfoot Bone Marrow Edema Identified By Magnetic Resonance Imaging in Feet of Subjects With Diabetes and Neuropathic Ulceration Is Common but of Unknown Clinical Significance

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OBJECTIVE — We conducted a retrospective cohort study assessing the prevalence and clinical and radiological outcome of remote areas of bone marrow edema on magnetic resonance imaging (MRI) in the feet of subjects with diabetes and neuropathic foot ulceration.

RESEARCH DESIGN AND METHODS — MRIs performed over 6 years looking for osteomyelitis associated with neuropathic lesions were assessed for remote areas of signal change.

RESULTS — Seventy MRI studies were assessed. Remote areas of signal change were present in 21 (30%) subjects, involved midfoot or hindfoot in 20 subjects, were associated with younger age and renal replacement therapy, and did not predict future Charcot neuroarthropathy or infection at that site. Repeat MRIs in 11 subjects with such areas found that none had progressed, six had improved, and two had resolved; in 29 subjects without such areas, five had developed new areas.

CONCLUSIONS — Bone marrow edema in the midfoot and hindfoot of subjects with diabetes and neuropathic lesions is common, often transient, and of unknown significance.

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We have previously described the value of magnetic resonance imaging (MRI) to assess for osteomyelitis in association with neuropathic foot lesions in subjects with diabetes whereby the MRI criteria for diagnosis require bone signal change to be in direct contiguity with signal change in the soft tissue adjacent to the area of ulceration (1). We have often incidentally observed hyperintensity on T2-weighted images, consistent with bone marrow edema, remote from the area of neuropathic ulceration (Fig. 1) that often involves the midfoot and hindfoot and is usually not associated with adjacent clinical or radiological signs of infection, clinical signs suggesting acute Charcot neuroarthropathy, or pain. We performed a retrospective cohort study to assess the prevalence of such remote areas of signal change and their subsequent clinical and radiological outcome.

RESEARCH DESIGN AND METHODS

— MRIs performed between February 2003 and January 2009 to look for osteomyelitis associated with neuropathic foot lesions in subjects with diabetes where Charcot neuroarthropathy had not been suspected clinically were assessed by two independent radiologists (a third adjudicated where necessary) for the presence or absence of remote areas of signal change and osteomyelitis. MRI acquisition was described previously (1). Medical records were assessed for the subsequent development of both Charcot neuroarthropathy and clinical infection associated with the remote area of signal change. Repeat MRIs performed in a subgroup (often to follow the response of osteomyelitis to conservative management) were also assessed.

Continuous variables with normal and skewed distributions are expressed as means (SDs) and medians (interquartile ranges), respectively. The unpaired *t* test or Fisher exact test was used to compare the continuous and categorical variables, respectively, between two groups. Cohen's kappa coefficient was used to assess inter-observer correlation. Analyses were performed using the SigmaStat package (Systat, San Jose, CA). Our Caldicott Guardian established that approval of the local research ethics committee was not required for analysis of the outcome of routine clinical management and the publication of anonymous data derived from it.

RESULTS

— Seventy MRI studies in 66 subjects were assessed; both feet had been studied in 4 subjects. There were 66 forefoot and 4 hindfoot lesions. Age was 64 (13) years; duration of diabetes 21 (14) years; A1C 8.6 (2.1) percent; 8 (12%) had type 1 diabetes; and 13 (20%) were on renal replacement therapy (hemodialysis or renal transplantation).

Remote areas of signal change in bone were present in 21 studies (30%). The neuropathic lesion involved the forefoot in 20 studies, and the remote areas of signal change involved the forefoot in 1 study, the midfoot in 14, the hindfoot in 3, the midfoot and hindfoot in 1, and the ankle and midfoot in 1; in 1 study, the neuropathic lesion and the remote area both involved the hindfoot.

Osteomyelitis underlying the neuro-

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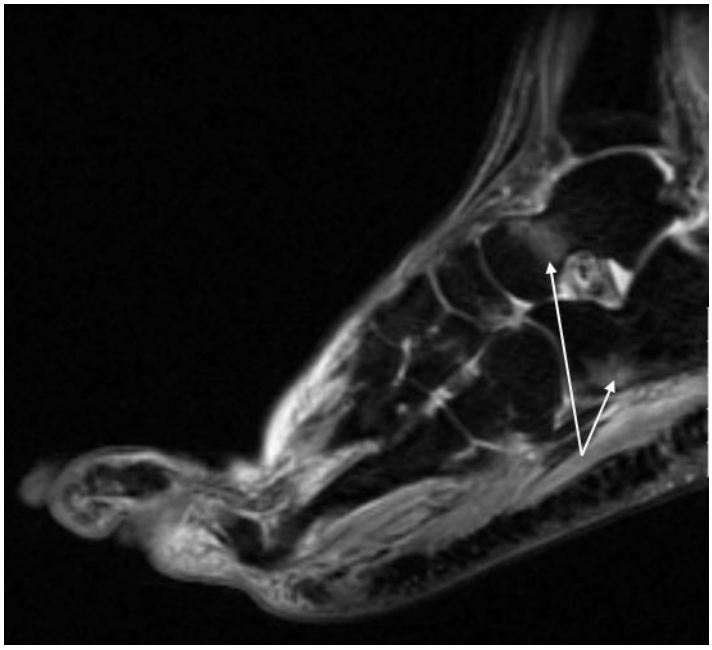

Figure 1—*Sagittal T2 fat-saturated magnetic resonance image shows remote areas of signal change in the talus and calcaneum (arrows).*

pathic lesion was present in 48 (69%) studies, reflecting the high pretest probability. Fifty-four of the 70 neuropathic lesions (77%) healed with conservative management alone. Inter-observer correlation for the detection of both remote areas of signal change ($\kappa = 0.7$) and osteomyelitis ($\kappa = 0.7$) was high (2).

Subjects with remote areas of signal change were younger (56 [13] vs. 67 [12] years; $P < 0.001$) and more likely to require renal replacement therapy (43 vs. 9%; $P = 0.002$) but were not more likely to have type 1 diabetes (24 vs. 7%; $P = 0.098$). Duration of diabetes, A1C, sex distribution, and prevalence of concurrent osteomyelitis were not different.

Duration of observation following the index MRI was 13 (7–19) months (range 3–62). Of the 21 feet with remote areas of signal change, none developed Charcot neuroarthropathy clinically and none developed clinical infection associated with that area. Charcot neuroarthropathy developed in one foot 19 months following the index MRI, which had demonstrated neither remote areas of signal change nor osteomyelitis.

Repeat MRIs were assessed in 11 of the 21 feet (52%) with remote areas of signal change and in 29 of the 49 feet (59%) without remote areas of signal change on the index MRI. The interval between index and repeat MRI was 6 (4–14) months for those with remote areas of signal change and 3 (3–5) months for those without. For those with remote areas of signal change, the areas had resolved in two subjects, improved in six, and had not changed in three; in none had they worsened. For those without areas of signal change, they were absent as before in 24, but had developed in 5: involving the midfoot in 1, the hindfoot in 3, and the midfoot and hindfoot areas in 1.

CONCLUSIONS — We report for the first time that remote areas of signal change on MRI consistent with bone marrow edema in the feet of subjects with diabetes and neuropathic lesions are common, with a prevalence of 30%, and tend to involve midfoot and hindfoot areas. Their clinical significance is unclear. They are not due to red marrow replacement, as the hyperintensity on T2-weighted imaging was not associated with the reduction in signal on T1-weighted imaging (3,4). They were in the substance of bone so could be consistent with Charcot neuroarthropathy; like others (4,5), we have found MRI changes with Charcot to be widespread and not limited to subchondral areas. Although they did not predict future clinical Charcot, all subjects had had offloading of the neuropathic lesions with appropriate orthoses as part of routine management, which may have interrupted the progression to Charcot. Furthermore Charcot is rare, so that the failure to predict future clinical Charcot may represent a type II error.

While it is unlikely that the areas represented infective foci, many subjects received antibiotics. However, almost all cases of diabetic foot osteomyelitis result from the contiguous spread of infection from adjacent tissue (6).

Other causes of bone marrow edema identified by MRI and collectively referred to as bone marrow edema syndrome (7) are associated with pain and include transient osteoporosis of the hip, regional migratory osteoporosis, and reflex sympathetic dystrophy. Pain was not a feature in the current study, although subjects were neuropathic.

Analysis of repeat MRI studies suggests a situation whereby remote areas of signal change improve or resolve in many affected individuals, but subsequently develop in some previously unaffected individuals.

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