Original Article: Complications

Conservative management of diabetic forefoot ulceration complicated by underlying osteomyelitis: the benefits of magnetic resonance imaging

J. Valabhji, N. Oliver, D. Samarasinghe*, T. Mali⁺, R. G. J. Gibbs⁺ and W. M. W. Gedroyc§

Departments of Diabetes and Endocrinology, *Microbiology, †Podiatry, ‡Vascular Surgery and §Radiology, St Mary's Hospital, Imperial College Healthcare NHS Trust, London, UK

Accepted 1 August 2009

Abstract

Aims To assess efficacy of conservative management of neuropathic forefoot ulcers with underlying osteomyelitis in subjects with diabetes when magnetic resonance imaging (MRI) is used to confirm or establish diagnosis and to guide antibiotic duration.

Methods A retrospective cohort study over 6 years assessing rates of ulcer healing, relapse and amputation. Antibiotics were continued for 3-month cycles with interval MRI: if the lesion had healed and bone signal change resolved or improved, antibiotics were discontinued; if the lesion had not healed or there was no difference in bone signal change, antibiotics were continued for a further 3-month cycle; clinical or radiological deterioration resulted in endoluminal or open vascular surgical intervention where appropriate, or digital or more proximal amputation.

Results There were 53 episodes in 47 subjects (mean \pm sD age 62 \pm 13 years, duration of diabetes 19 \pm 13 years, glycated haemoglobin 8.4 \pm 1.6%; six with Type 1 diabetes and seven with end-stage renal failure). Successful healing without relapse was achieved in 40 episodes (75%) [median (range) duration of antibiotics 6 (3–12) months and follow-up post-cessation of antibiotics 15 (3–58) months]. Relapse occurred in six episodes (13%) at 31 (2–38) months post-cessation of antibiotics. There were one major (2%) and eight minor (15%) amputations. Five subjects have died (11%), all without foot ulcers.

Conclusions High rates of healing and low rates of amputation were achieved. The use of MRI was associated with long courses of antibiotics, but particularly low relapse rate.

Diabet. Med. 26, 1127-1134 (2009)

Keywords diabetic foot, magnetic resonance imaging, osteomyelitis

Abbreviations HIV, human immunodeficiency virus; MRI, magnetic resonance imaging; MRSA, methicillin-resistant staphylococcus aureus; PVD, peripheral vascular disease

Introduction

The annual incidence of foot ulceration in people with diabetes in a UK population is 2.2% [1]. Approximately 20% of diabetic foot ulcers are complicated by underlying osteomyelitis [2,3] and, in patients with diabetes with foot ulceration and histologically confirmed bone involvement, the forefoot (metatarsal head and distally) was the involved site in 90% of cases [4]. Therefore, around 8000 people with diabetes will suffer forefoot ulceration complicated by underlying osteomyelitis each year in the UK. Many of these will undergo at least minor amputation, with the associated risks of failure to heal and prolonged inpatient stays. Furthermore, digital or ray amputation often results in abnormal weight distribution across other parts of the foot, leading to secondary lesions, or transfer ulcers, in up to 40% of cases [5].

There have now been several series of cases treated conservatively with prolonged courses of antibiotics, without surgical resection of infected bone, reporting rates of healing and eradication of underlying osteomyelitis of between 29 and 82% [6–15]. However, others still argue for surgical intervention [4,16]. There are also concerns regarding the potential for relapse with non-surgical management, with relapse rates of up to 32% [14,15]. The diagnosis of underlying osteomyelitis in this situation is difficult and there is no consensus definition [17]. A role for magnetic resonance imaging (MRI) as a primary imaging

Correspondence to: Dr Jonathan Valabhji, Department of Diabetes and Endocrinology, St Mary's Hospital, Imperial College Healthcare NHS Trust, London W2 1NY, UK. E-mail: jonathan.valabhji@imperial.nhs.uk

modality to confirm or establish osteomyelitis and the role of serial MRI in guiding subsequent management has not been described previously. MRI offers excellent spatial resolution of both the bone and the associated soft tissue involved. Sensitivities of MRI approach 100%, although specificities are lower at 80-90%. The lower specificity in diabetes is usually attributable to diagnostic confusion with Charcot neuroarthropathy. Recent meta-analyses have demonstrated the performance of MRI to be very good and consistently better than plain X-ray, bone scanning and white blood cell labelled studies [18-20]. However, in all three meta-analyses (which included largely the same studies), individual studies had often not considered Charcot neuroarthropathy in the differential diagnosis, so that true specificities for MRI could be lower. Furthermore, comparisons between performance characteristics of MRI and plain X-ray were based only on plain X-ray at presentation, rather than sequential plain X-rays, where performance for the diagnosis of osteomyelitis is better.

We report a retrospective cohort study that assesses efficacy over a 6-year period of a clinical algorithm for the conservative management of forefoot osteomyelitis in which diagnosis is confirmed or established in all cases by MRI, in diabetic subjects presenting with neuropathic forefoot ulcers. Sequential MRI is then used to dictate duration of antibiotics. On treatment, improvement in the MRI bone signal change consistent with osteomyelitis is slow. Whether this is a true reflection of the time taken to achieve complete eradication of infection in bone, or whether the improvement in signal change lags behind clinical resolution of the osteomyelitis, is not known. However, because of the slow rate of change in MRI bone signal abnormality, we performed sequential MRI at 3-monthly intervals, necessitating the continuation of antibiotics for a minimum 3-month period. We have found that remote bone signal change on MRI not associated with the neuropathic lesion, and so not attributed to osteomyelitis, is common in the mid- and hindfoot areas [21] and its clinical significance is not known, so that specificity of MRI in the diagnosis of mid- and hindfoot osteomyelitis may be poorer. Furthermore, over the 6-year period, 90% of neuropathic lesions associated with osteomyelitis involved the forefoot, 5% the midfoot and 5% hindfoot, so that the numbers of mid- and hindfoot episodes were very small. While the same clinical algorithm is used for fore-, mid- and hindfoot lesions in our multidisciplinary clinic, the focus of the current report is therefore forefoot neuropathic lesions complicated by underlying osteomyelitis. All subjects were managed by a multidisciplinary team within the outpatient clinic setting, including podiatrists, a diabetologist, an orthotist, a vascular surgeon, a microbiologist and a radiologist with a special interest in MRI.

Subjects and methods

Subjects

Subjects with diabetes presenting with neuropathic forefoot ulceration underwent MRI of the affected foot if underlying

osteomyelitis was suspected clinically (lesion present for more than 3 weeks, positive probe-to-bone test [2,3,22], characteristic 'sausage toe' appearance [23] or characteristic changes of osteomyelitis on plain X-ray). Subjects with a permanent pacemaker and subjects whose weight exceeded the limit for the MRI scanner (*ca.* 150 kg) could not undergo MRI. Subjects managed between January 2003 and December 2008 were included in this retrospective cohort study. All subjects with neuropathic foot ulceration and MRI-confirmed underlying osteomyelitis were managed according to a predefined treatment algorithm.

Magnetic resonance imaging

MRI was performed on a GE scanner (GE Medical Systems, Milwaukee, WI, USA) using a quad knee/ankle coil prior to June 2008. Scans performed from June 2008 were performed using a dedicated HD foot coil. The foot was immobilized with pads. Imaging included sagittal T2 fat-saturated images (FSE TR/TE:4600/68; ET:16; FOW:26; matrix 320 × 192, slice thickness 4 mm), coronal T2 fat-saturated images (FSE TR/TE:7600/68; ET:16; FOW:15; matrix 256 × 224, slice thickness 5 mm) and coronal T1 weighted images (FSE TR/TE:700/min full; ET:2; FOW:15; matrix 256 × 193, slice thickness 5 mm). If the fat saturation was not uniform on the T2 fat-saturated images, the IDEAL sequence was used (FSE TR/TE:3400/102; ET:12; FOW:26; matrix 320 × 224, slice thickness 4 mm) (GE Medical Systems, Milwaukee, WI, USA). The criteria for diagnosing osteomyelitis were hypointense signal within the bone on T1 weighted images and hyperintense signal within the bone on T2 weighted images, in direct continuity with abnormal high signal in the surrounding soft tissues which led to the abnormal skin and subdermal area associated with the ulcer (Fig. 1). Almost all cases of diabetic foot osteomyelitis result from contiguous spread of infection from adjacent soft tissue; unlike childhood osteomyelitis, haematogenous seeding is extremely rare in this situation [17]. Remote areas of focal hyperintensity in the bone not associated with the soft tissue abnormality were common, particularly in the mid- and hindfoot areas, are of unknown clinical significance and were not therefore diagnosed as osteomyelitis.

Subsequent MRI scans were compared directly with the baseline images by a single radiologist (WMWG) and were categorized as demonstrating resolution, improvement, no change or deterioration in the bone signal change associated with the site of neuropathic ulceration.

Treatment algorithm

When subjects presented with an infected neuropathic forefoot lesion, a deep wound swab was taken following cleaning of the lesion with saline and podiatric debridement of callous, slough and necrotic tissue. Empirical antibiotic therapy was then instituted. As *Staphylococcus aureus* and β haemolytic *streptococci* are the most common organisms involved in the

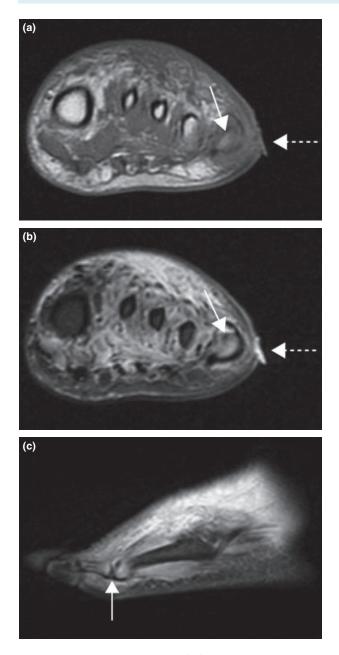


FIGURE 1 Magnetic resonance images of a foot with a neuropathic lesion at the lateral aspect of the fifth metatarsal head area: (a) coronal T1 weighted image demonstrating the ulcer (dashed arrow) and low signal intensity in the marrow of the fifth metatarsal (solid arrow) consistent with bone marrow oedema and osteomyelitis; (b) coronal T2 fat saturated image demonstrating the ulcer (dashed arrow) and hyperintensity in the underlying soft tissue extending down to the fifth metatarsal which is also returning hyperintense signal (solid arrow) consistent with bone marrow oedema and osteomyelitis; (c) sagittal T2 fat saturated image showing hyperintensity in the fifth metatarsal head and fifth proximal phalanx (solid arrow).

pathogenesis of osteomyelitis, empirical antibiotics were chosen which were active against these organisms and had good oral bioavailability and good bone penetration. Co-amoxiclav was the first-line treatment [preferred to flucloxacillin for covering methicillin-sensitive staphylococcus aureus because of its better oral bioavailability]; the combination of clindamycin and ciprofloxacin was used in those with a history of penicillin allergy; the combination of rifampicin and doxycycline was used in those in whom methicillin-resistant staphylococcus aureus (MRSA) has previously been identified, assuming the previously identified MRSA was sensitive to both agents. Antibiotic regimens were subsequently modified only if organisms were isolated which were thought to be significant and which were not treated by the initial regimen. Subjects were only admitted for inpatient intravenous antibiotic therapy if there were systemic signs of infection or if soft tissue infection or cellulitis was considered sufficiently severe to warrant it. However, for a proportion of episodes, first contact with the multidisciplinary foot team followed admission under another team where initial contact with the multidisciplinary team may have facilitated exclusive outpatient management; this was a more common occurrence in the early years of the study period.

Inflammatory markers and white blood cell count were not measured routinely to guide clinical management, unless there were concerns about systemic infection. Plain X-rays were performed on first presentation, but not sequentially. Reliable data on ulcer size at presentation were not available for the whole cohort. The neuropathic lesions at presentation were not associated with areas of gangrene, so that all were Wagner [24] grade 3. Bone biopsy was not performed.

All subjects had optimum offloading of the neuropathic lesion using a variety of devices and regular outpatient podiatric debridement of callous, slough and necrotic tissue. All subjects were screened for the presence of peripheral vascular disease (PVD). Those with one or more foot pulse not palpable underwent duplex scanning to define potential target lesions for vascular surgical intervention. Only those whose neuropathic lesions were failing to improve or were deteriorating proceeded to digital subtraction angiography and vascular surgical intervention if such intervention was possible.

MRI was repeated at 3 months and antibiotics continued in the interim. If the neuropathic forefoot lesion had healed at 3 months and the repeat MRI demonstrated resolution or improvement in underlying bone signal change, then the antibiotics were discontinued. If healing had not yet been achieved or if there was no change in the associated bone signal change on MRI, then antibiotics were continued for a further 3-month cycle with repeat MRI. If the lesion was clearly deteriorating clinically or radiologically, despite vascular surgical intervention if such intervention had been possible, then digital or more proximal amputation was undertaken.

Success rate was the proportion of episodes resulting in a healed lesion, with resolution or significant improvement in underlying bone signal change on MRI, and non-recurrence of a lesion at the same or a contiguous site at least 3 months after discontinuation of antibiotics. Failure rate was the proportion of episodes deteriorating on treatment to require digital or more proximal amputation, plus episodes of recurrence of a lesion following healing at the same or a contiguous site, regardless of the time elapsed following discontinuation of antibiotics. Relapse rate was the proportion of those episodes that initially achieved healing in which there was recurrence of a lesion at least 3 months following discontinuation of antibiotics at the same or a contiguous site.

Statistical analysis

Continuous variables with normal distributions are expressed as means with standard deviations; continuous variables with skewed distributions are expressed as medians with interquartile ranges. To compare a continuous variable between two groups, the unpaired *t*-test or the Mann–Whitney *U*-test was used for variables with normal and skewed distributions respectively. To compare categorical variables between two groups, Fisher's exact test was performed. Binary categorical variables are expressed as number of subjects with the percentage in each category. The SIGMASTAT package was used for the analyses (Systat, San Jose, CA, USA).

The Caldicott Guardian gave approval for analysis of the outcome of routine clinical management within the setting of the multidisciplinary diabetic foot clinic and for the publication of anonymized data derived from it.

Results

There were 53 episodes in 47 subjects of neuropathic forefoot ulceration with underlying MRI-confirmed osteomyelitis. A second episode in the same individual was at an anatomically distant site. Six of the 47 subjects had Type 1 diabetes (13%). Although Type 1 diabetic subjects were younger $(49 \pm 9 \text{ vs.})$ 65 ± 12 years; *P* = 0.0026), the age distribution for the whole cohort was not obviously bimodal and mean age was 62 ± 13 years and mean duration of diabetes 19 ± 13 years. Meanglycated haemoglobin (HbA_{1c}) was 8.4 \pm 1.6%. Thirty-six subjects were male (77%), 33 were of European (70%) origin, five of African-Caribbean (11%) origin, seven of South Asian (15%) origin and two of Middle Eastern (4%) origin. All had peripheral neuropathy and 37 of the 40 subjects in whom retinopathy status could be ascertained had concurrent retinopathy (93%). Seven subjects (15%) required renal replacement therapy and 25 (53%) had chronic kidney disease stages 3, 4 or 5, equivalent to a glomerular filtration rate < 60 ml/min. Twenty-nine subjects (62%) had PVD, as determined by the absence of one or more foot pulse. Five subjects (11%) had Charcot neuroarthropathy, although the Charcot process had involved midfoot, hindfoot or ankle in these subjects, rather than forefoot.

The commonest sites of osteomyelitic involvement were the phalanges of the great toe (16 episodes), the 5th metatarsal head (13 episodes) and the phalanges of the second toe (10 episodes). Frequency of other sites involved were as follows: phalanges of the third, fourth and fifth toes in four, five and three episodes, respectively; metatarsal heads of the first, second, third and fourth digits in zero, three, four and four episodes, respectively.

The commonest organism identified on deep wound swab was Staphylococcus aureus. Staphylococcus aureus was identified in 32 episodes (60%), six of which (15%) were methicillinresistant. Beta-haemolytic *streptococcus* was identified in nine episodes (17%), seven of which were Lancefield Group B and two Lancefield Group G. Enterobacteriaceae were identified in four episodes (8%), anaerobes in three episodes (6%), *Pseudomonas* in two episodes (4%), *Staphylococcus epidermidis* in one episode (2%), *Proteus* in one episode (2%) and *Enterococcus* in one episode (2%). In nine episodes (17%), two organisms were identified and, in two episodes (4%), three organisms were identified. In 13 of the 53 episodes (25%), no organisms were identified on deep wound swab.

Co-amoxiclav was the only antibiotic used in 28 of the 53 episodes (53%), the combination of clindamycin and ciprofloxacin was used in five episodes (9%) and the combination of rifampicin and doxycyline was used in five episodes (9%). Gastrointestinal side effects (nausea, vomiting or diarrhoea) led to modification of the initial antibiotic regimen in 11 episodes in eight subjects. Other antibiotics used in these eight subjects were fucidic acid, flucloxacillin and trimethoprim. One subject with MRSA took antiretroviral therapy to treat human immunodeficiency virus (HIV), so that rifampicin was contraindicated and doxycycline was combined with fucidic acid instead. A further three episodes in three subjects were treated with outpatient intravenous vancomycin and meropenem administered three times weekly at haemodialysis, as this was preferred by the subjects and their renal physician. There were no cases of Clostridium difficile-associated diarrhoea.

Over the first 3 years of the study period, 16 of the 19 episodes treated (84%) involved initial inpatient care (median length of stay 16 days), although many were admitted by other teams prior to first contact with the multidisciplinary team. Over the second 3 years of the study period, 16 of the 34 episodes treated (47%) involved initial inpatient care (median length of stay 11 days).

Outcomes are demonstrated in Fig. 2. Healing without subsequent relapse was achieved in 40 episodes, so that the rate of success of our conservative treatment algorithm was 75%. For the 40 successfully treated episodes, duration of antibiotic treatment was 3 months in 15 episodes (38%), 6 months in 20 episodes (50%), 9 months in four episodes (10%) and 12 months in one episode (3%). Median duration of follow-up post-cessation of antibiotics was 15 (7–25) months, with a range of 3–58 months.

Of the 13 episodes in which treatment failed (failure rate 25%), seven episodes (13%) resulted in deterioration on treatment, despite vascular surgical intervention in two, to require amputation: one digital, three ray, two transmetatarsal and one below knee. In six of the 46 episodes in which healing was initially achieved, relapse occurred at 2, 17, 24, 31, 33 and 39 months post-cessation of antibiotics, giving a relapse rate in those initially achieving healing of 13%. The relapses at 2 and 17 months resulted in ray and transmetatarsal amputations, respectively. The other four relapses, in which a different organism was identified at relapse compared with initial

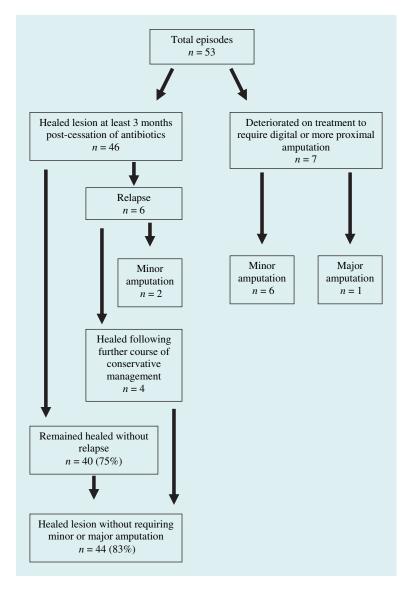


FIGURE 2 Flow diagram illustrating outcome in 53 episodes of diabetic forefoot ulceration complicated by underling ostoemyelitis managed conservatively, with magnetic resonance imaging used both to confirm or establish diagnosis and to guide duration of antibiotic therapy.

presentation in three, underwent a further period of conservative management and remain healed currently. Therefore, some form of amputation was required in only nine of the 53 episodes treated (17%). Eight were minor amputations (15%) and one major (2%).

Table 1 explores potential predictors of success using our conservative treatment algorithm. Neither age, duration of diabetes, level of glycaemic control, renal function, gender, ethnicity, Type 1 diabetes status, identification of MRSA nor the presence of PVD were significant predictors of outcome. All eight episodes that occurred in patients with end-stage renal failure were treated successfully with the current treatment algorithm. Six of these episodes were in five subjects on haemodialysis and two episodes were in two subjects with previous end-stage renal failure but who had subsequently undergone renal transplantation and were on immunosuppressive therapy at the time of treatment for the foot lesion. The episode in the subject with HIV was also successfully treated.

Three of the 47 subjects were lost to follow-up at 10, 17 and 37 months post-cessation of antibiotics, all without foot ulceration at last review. Of the other 44 subjects, five have died (11%), giving a mortality rate of 6.2 deaths per hundred patient years. All five had achieved a successful outcome with the treatment algorithm and died without foot ulcers at 7, 14, 21, 22 and 34 months post-cessation of antibiotics.

Although not the focus of the current report, over the same period of time there were only three episodes of midfoot and three episodes of hindfoot neuropathic ulceration in which MRI was suggestive of underlying osteomyelitis seen in the multidisciplinary clinic. Following the same clinical algorithm, healing without subsequent relapse was achieved in two of the three midfoot episodes and in one of the three hindfoot episodes.

	Success	Failure	P-value
Number	40	13	
Age (years)	62 ± 14	63 ± 11	0.81
HbA _{1c} (%)	8.3 ± 1.8	8.2 ± 1.2	0.85
Creatinine (µmol/l)	119 ± 58	139 ± 80	0.33
End-stage renal failure	8 (20%)	0 (0%)	0.18
Sex (number male)	31 (78%)	11 (85%)	0.71
European	25 (63%)	11 (85%)	0.18
Type 1 diabetes	5 (13%)	2 (15%)	1.00
MRSA	6 (15%)	2 (15%)	1.00
Peripheral vascular disease	21 (53%)	8 (62%)	0.75

Parameters are expressed as means \pm standard deviations or as numbers (percentages) as appropriate. HbA_{1c}, glycated haemoglobin; MRSA, methicillin-resistant staphylococcus aureus.

Discussion

We describe a conservative treatment algorithm for the management of diabetic forefoot neuropathic ulceration complicated by underlying osteomyelitis based on MRI as the primary imaging modality. The algorithm achieved healing and resolution without subsequent relapse in 75% of episodes and avoided any form of amputation in 83% of episodes. The rates of major, minor and total amputations of 2, 15 and 17%, respectively, compare favourably with rates reported in other series describing conservative management of osteomyelitis (0-29, 5-38 and 7-47%, respectively) [6,8-10,12-15]. A concern of non-surgical approaches in this situation has been the potential for subsequent relapse. The relapse rate using MRI to guide the duration of antibiotic treatment is 13% according to our definition of relapse, but it is possible that three of the relapses in the current study were second episodes at the same site, in that a different organism was identified, so the true relapse rate with the current treatment algorithm could be as low as 7%. We have follow-up data up to 5 years post-cessation of antibiotics in the current study.

We assessed consecutive patients attending the multidisciplinary foot clinic over a 6-year period. It is possible that additional subjects who had never attended the clinic attended Accident and Emergency where a clinician judged early surgery to be necessary, so that minor or major amputation may have taken place without involvement of the multidisciplinary team. Furthermore, there will always be some cases in which conservative management is inappropriate and early surgery is judged inevitable and potentially life-saving. Such cases were not necessarily captured in the current study. The series reported by Game and Jeffcoate [15] had the advantage of including such subjects who constituted 23% of the entire series; the other subjects were treated non-surgically initially, of whom 82.3% had achieved remission at 12 months without surgery. While this is very similar to those achieving remission without surgery in the current study (83%), the median duration of antibiotics in

the study by Game and Jeffcoate was 2 months compared with 6 months in the current study, so exposing subjects to less antibiotics, with their inherent risks of side effects and selection of resistant organisms. However, while the use of MRI in the current study is associated with a much longer course of antibiotics, only one (2%) episode relapsed by 12 months (follow-up data beyond 12 months was available for 65% of episodes that initially healed), as opposed to 31% by 12 months in the series reported by Game and Jeffcoate. The majority of relapses in the current study occurred beyond 12 months. Another recent report describing conservative management of diabetic foot osteomyelitis that used shorter courses of antibiotics (mean 11.8 weeks), in which bone biopsy samples guided choice of antibiotics in a proportion, had similarly high relapse rates of 32% [14]. In contrast, a study that used very long courses of antibiotics (mean 40 weeks) reported a relapse rate of only 2% [13]. It is therefore possible that the slow resolution of bone signal

eradication of infection in bone with antibiotics. It is possible that some of the episodes of neuropathic forefoot ulceration were associated with underlying bone signal change as a result of Charcot neuroarthropathy rather than because of osteomyelitis. Charcot neuroarthropathy may be under-diagnosed in the forefoot area. Ndip and colleagues [25] recently described osteomyelitis as the trigger to a subsequent Charcot process elsewhere in the foot, which may be particularly relevant for what we have described as second episodes in the same individuals at anatomically distant sites. We did, however, try to minimize this risk by ensuring bone signal change was contiguous with surrounding soft tissue signal change that extended from the site of ulceration (Fig. 1).

change on MRI more closely reflects the time taken to achieve

Our treatment algorithm involves using antibiotics with good oral bioavailabilty and bone penetration and which are active against *S. aureus* and β haemolytic *streptococci*. The regimens used will also be active against a wide spectrum of organisms. There are known limitations of deep wound swab as an investigative tool when underlying osteomyelitis is present, with concordance between bone and non-bone specimens only 20–30% [26,27]. Furthermore, infection is often polymicrobial, particularly if the ulcer has been chronically infected or if the foot is ischaemic [28].

Senneville and colleagues [14] in a multi-centre study demonstrated bone culture-based antibiotic therapy in diabetic forefoot ulceration complicated by osteomyelitis to be a significant predictor of cure (82% in those with bone culture-based antibiotics vs. 50% in those without). However, the success rate in our study is comparable with that in the bone culture-based antibiotic group in the study of Senneville *et al.* [14].

There are no agreed criteria for the diagnosis of osteomyelitis associated with neuropathic foot lesions. While positive histological and concurrent positive microbiological examination of bone can be considered definitive, clinicians tend to rely on clinical presentation combined with imaging. The International Working Group on the Diabetic Foot has recently proposed a consensus diagnostic scheme initially for research purposes, in which MRI criteria fall into the 'probable' rather than the 'definitive' diagnostic category [17]. However, diagnostic schemes for research purposes require a greater degree of specificity, whereas greater levels of sensitivity are required for clinical practice, so that the authors acknowledge that the clinical usefulness of the scheme is currently uncertain [17].

It is somewhat surprising that the presence of PVD was not a significant predictor of poorer outcome, as has been the case in other studies [6]. However, the categorical divide for presence of PVD, the absence of one or more foot pulse, may have been too early a feature in the disease process for PVD to emerge as a statistically significant predictor of poor outcome.

Similarly, impaired renal function was not a significant predictor of poorer outcome in the current study. Other studies have suggested that impaired renal function does predict poorer outcome [11]. It is possible that the longer duration of antibiotics used in the current study negated the detrimental effect of uraemia.

The low mortality rate in the current study is consistent with a recent UK study reporting reductions in 5-year mortality in diabetic patients with neuropathic lesions from 36 to 19% over a 13-year period, with intensive cardiovascular disease risk modification [29]. We aimed to treat overall cardiovascular risk with aggressive medical therapy throughout the study period and demonstrate only 11% mortality.

In conclusion, we report a successful clinical algorithm for the conservative management of diabetic forefoot neuropathic ulceration complicated by underlying osteomyelitis in which MRI is used both to confirm or establish diagnosis and to dictate duration of antibiotic therapy. While this approach is associated with longer courses of antibiotics, it is associated with a particularly low relapse rate.

Competing interests

Nothing to declare.

References

- 1 Abbott CA, Carrington AL, Ashe H, Bath S, Every LC, Griffiths J et al. The North-West Diabetes Foot Care Study: incidence of, and risk factors for, new diabetic foot ulceration in a community-based patient cohort. *Diabet Med* 2002; 19: 377–384.
- 2 Shone A, Burnside J, Chipchase S, Game F, Jeffcoate W. Probing the validity of the probe-to-bone test in the diagnosis of osteomyelitis of the foot in diabetes. *Diabetes Care* 2006; 29: 945.
- 3 Lavery LA, Armstrong DG, Peters EJ, Lipsky BA. Probe-to-bone test for diagnosing diabetic foot osteomyelitis: reliable or relic? *Diabetes Care* 2007; **30**: 270–274.
- 4 Aragon-Sanchez FJ, Cabrera-Galvan JJ, Quintana-Marrero Y, Hernandez-Herrero MJ, Lazaro-Martinez JL, Garcia-Morales E *et al.* Outcomes of surgical treatment of diabetic foot osteomyelitis: a series of 185 patients with histopathological confirmation of bone involvement. *Diabetologia* 2008; **51**: 1962–1970.
- 5 Berner A, Sage R, Niemela J. Keller procedure for the treatment of resistant plantar ulceration of the hallux. J Foot Ankle Surg 2005; 44: 133–136.

- 6 Bamberger DM, Daus GP, Gerding DN. Osteomyelitis in the feet of diabetic patients. Long-term results, prognostic factors, and the role of antimicrobial and surgical therapy. *Am J Med* 1987; 83: 653– 660.
- 7 Nix DE, Cumbo TJ, Kuritzky P, DeVito JM, Schentag JJ. Oral ciprofloxacin in the treatment of serious soft tissue and bone infections. Efficacy, safety, and pharmacokinetics. *Am J Med* 1987; 82: S146–S153.
- 8 Peterson LR, Lissack LM, Canter K, Fasching CE, Clabots C, Gerding DN. Therapy of lower extremity infections with ciprofloxacin in patients with diabetes mellitus, peripheral vascular disease, or both. Am J Med 1989; 86: 801–808.
- 9 Ha Van G, Siney H, Danan JP, Sachon C, Grimaldi A. Treatment of osteomyelitis in the diabetic foot. Contribution of conservative surgery. *Diabetes Care* 1996; 19: 1257–1260.
- 10 Venkatesan P, Lawn S, Macfarlane RM, Fletcher EM, Finch RG, Jeffcoate WJ. Conservative management of osteomyelitis in the feet of diabetic patients. *Diabet Med* 1997; 14: 487–490.
- 11 Pittet D, Wyssa B, Herter-Clavel C, Kursteiner K, Vaucher J, Lew PD. Outcome of diabetic foot infections treated conservatively: a retrospective cohort study with long-term follow-up. *Arch Intern Med* 1999; **159**: 851–856.
- 12 Eneroth M, Larsson J, Apelqvist J. Deep foot infections in patients with diabetes and foot ulcer: an entity with different characteristics, treatments, and prognosis. *J Diabetes Complications* 1999; 13: 254–263.
- 13 Embil JM, Rose G, Trepman E, Math MC, Duerksen F, Simonsen JN *et al.* Oral antimicrobial therapy for diabetic foot osteomyelitis. *Foot Ankle Int* 2006; 27: 771–779.
- 14 Senneville E, Lombart A, Beltrand E, Valette M, Legout L, Cazaubiel M *et al.* Outcome of diabetic foot osteomyelitis treated nonsurgically: a retrospective cohort study. *Diabetes Care* 2008; 31: 637–642.
- 15 Game FL, Jeffcoate WJ. Primarily non-surgical management of osteomyelitis of the foot in diabetes. *Diabetologia* 2008; 51: 962–967.
- 16 Henke PK, Blackburn SA, Wainess RW, Cowan J, Terando A, Proctor M *et al.* Osteomyelitis of the foot and toe in adults is a surgical disease: conservative management worsens lower extremity salvage. *Ann Surg* 2005; 241: 885–892.
- 17 Berendt AR, Peters EJ, Bakker K, Embil JM, Eneroth M, Hinchliffe RJ *et al.* Diabetic foot osteomyelitis: a progress report on diagnosis and a systematic review of treatment. *Diabetes Metab Res Rev* 2008; 24: S145–S161.
- 18 Kapoor A, Page S, Lavalley M, Gale DR, Felson DT. Magnetic resonance imaging for diagnosing foot osteomyelitis: a meta-analysis. Arch Intern Med 2007; 167: 125–132.
- 19 Butalia S, Palda VA, Sargeant RJ, Detsky AS, Mourad O. Does this patient with diabetes have osteomyelitis of the lower extremity? *J Am Med Assoc* 2008; 299: 806–813.
- 20 Dinh MT, Abad CL, Safdar N. Diagnostic accuracy of the physical examination and imaging tests for osteomyelitis underlying diabetic foot ulcers: meta-analysis. *Clin Infect Dis* 2008; 47: 519–527.
- 21 Valabhji J, Hui E, Thorning C, Tyler PA, Dick EA, Gedroyc WMW. Remote areas of bone marrow oedema identified by magnetic resonance imaging in feet of subjects with diabetes presenting with neuropathic lesions are common but do not predict future Charcot neuroarthropathy. *Diabetologia* 2009; **52** (Suppl 1): S447 (Abstract 1153).
- 22 Grayson ML, Gibbons GW, Balogh K, Levin E, Karchmer AW. Probing to bone in infected pedal ulcers. A clinical sign of underlying osteomyelitis in diabetic patients. J Am Med Assoc 1995; 273: 721–723.
- 23 Rajbhandari SM, Sutton M, Davies C, Tesfaye S, Ward JD. 'Sausage toe': a reliable sign of underlying osteomyelitis. *Diabet Med* 2000; 17: 74–77.

- 24 Wagner F. The dysvascular foot: a system of diagnosis and treatment. Foot Ankle 1981; 2: 64-122.
- 25 Ndip A, Jude EB, Whitehouse R, Prescott M, Boulton AJ. Charcot neuroarthropathy triggered by osteomyelitis and/or surgery. *Diabet Med* 2008; 25: 1469–1472.
- 26 Senneville E, Melliez H, Beltrand E, Legout L, Valette M, Cazaubiel M *et al.* Culture of percutaneous bone biopsy specimens for diagnosis of diabetic foot osteomyelitis: concordance with ulcer swab cultures. *Clin Infect Dis* 2006; **42**: 57–62.
- 27 Zuluaga AF, Galvis W, Jaimes F, Vesga O. Lack of microbiological concordance between bone and non-bone specimens in chronic osteomyelitis: an observational study. *BMC Infect Dis* 2002; **2**: 8.
- 28 Gadepalli R, Dhawan B, Sreenivas V, Kapil A, Ammini AC, Chaudhry R. A clinico-microbiological study of diabetic foot ulcers in an Indian tertiary care hospital. *Diabetes Care* 2006; 29: 1727– 1732.
- 29 Young MJ, McCardle JE, Randall LE, Barclay JI. Improved survival of diabetic foot ulcer patients 1995–2008: possible impact of aggressive cardiovascular risk management. *Diabetes Care* 2008; **31**: 2143–2147.