MRSA and osteomyelitis of the foot in diabetes

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A 52-year-old man is referred to the diabetic clinic by his general practitioner (GP). He has a history of Type 2 diabetes diagnosed 8 years ago which is treated with a combination of Metformin and Gliclazide (last HbA1c 8.6%). He also has hypertension for which he takes aspirin and Ramipril. The referral is prompted by the presence of a foot ulcer that has failed to heal over an 8-week period. The patient has had repeated courses of Co-Fluampicil prescribed by the GP. The referral is accompanied by a wound swab result that demonstrates isolation of methicillin-resistant *Staphylococcus aureus* (MRSA).

Clinically the patient is well. Both feet appear neuropathic and are insensate, while peripheral pulses are palpable. On the right foot there is an ulcer under the first metatarso-phalangeal joint with surrounding callus, this foot is 3° hotter than the left. After debridement bone is palpable at the base of the wound.

- **What is the immediate management plan?**
- **What is the clinical relevance of the wound swab result?**
- **Should the patient be started on antibiotics? If so, which antibiotics are appropriate?**
- **What is the long-term management of MRSA in the diabetic foot?**

**Immediate management**

Immediate management would vary considerably from unit to unit and from country to country. This variation reflects

- the lack of evidence upon which to base clinical decisions,
- the availability—or lack—of healthcare resources, and
- the structure of remuneration of hospitals and professionals.

The plan, which follows, is the one that we would adopt.

**Diagnosis**

The man has a neuropathic ulcer, with redness, warmth and swelling of the foot. The most likely diagnosis is that of osteomyelitis—limited, presumably, to the bones immediately underlying the ulcer. There is also a possibility that he has acute neuropathic osteoarthropathy (acute Charcot foot). One of the anomalies of the Charcot literature lies in the high prevalence of lesions diagnosed in the hind- and mid-foot, when compared with the forefoot, and this raises the possibility that in at least some cases managed as acute osteomyelitis of a digit, the real problem is that of Charcot osteoarthropathy.

**Probe to bone test**

Many clinicians base the diagnosis of osteomyelitis on the ability to touch bone or joint capsule with a sterile probe. This, the so-called ‘probe to bone’ test has a catchy name, but the positive predictive value derived was artefactually enhanced by the high pretest probability of bone infection in the original small cohort studied [1]. It is worth remembering that in general medical practice, when bone is palpable—or even visible—through pressure ulcers over the hip or sacrum, there is rarely any suspicion of underlying osteomyelitis.

Magnetic resonance imaging (MRI) may distinguish between osteomyelitis and Charcot, when reviewed by experts, but imaging is generally unreliable. Blood tests for inflammatory or bone turnover markers are of no value (for review, see [2]). Bone biopsy may be the gold standard but is not part of routine practice in UK. If, however, the skin is broken, and plain X-ray confirms cortical disruption, the safest option is to assume that the bone is infected.

**X-ray**

The radiological changes of osteomyelitis are loss of the normal bone architecture, with interruption of the cortex and patchy lucency. The appearance of subperiosteal new bone is less specific than in cases of haematogenous osteomyelitis. These changes may not be apparent when the patient presents. Although most agree that they usually become clear within 4 weeks, we have one patient in whom there were no bone changes for 7 months after clinical diagnosis, and another in which they did not appear at all in 12 months of follow-up.

**Microbiological studies**

It is most likely that bone will be infected by Gram-positive cocci [3], although earlier use of broad-spectrum antibiotics may have encouraged the involvement of other species, including anaerobic bacteria. Hence, it would be usual to choose a wide-spectrum regimen for a patient like this, who had received repeated courses of cofluampicin. Ultimately, therapy
should be targeted at the sensitivities of known infecting organisms, but these may be difficult to define. Surface swabs are of no value. Even deep soft tissue samples may be misleading [4]. Blood cultures will be useful if the patient has systemic signs, but meaningful results are only likely to be provided by bone biopsy handled by the microbiology services with precision and speed. Without such information, antibiotic choice is to a large extent pragmatic.

**Practice point**

If all or part of the foot underly ing a neuropathic ulcer is inflamed, the diagnosis of osteomyelitis should be assumed—whether or not the bone destruction is confirmed on X-ray at presentation.

**Management**

**Glycaemic control**

While attention will focus on the management of his foot, other aspects of his diabetes and other conditions need to be reviewed. These include glycaemic control, which is not optimal. There is good evidence that those with a history of poor control are more likely to get new ulcers [5,6], but none to substantiate the belief that close control of blood glucose hastens healing. It may, or may not, help. It may, or may not, be feasible.

**Practice point**

It is usual to recommend tightened glycaemic control in patients with established ulcers. While likely to be beneficial, if achieved, there are no data to prove the point.

**Ulcer care**

The neuropathic ulcer will need managing by regular cleansing, debridement and off-loading. Given underlying infection, choice of dressings probably has little effect on healing, although an effort should be made to eliminate excessive exudate while maintaining adequate wound moisture.

**Surgery**

Traditional teaching is that infected bone should be resected, sooner rather than later. This view dates from an era in which antibiotic preparations with appropriate spectrum and good bone penetrance were not available. It now needs to be reconsidered. First, there is evidence from a large number of retrospective observational series that prolonged therapy with antibiotics may induce apparent cure [2]. Second, and perhaps less recognized, is the fact that early surgery may not be as effective as is thought. Data from two large studies of toe amputation suggest that the cure rate is only of the order of 40% [7,8]. Surgery also necessitates admission to hospital, and this increases the chances of secondary infection with resistant organisms.

**Practice point**

The evidence to substantiate the need for early surgery is poor. Minor surgery may be associated with relapse or recurrence in approximately 60%. On the other hand, evidence from the study of over 500 patients has suggested that prolonged treatment with antibiotics may be curative in the majority.

**Antibiotics**

There are no data upon which to make an informed decision concerning breadth of antimicrobial spectrum, route or duration of administration [2]. If the patient is systemically unwell or cannot cope at home, then they will be admitted to hospital, assuming there is a bed available. If admitted, the patient will usually be given broad-spectrum therapy intravenously. When, however, the patient is well, as in this particular case, we would manage him as an out-patient with an oral regimen that was initially broad spectrum.

**Significance of the finding of MRSA**

The increasing prevalence of MRSA (and other multiresistant organisms) is becoming a major health hazard. While the evolution of resistant organisms is likely to have been encouraged by the profligate use of antibiotics, both in medicine and agriculture, it is transmitted primarily within hospitals and other institutions. Nevertheless, community-acquired MRSA, as in this case, is recognized increasingly, and accounted for some 12% cases identified in a recent study from the USA [9]. There is a suggestion that community-acquired MRSA may be more virulent [10]. Even so, there is currently little evidence that involvement of MRSA affects the outcome of diabetic foot ulcers. One study from the UK suggested a worse outcome, but this conclusion was undermined by the inappropriate use of parametric statistics [11]. We found no effect of MRSA on outcome in 147 sequential ulcers [12], even though no specific steps were taken to eradicate the organism. Similarly, Hartemann-Heurtier and colleagues documented no difference between those colonized or not by MRSA and other multiresistant organisms in 180 consecutive admissions to a specialized unit [13].

Despite these observations, we, like most, would assume that the results of the surface swab in this case indicated that MRSA was involved in any underlying infection of bone, and would include antibiotics likely to be active against it (e.g. vancomycin, fusidic acid, rifampicin, linezolid, doxycycline) in the broad-spectrum regimen. Ideally, however, good samples should be obtained for further microbiological study, and this should be used to target second-stage therapy.
Although MRSA may or may not compromise outcome in this patient group, its identification has other implications: specifically, the need to take steps to minimize cross-infection. In countries in which hospital admission for osteomyelitis is usual, and in which the risk of acquiring MRSA is correspondingly higher, such steps have been shown to be effective [14]. Since hospital admission remains the factor most likely to result in a wound being infected by MRSA, this is an additional reason for avoiding it if possible—by opting for medical rather than surgical treatment, and by using oral antibiotics as first-line treatment (unless facilities are available for domiciliary intravenous management) [15].

Practice point

There is no convincing evidence that MRSA worsens outcome in diabetic foot infections. The main significance of its isolation is that of taking steps to limit cross-infection of others.

Practice point

Hospital admission is the most likely reason for a foot ulcer being infected by MRSA. This is a reason for avoiding admission if at all possible—for selecting a non-surgical approach and administering antibiotics orally rather than intravenously.

Long-term care

Unless all infected bone is resected successfully, antibiotic therapy should be continued for 2–3 months. Some treatment for longer. There are few firm factors upon which to base the decision to discontinue: it is largely pragmatic, and dependent on resolution of the signs of inflammation. C-reactive protein is of little value. Such prolonged treatment requires a considerable investment of effort by the patient, and it is likely that compliance with antibiotics and with off-loading is not 100%, especially in younger people, those with other responsibilities and/or those less ready to adopt the patient role.

Involved bone recalcifies but is often left shortened and deformed. Provision of fitted footwear must be considered in order to prevent new ulceration. As people with neuropathy who have had one lesion already, the likelihood of recurrence is very high and patients must be offered the opportunity for rapid assessment at the earliest sign of any new problem.

Practice point

It is difficult for many people to comply with continued rest, off-loading and antibiotics for the required number of months. Many have a job of work to do. Non-compliance should be regarded as an aspect of normal human behaviour.

Practice point

Once the lesion is healed, the patient remains at very high risk of acquiring a new lesion. Appropriate footwear and education should minimize the chances of recurrence, but the most important information the patient needs is a phone number for him/her to contact to arrange urgent reassessment at the first sign of new trouble.

Counselling

One final point needs to be considered, and it is one which is probably neglected by the vast majority of clinicians: the need to alleviate fear about MRSA. The failure of newspapers (and some paramedical professionals) to discriminate between MRSA and necrotizing fasciitis is a continuing course of popular misinformation, which induces inappropriate anxiety. Each unit should consider producing a small handout about MRSA, designed to combine necessary precautions with common sense and reassurance.

Practice point

Units should devise simple handouts for people infected with (or colonized by) MRSA, designed to combine necessary precautions with common sense and reassurance.

References


General description and methods

Aims and editorial philosophy

This section of Diabetic Medicine aims to promote good care of people with diabetes by meeting the educational needs of trainee and trained professionals. Its goals are to:

- Respect adult learning principles.
- Report and comment on important changes in the evidence base of diabetes care.
- Explore problems and controversies in care and offer expert solutions when the evidence base is weak.
- Explain scientific concepts and developments that impact on diabetes care.
- Support the readers’ development of study skills.
- Promote and report interaction with the readership.
- Be concise.

It aims to be rigorous, always clinically relevant, and to draw on the discipline of evidence-based medicine.

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Publication details

Continuing Education is published three times per annum. Full-text and PDF versions are available to Diabetic Medicine subscribers on the Blackwell Science Synergy website (http://www.blackwell-synergy.com). The electronic version of the section provides an electronic link to MedLine and, whenever available, to the full electronic text of any original article cited. An electronic discussion forum will be linked to the website to promote communication between readers (http://www.mediabetes.com).

Contents

Each issue contains some or all of the following types of article:


Learning and teaching skills. These commissioned articles on topics related to professional development aim to help readers develop their learning skills.

Clinical practice question. The Editorial Panel commissions an expert to write a short commentary around a difficult situation arising in clinical practice. The article begins with self-assessment questions, and then answers them as far as existing evidence and the experience of the commentator permit. The Editorial Panel invites readers to submit questions and nominate commentators. The electronic discussion forum will, with time, act as a source of topics.

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Having identified a paper, the screener scores it for its potential to change practice, originality, importance and strength of evidence. At present, the journals are not second-screened. Six months before an issue is due to be published, all articles identified in the preceding 4 months are ranked. A structured abstract of the highest-ranking article is prepared, prefaced by self-assessment questions, and an expert in the field is commissioned to write a short commentary discussing the article and putting it in the context of the current medical literature, and clinical practice generally. Other articles are cited with a short comment.

Horizons. These articles aim to give a succinct discussion of a new or evolving aspect of basic science that impacts on clinical practice. They are commissioned in response to important biomedical developments.

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