



VANCOMYCIN-IMPREGNATED CALCIUM SULFATE TREATMENT FOR

DIABETIC FOOT ULCERATION

Calcium sulfate can be mixed with a broad range of antibiotics for the local treatment of bone or soft-tissue infection, in many cases avoiding the need for prolonged oral or parenteral antibiotic treatment. Here we present a case of plantar hallux ulceration in a patient with diabetes complicated by a history of osteomyelitis. The combination of antibiotic-impregnated calcium sulfate and a multidisciplinary approach achieved successful resolution of an ulceration that had been present for six years

A 43-year-old male was referred for treatment of an osteomyelitic left hallux and plantar ulcer infected with MRSA. The patient was a non-smoker and had a history of long-standing type 1 diabetes with good control (HbA1c 53 mmol/mol), essential hypertension and hypercholesterolaemia. The patient's regular treatment included enalapril, Levemir®, NovoRapid®, rosuvastatin and tadalafil. He had palpable biphasic pulses and peripheral sensory neuropathy (absent response to a 10g monofilament).

The patient had a six-year history of recurrent ulceration to the plantar aspect of the left hallux inferior to the interphalangeal joint (IPJ). The lesion was thought to have been caused by verruca pedis complicated by keratosis. The hallux had ulcerated and healed on four previous occasions. He then developed osteomyelitis and Charcot arthropathy. Treatment of the ulcer at the multidisciplinary team (MDT) foot clinic consisted of oral antibiotics, offloading with a removable cast and regular debridement.

The most recent episode of ulceration had persisted for 11 months and was complicated by osteomyelitis. An amputation of the hallux was discussed as a treatment option. Clinically the hallux appeared acutely infected with a plantar ulceration measured at 15mm maximum diameter (Figures 1 & 2). A

wound aspirate was positive for MRSA and sensitive to clarithromycin and vancomycin. In addition, a hallux rigidus was evident with significant loss of motion at the first metatarsophalangeal joint (MTPJ). X-Ray examination showed end-stage osteoarthritis at first MTPJ and destruction of the distal phalanx (Figure 3).

The patient had completed a six-week course of clarithromycin prior to surgery. Referral was made to the Podiatric Surgery Department for consideration of treatment with antibiotic-impregnated calcium sulfate.

MANAGEMENT BY THE PODIATRIC SURGERY TEAM

The patient and the diabetes team were keen to avoid amputation of the hallux. Localised antibiotic therapy was deemed a potentially helpful alternative form of treatment. However, the presence of hallux rigidus suggested that treating the ulcer in isolation would lead to recurrence and so an arthroplasty was planned to decompress the IPJ and reduce peak plantar pressures. The patient was admitted to a community-based day-case surgery unit. He completed topical treatment for MRSA carriage (Mupirocin nasal ointment and chlorhexidine 4% skin cleanser) five days before the surgery.

SURGERY

Local anaesthesia was achieved with a proximal digital block using a combination of mepivacaine 3% plain and levobupivacaine 5.0mg/ml. The foot

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was exsanguinated and haemostasis achieved with an ankle tourniquet. The plantar ulcer was debrided and found to readily probe through the IPJ to the dorsal surface. A dorsal lazy S incision was made over the hallux to the IPJ. The head of the proximal phalanx appeared osteomyelitic and was excised with the surrounding tissue and the remaining fragment of the distal phalanx debrided. The void and ulcer were packed with calcium sulfate pellets impregnated with 1g vancomycin (Figures 4 & 5). The dorsal wound was sutured in layers with 3/0 Vicryl and 4/0 Prolene and the plantar ulcer was left to heal by secondary intention. The patient was issued with a post-op shoe as well as Ibuprofen and paracetamol for post-operative analgesia. He was advised to rest and elevate the foot for two weeks.

The calcium sulfate is supplied as 10cc Stimulan® powder and must be mixed in theatre with the antibiotic of choice. It can be mixed with powdered antibiotics such as vancomycin or liquid antibiotics such as gentamicin. The mixture must set in a silicone mould to produce pellets of approximately 3mm diameter. Once set, these can be packed individually into the wound or even drilled into bone.

OUTCOME

The patient returned to the Podiatric Surgery Outpatient clinic at two and seven days post-operation at which point care was transferred back to the MDT (Figure 6). At 15 days



Figure 1. Pre-operative image.

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post-operation sutures were removed with no sign of secondary infection although the hallux continued to show chronic swelling. At this point, the calcium sulfate pellets were still well defined in the plantar wound. By the next MDT appointment, five weeks post-operation, the plantar ulcer had significantly improved, with a fully healed wound noted by nine weeks (Figure 7). Following surgery, orthotics were also renewed with the MDT orthotists

LEARNING OUTCOMES

Diabetes is one of the UK's most common chronic diseases. It is estimated that 10% of those with diabetes will, at some point, develop a foot ulcer, with diabetes being the most common cause of non-traumatic limb amputation. According to NICE guidance, standard care for diabetic foot ulcers should include the offer of at least offloading, control of foot infection, control of ischaemia, wound debridement or wound dressings.¹

In this case, treatment of the mechanical foot abnormalities had already been addressed with the use of orthotic inlays initially and then casting after ulcer development which attempted to offload the hallux. Foot infection had been identified but standard methods of control had failed. The patient did not present with clinical signs of ischaemia and he attended regularly for wound debridement. Wound dressings consisted of simple, dry dressings with additional absorbent layers as required.

The use of localised antibiotic therapy coupled with calcium sulfate is a relatively new concept for the treatment of osteomyelitis. Calcium-based crystalline materials have been recognised as a potential bone void filler or graft material since the 1920s.² The use of calcium sulfate for delivery of

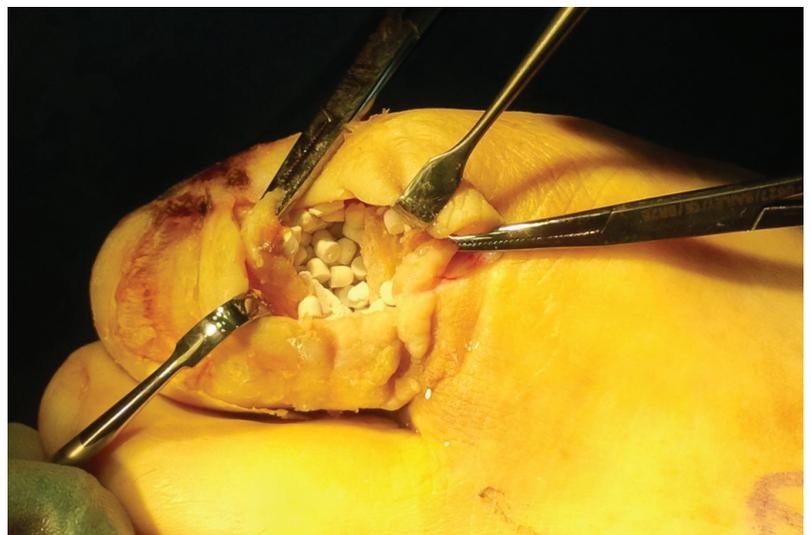
antibiotics is growing in popularity, with a shift away from non-biodegradable polymethylmethacrylate which was the medium of choice for over 20 years.³

Early use of calcium sulfate in infected wounds was complicated by excessive drainage, a result of the production process that failed to remove impurities which, in turn, gave rise to an exaggerated inflammatory response.⁴ The product used in this case, Stimulan[®], is derived from a laboratory manufacturing process resulting in a pure synthetic form of calcium sulfate, which is much less likely to provoke an inflammatory response and the exudate associated with it.⁵ That said, some caution should be taken as any void filler of this nature will likely induce a degree of drainage or exudate and so appropriate post-operative wound care techniques will need to be in place.

Recent studies have shown that the use of antibiotic-impregnated calcium sulfate as a treatment for radiologically confirmed osteomyelitis has been safe and effective, particularly in the management of diabetic foot ulcers.⁶

The key benefit of calcium sulfate is that once in the wound it will dissolve slowly over a six-week period and during this time will steadily release the antibiotic, delivering doses significantly in excess of the minimum inhibitory concentration (the dose of drug required to kill bacteria) but achieved with only a single dose of antibiotic. Delivery of antibiotics into the infected tissues means that the infection can be directly targeted avoiding the need for long courses of intravenous or oral antibiotics.⁷ The caveat here is that locally targeted treatments will not fight systemic infection and so in severe infection local treatment must be used alongside traditional measures.

Calcium sulfate as mentioned above can be mixed with a variety of antibiotics but in this case the patient was confirmed MRSA positive following a wound aspirate. The decision to use vancomycin was made jointly by the MDT foot clinic and microbiologists. Vancomycin is a glycopeptide bactericidal antibiotic and like penicillin it acts to inhibit the formation of peptidoglycan chains and therefore cell-wall



Top Left - Figure 2. Pre-operative image, dorsal view. **Top Right - Figure 3.** X-ray demonstrating hallux 1PJ osteomyelitis. **Bottom - Figure 4.** Intra-operative image demonstrating Stimulan[®] in situ.



Left - Figure 5. Stimulan mixed with vancomycin and ready for packing into wound. **Centre - Figure 6.** One week post operation. **Right - Figure 7.** Appearance of hallux nine weeks following surgery.

synthesis.^{8,9} Vancomycin is active against most gram positive bacteria, including MRSA, and when combined with aminoglycosides such as gentamicin it can have a synergistic effect, enhancing its spectrum of activity.^{8,9} Vancomycin is often reserved for MRSA infections or for patients with severe gram positive infections who are allergic to penicillin.⁹ Vancomycin is not absorbed through the gastrointestinal tract when taken orally but it may be used orally for the local treatment of pseudomembranous colitis cause by *Clostridium difficile* infection.⁹

Plantar hallux ulcerations in the diabetic neuropathic foot are often due to abnormal foot biomechanics involving the 1st ray and the foot as a whole. Precursors to ulceration may include over-pronation or hallux rigidus.^{10,11} Hallux rigidus creates a rocker bottom adaptation to the first ray, with the hallux often becoming hyperextended, the foot then pivots around the head of the proximal phalanx during toe off ultimately leading to ulceration.¹²

Hallux IPJ arthroplasty has been shown to be beneficial in the treatment of plantar hallux ulcerations,¹³ possibly due to the increased mobility at the joint compensating for the lack of MTPJ movement. In this case, alongside the arthroplasty calcium sulfate was inserted, a bone void filler that may encourage osteoconduction and bony bridging of the arthroplasty; however, the destruction of the distal phalanx was such that this was considered unlikely to be a clinical concern.

This case demonstrates the value of including podiatric surgery as an

option in the extended diabetes MDT. The specialist foot clinic had followed NICE guidance in managing the ulcer but the lesion proved recalcitrant and so a surgical option was considered. The surgery was organised conveniently at a community setting, avoiding the need for and resources associated with an acute admission to a surgical ward. Surgery was performed safely under local anaesthetic and once the surgical team were happy with the wound, care was transferred back to the MDT. ■

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