Mid- to Long-Term Results of Single Stage Management of Chronic Osteomyelitis Facilitated by a Bioabsorbable, Gentamicin-Loaded Ceramic in Dead Space Filling

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INTRODUCTION:
Chronic osteomyelitis is often treated with staged surgery, delivering the principles required to eradicate the infection. Adequate debridement is essential to remove dead tissue and biofilm, but this creates a dead space which must be managed. Systemic antibiotic penetration of this space may be poor, so effective antimicrobial delivery can be ensured with implantation of local antibiotics. This study evaluated a bioabsorbable antibiotic-loaded ceramic, as a post-debridement defect filler, in a single-stage protocol for the eradication of chronic infection.

METHODS:
We report a prospective study of patients with Cierny and Mader types III and IV chronic osteomyelitis. Infection was confirmed with strict clinical, microbiological, and histological criteria.

All patients were treated by a multidisciplinary team with a single-stage protocol including preoperative patient optimization, debridement, multiple deep tissue sampling, initial empiric and then culture-specific systemic antibiotics, stabilization (if needed), dead space filling with a gentamicin-loaded, bioabsorbable ceramic, and immediate primary skin closure. The ceramic contained 60% Calcium Sulphate, 40% Hydroxyapatite, and 17.5mg gentamicin per ml.

Patients were reviewed for the primary outcome of infection eradication at 3, 6, 12, 24, 48, and after 48 months from surgery (mean 72 months; range 12-100.5). Adverse events and complications were also recorded at all timepoints.

RESULTS:
One-hundred consecutive patients (mean age 51.6yrs; 23-88) with confirmed infection in 105 bones were treated. Osteomyelitis followed open fracture or internal fixation of closed fractures in 71%. Nine had adjacent septic arthritis, 80% had co-morbidities (Cierny-Mader Class B hosts), and 10 had infected nonunions. Osteomyelitis affected the tibia/fibula in 39 cases, 24 in the femur, 28 upper limb bones, 3 calcanei and 1 sacrum. Five patients had 2 bones affected.

Stabilization was required in 21 cases and 5 required joint fusion as part of the initial surgery. Plastic surgical skin closure was needed in 23 cases (18 free flaps and 5 local flaps). Mean bone defect volume was 10.9mls (1-30) (Figure 1).

Staphylococci were the commonest organism (41.8%), with Methicillin-resistant Staph. aureus in six patients. Proteus mirabilis and Pseudomonas spp were more common in polymicrobial infection, often with a gram-positive organism (usually Staphylococcus aureus).

All 100 patients were reviewed at one year; 97 patients at two years (1 death and 2 lost to follow up (LTF)); 92 at four years (3 deaths and 2 LTF), and 91 finally at a mean of 6.05 years (range 4.2-8.4)(1 death). All five deaths were unrelated to the surgery or to bone infection and all were infection free at death.

At one year after surgery, 97% of patients were infection free. There were two further recurrences by two years and one final recurrence at 4.5 years, giving an overall success rate of 94% at a mean of six years follow up (Figure 2). All five fusions healed and 8/10 nonunions healed with the primary surgery alone. Four patients had joint replacement during follow up for degenerative arthritis in the same limb as the infection, without recurrence. Adverse events were uncommon, with three fractures occurring between one and eleven months after surgery. Six patients had early leakage of the ceramic material from the wound which was treated expectantly and dried up without intervention and without later recurrence of infection. Outcome was not dependent on C-M host class, aetiology of infection, microbial culture, wound leakage or presence of nonunion.

DISCUSSION AND CONCLUSION:
This study presents a consecutive series of patients with the more severe stages of osteomyelitis. Recent studies have frequently reported much higher recurrence rates. As our patients now present with more complex infections and comorbidities, we need treatment strategies which can be applied widely. The use of local delivery of antibiotics may prevent the problems of antibiotic intolerance, poor compliance, and adverse reactions due to toxicity of systemic therapy. These are common in older or more comorbid populations.

This protocol, facilitated by the absorbable local antibiotic, was highly effective, with few recurrences even up to 8 years after surgery. The ability to completely fill the dead space with a material which will deliver antibiotics over several weeks and then be remodeled allows a single operation which is more patient-friendly. With no further hospital admissions, it may also offer cost savings compared to standard staged therapy.

We have applied this treatment to all patients regardless of comorbidities, requirement for flaps, or nature of infection. The single stage protocol was robust, giving effective treatment in all these groups.
Figure 1.
This large defect in the upper tibia was filled with gentamicin-impregnated ceramic and the skin closed with a local gastrocnemius muscle flap and skin graft.

Figure 2.
Kaplan-Meier Survival Analysis from 3-8 years after surgery.