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BRIEF REPORT

Through the looking glass; bioactive glass S53P4 (BonAlive®) in the treatment of chronic osteomyelitis

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Abstract
Background In terms of eradication, osteomyelitis represents one of the most challenging infective conditions in medicine and surgery. In recent years, the use of bioactive glass in conjunction with antimicrobial therapy has emerged as a viable new treatment.
Aim We present a short study, from a regional orthopaedic unit, demonstrating its successful use in three patients with chronic osteomyelitis.
Methods Between September 2010 and May 2011, bioactive glass S53P4 was used in conjunction with intravenous and oral antibiotics to treat chronic osteomyelitis in three patients (two male, one female). All patients underwent debridement and sequestrectomy procedures with the insertion of bioactive glass followed by antimicrobial regimens tailored to isolated pathogen sensitivities. Patient age ranged from 28 to 68 years, with a mean age of 44.7 years. The presentation period, from time of initial diagnosis to treatment, varied from 16 months to 16 years and all three patients had undergone multiple previous debridements and antimicrobial regimens to no avail.
Results A follow-up of 14–21 months has been achieved with a mean follow-up of 17.3 months. We have seen excellent results in all three patients. All haematological and biochemical parameters have returned to normal, pain has ceased and function has returned in the affected limbs. All antibiotics have stopped and there is no radiological evidence of osteomyelitis. The bioactive glass has integrated with the surrounding bone.
Conclusions Though a relatively recent development, bioactive glass used in concurrence with antibiotic therapy has significant potential in the treatment of chronic osteomyelitis.

Background

In terms of eradication, osteomyelitis represents one of the most challenging infective conditions in medicine and surgery. In recent years the use of bioactive glass in conjunction with antimicrobial therapy has emerged as a viable new treatment. We present a short study, from a regional orthopaedic unit, demonstrating its successful use in three patients with chronic osteomyelitis.

Osteomyelitis may be defined as a destructive bony lesion caused by infecting pathogenic organisms. There are multiple triggering aetiologies. Commonly the pathogens gain access via trauma or surgery resulting in direct inoculation. The infection may originate via haematogenous spread, and in certain populations (diabetics, immunocompromised) the infection may occur as an indirect result of the underlying systemic condition [1].

Acute osteomyelitis often displays the cardinal features of inflammation along with bone and soft tissue oedema and locally reduced vascular supply. Pathogens which are responsible include *Staphylococcus aureus*, *Pseudomonas* species and *Enterobacteriaceae* [2]. Some of these organisms can exhibit surface adhesins capable of bonding with host proteins. Acidosis may occur during the acute setting resulting in breakdown of the bone matrix [3]. In the chronic setting, lesions of de-vascularised and necrotic bone occur (sequestrums) [1] providing a haven for bacteria and a source of recurrence.

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Aim

The aim of our study was to demonstrate bioactive glass S53P4 as a safe and efficacious adjunct to antimicrobials in the treatment of chronic osteomyelitis.

Methods

Between September 2010 and May 2011, bioactive glass S53P4 was used in conjunction with intravenous and oral antibiotics to treat chronic osteomyelitis in three patients (two male, one female). The diagnosis was confirmed both radiologically and histopathologically. All patients underwent debridement and sequestrectomy procedures with the insertion of bioactive glass followed by antimicrobial regimens tailored to isolated pathogen sensitivities. Age at time of treatment ranged from 28 to 68 years, with a mean age of 44.7 years. The presentation period, from time of initial diagnosis to treatment, varied from 16 months to 16 years and all three patients had underwent multiple previous debridements and antimicrobial regimens to no avail. None of the patients were diabetic or had any other significant medical or surgical history.

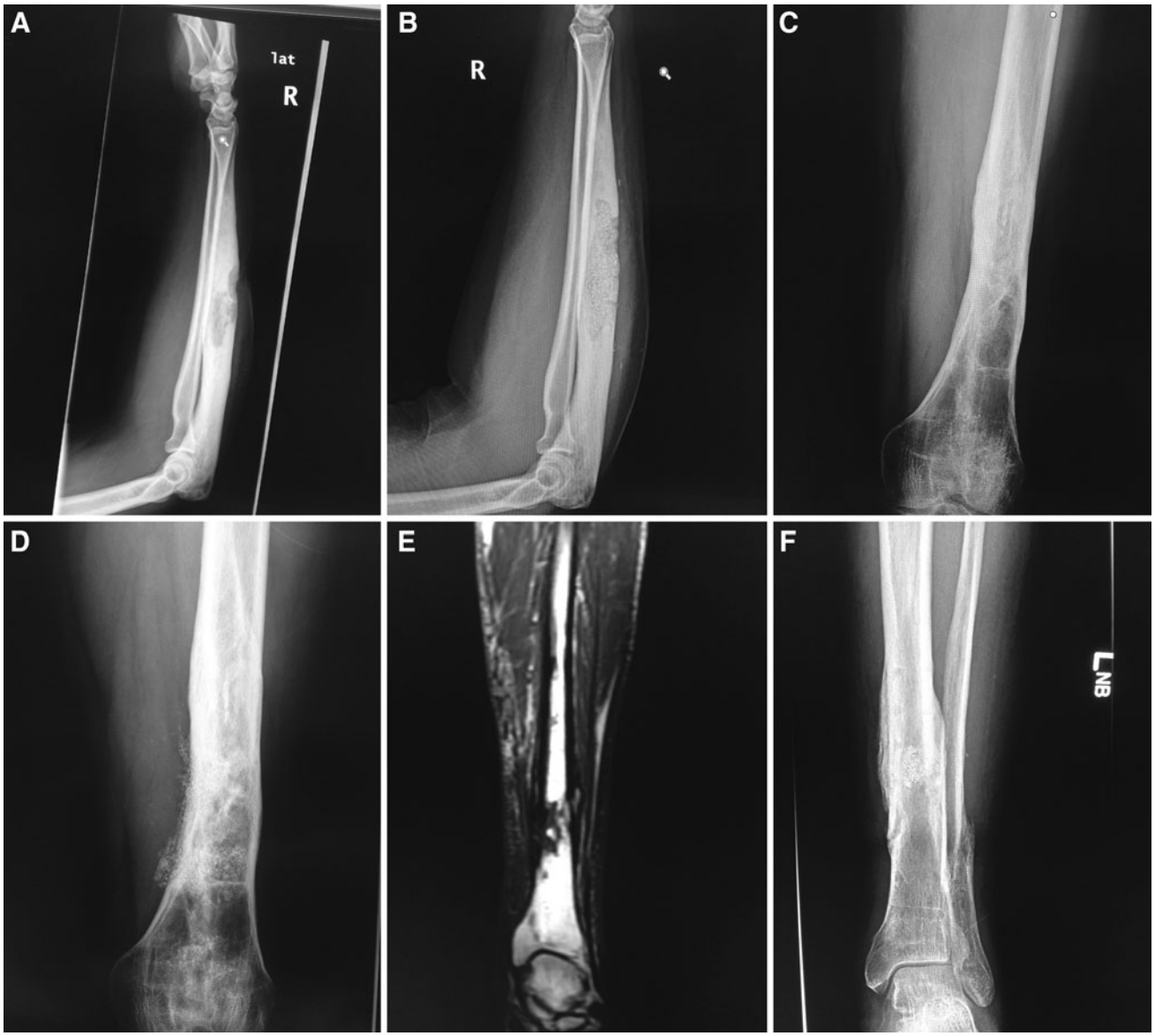

Fig. 1 **a**, **b** Plain radiograph lateral views of patient A's right ulna immediately prior to and 1 year post procedure. **c**, **d** Plain radiograph AP views of patient B's distal left femur again taken immediately prior to surgery and then 8 months subsequent. **e**, **f** An MRI coronal section and a plain radiograph AP view of patient C's left distal tibia prior to and 6 months post bioactive glass insertion. In all cases a clear bone defect was identifiable which appears to have been repaired successfully by the incorporating bioactive glass

Results

A follow-up of 14–21 months has been achieved to date with a mean follow-up of 17.3 months. We have seen excellent results in all three patients. All haematological and biochemical parameters have returned to normal levels, pain has ceased and function has returned in the affected limbs. All antibiotics have stopped. There is no further radiological evidence of osteomyelitis and the bioactive glass has integrated well with the surrounding bone (Fig. 1).

Conclusions

For many years antibiotic therapy has formed the cornerstone of osteomyelitis treatment. Notwithstanding the high cost of long-term intravenous antibiotic therapies and the large side-effect profiles of many antimicrobial agents, antibiotic therapy alone often fails to eradicate the infection.

Surgical options include debridement of infected/necrotic bone with copious irrigation. Local delivery of high-dose antibiotics may be achieved via the deployment of antimicrobial impregnated delivery systems (gentamicin loaded PMMA beads, or antibiotic-loaded spacers) [4]. Following the surgical debridement, however, there often remains extensive sequestrums [1] and recurrence of infection remains problematic.

Bioactive glasses are synthetic, osteoconductive and biocompatible materials [1]. Their ability to integrate with bone and soft tissue was first described in 1971 [5]. An exchange of ions (H^+, Na^+, Ca^{2+}) occurs between the glass surface and the surrounding body fluid. This leads to the creation of silanol groups followed by a silicon dioxide layer. An amorphous calcium phosphate (ACP) layer forms over this and crystallises into a hydroxyapatite (HA) layer. Once the HA layer has formed absorption of growth factors occurs, followed by the inward migration of osteoprogenitor cells which trigger the synthesis of extracellular matrix and new bone formation [6].

As well as their potential for complete bone and tissue integration/repair, bioactive glasses have also demonstrated considerable antibacterial and angiogenesis-promoting properties. The antibacterial properties exhibited are likely multifactorial involving the creation of a local alkaline environment and the resistance of the material to bacterial adhesion and biofilm formation [7]. Integration of mesenchymal stem cells and various growth factors such as vascular endothelial growth factor (VEGF) serve to augment the materials ability to repair tissue defects and stimulate neovascularization [6].

Though a relatively recent development, the use of bioactive glass in concurrence with antibiotic therapy has significant potential in the treatment of osteomyelitis as demonstrated in this short study. Of particular note is its ability to repair longstanding bone defects whilst simultaneously exhibiting potent antimicrobial properties. Due to our limited data set, we feel that continuing collation of data and research on the treatment of osteomyelitis with bioactive glasses is merited to further validate our results and improve our understanding of this difficult and debilitating condition.

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