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Case Report

A case of chronic ankle osteomyelitis treated with bioactive glass and tibiocalcaneal fusion

Miriam Grassi[1], Marco Mattia Larghi[1], Davide Brioschi[1], Marianatonietta Scazzarriello[1,2], Alfonso Manzotti[1]

1. ASST-Fatebenefratelli L. Sacco University Hospital, Milano, Italy.
2. Università degli studi di Milano, Milano, Italy.

Abstract

Limb-salvage surgery in cases of chronic osteomyelitis poses significant challenges for orthopedic surgeons. This case report presents the first documented instance of a successful staged limb-salvage treatment for chronic ankle osteomyelitis, combining tibiocalcaneal fusion with bioactive glass (BAG). Bioactive glass S53P4 is a synthetic, biocompatible, osteoconductive bone substitute known for its bone-bonding capabilities, antibacterial and angiogenesis-promoting properties, which could be suitable for treating bone defects in infections. The subject of this case is a 68-year-old male with long-standing uncontrolled diabetes, who presented with a seven-day history of progressive left ankle arthralgia, purulent drainage in the medial aspect of the ankle, and low-grade fever. Imaging studies confirmed the diagnosis of chronic ankle osteomyelitis. The treatment involved a multidisciplinary approach including early antibiotic therapy, rigorous glycemic control, and staged surgical interventions using biomaterials. The first surgery was debridement and adequate irrigation, bone-void filling with antibiotic cemented spacer. Later targeted antibiotic therapy, after cultural examination, progressed to total contact casting and partial progressive weight-bearing. After 24 months of follow-up, with no clinical signs of infection, no gross alteration of gait pattern, and demonstrating complete bone healing, the patient was submitted to tibiocalcaneal fusion using bioactive glass. The BAG-S53P4 represents an interesting option as a bone substitute in chronic osteomyelitis with bone loss.

Level of evidence IV; Therapeutic study; Case report.

Keywords: Biocompatible materials; Osteomyelitis; Ankle; Bone substitutes.

Introduction

Chronic osteomyelitis often presents significant challenges in treatment, especially when it results in substantial bone loss. The standard approach usually involves surgical debridement to remove infected and necrotic tissue. In recent years, biomaterials have emerged as promising therapeutic options. The evolution of biomaterials can be categorized into three generations.

- **First generation**: These biomaterials were designed to be as bio-inert as possible, minimizing scar tissue formation at the interface with host tissues.
- **Second generation**: These biomaterials incorporated properties that actively stimulated tissue regeneration and repair, enhancing implant integration and stability.
- **Third generation:** These biomaterials were designed to stimulate tissue regeneration and repair through mechanisms such as gene activation.

Among the various bimaterials available, bioactive glass (BAG) has garnered attention, particularly due to its inventor, Lerry Hench, who developed it at the University of Florida in 1969, with a large use in craniomaxillofacial surgery in treating chronically infected bone.

Bioactive glass has unique properties that promote osteoconductivity and osteoinductivity, making it suitable for bone reparative procedures.

Specifically, BAG-S53P4 (composed of SiO_2, Na_2O, CaO, P_2O_5) has been shown to chemically bond with bone, promoting new bone formation. Its antibacterial properties

Study performed at the ASST FBF SACCO Luigi Sacco University Hospital, Milano, Italy.

Correspondence: Miriam Grassi. ASST-Fatebenefratelli L. Sacco University Hospital, Via G.B. Grassi 74, 20157 Milano, Italy. **Email:** miriam.grassi.mg@gmail.com, grassi.miriam@asst-fbf-sacco.it. **Conflicts of interest:** None. **Source of funding:** None. **Data received:** September 21, 2024. **Data accepted:** April 15, 2025.

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arise from localized increases in pH and osmotic pressure, resulting from the release of sodium and calcium ions along with phosphate salts. This environment inhibits bacterial adhesion and proliferation. Furthermore, BAG shows broad-spectrum bactericidal activity, and its ability to prevent biofilm formation has been well-documented. No induction of bacterial resistance to BAG-S53P4 has been reported to date. In this paper, we present our experience treating chronic ankle osteomyelitis in a patient with a history of an open distal tibia and fibula fracture. The case was managed by the same surgical team, at a single university center, in the North of Italy, during the COVID-19 pandemic lockdowns.

Case description

Preoperative management

A 68-year-old male patient sustained a displaced open fracture of the left distal tibia and fibula in July 1965 (AO Type 43-B3), following a high-energy motorcycle accident. He had no allergies. His medical history was significant for tobacco use (2 packs a day) and glycemic imbalance.

Upon admission, he was alert and oriented, with stable circulation and ventilation. Clinical examination of the left ankle revealed severe soft tissue contamination with a 3 cm laceration on the medial malleolus and a 2 cm laceration on the lateral malleolus, bone exposure, and significant deformity. Neurological and vascular assessments were normal. Wound cleaning, surgical debridement, and reduction with external fixation were performed. Antibiotic prophylaxis with 2 g Cefazolin intravenous and intramuscular tetanus toxoid was administered. However, by postoperative day seven, purulent drainage was observed from the wound sites, although no signs of infection were noted around the external fixator pins. The patient was diagnosed with an acute wound

Infection, prompting further debridement and tissue sampling, which identified *Staphylococcus aureus*. Targeted antibiotic therapy was administered for six weeks. The wounds evolved favorably, although a small ulceration area with a bleeding base persisted over the medial malleolar area and was slow to heal. Eight weeks later, the external fixator was removed, and definitive surgery with internal fixation was performed. Osteosynthesis material was removed after 12 months at the same center. He did well for several years with these procedures.

This patient came to our observation in June 2020 at the Emergency Department in a University reference center for infectious diseases, in Milan. The patient has a history of long-term uncontrolled glycemia and came to our observation for seven days of progressive left ankle arthralgia, present at weight-bearing, severe steppage, and local swelling. After three days of recovery, we noted the appearance of purulent drainage in the medial malleolar area and low-grade fever (between 37.5 and 38.5 c°). The patient was diagnosed with a chronic ankle osteomyelitis as shown by radiographs, computed tomography scans, and magnetic resonance imaging (Figure 1). A PET-CT scan confirmed the diagnosis of chronic osteomyelitis, and he was admitted to the Infectious Diseases Unit. A multidisciplinary team, including Infectious Disease specialists and orthopedic surgeons, evaluated the patient. Empirical antibiotic therapy was administered with 6 g Cefazolin intravenous, divided into three doses daily. Blood tests at the time of admission were: white blood cells 10.15 x 10^9/L, hemoglobin 130 gr/L, CRP 83.9 mg/L, glucose 130 mg/dL, fibrinogen 8.00 gr/L. The hemocultures for the search for aerobes and anaerobes were negative, as well as nasopharyngeal swabs tested for SARS-CoV-2 (RT-PCR), while the fistula swab resulted positive for Methicillin-sensitive *Staphylococcus aureus* (MSSA).

He was submitted to an initial surgical procedure in July 2020, which included debridement, multiple intraoperative culture tests, and the implantation of an antibiotic cement spacer, with resection of the medial and lateral malleolus. This created a large osseous rectangular deficit measuring approximately 3.75 x 2.5 cm^2. Intraoperative culture tests resulted positive for MSSA, Methicillin-resistant *Staphylococcus aureus* (MRSA), and *Escherichia coli*. Specific antibiotic therapy was administered with Piperacillin 4 g and Tazobactam 500 mg

Figure 1. Preoperative radiographs and computed tomography scans.

three doses daily and Teicoplanin 800 mg once daily. During the hospital stay the patient was submitted to a urinary tract infection by *Enterobacter aerogenes* and he was treated with Fosfomycin 3 g twice daily for one day and once daily for three days and subsequently with Sulfamethoxazole 800 mg and Trimethoprim 160 mg twice daily for five days and three doses daily for an additional five days. The patient remained hospitalized for 53 days.

A clinical and telephonic follow-up was performed six months postoperatively due to the COVID-19 lockdown.

In January 2021, after the second lockdown and after four months of antibiotic wash-out with a smoking cessation program and a diet for glycemic control he was admitted in the Orthopedics and Traumatology Unit and he was submitted to a second surgery of debridement, removal of antibiotic cemented spacer with a single transfibular approach, multiple intraoperative culture tests and tibiotalocalcaneal arthrodesis with a retrograde intramedullary nail and bioactive glass. Postoperative radiographs showed satisfactory results (Figure 2).

A non-weight-bearing cast was placed for four weeks, followed by a partial weight-bearing walker boot for an additional three weeks. Ten weeks postoperatively, radiological control was performed, and full weight-bearing was authorized. The follow-ups at 12, 24, 36, and 48 months the patient was pain free, he was walking without aids and no leg-length dysmetria and at 48 months follow-up he was submitted to surgery to remove a screw (Figure 3). The American Orthopaedic Foot and Ankle Society (AOFAS) ankle-hindfoot score, which is a health outcome score for patients after foot and ankle surgery, was used to assess the clinical outcome. This patient had a good outcome with a score equal to 86 at 48 months postoperatively, starting from a preoperative AOFAS score equal to 50 (poor outcome).

A stable union was achieved in radiological controls, and no wound-related complications were noticed.

Discussion

Our case report illustrates a successful application of isolated ankle joint fusion using BAG in the presence of extensive bone defects involving the tibia and talus.

This approach demonstrated an encouraging rate of osseous union and satisfactory functional outcomes. By integrating BAG with a meticulous surgical technique that included proper alignment and stabilization of the ankle joint, we achieved the dual goal of restoring ankle function and maintaining leg length. Various surgical techniques have been explored in the literature to restore bone stock and preserve leg length following ankle fusion.

These include: large structural iliac crest autografts (autografts are commonly employed due to their osteogenic potential, but they are limited by donor site morbidity); distal fibula autografts (Palisade technique) and femoral head

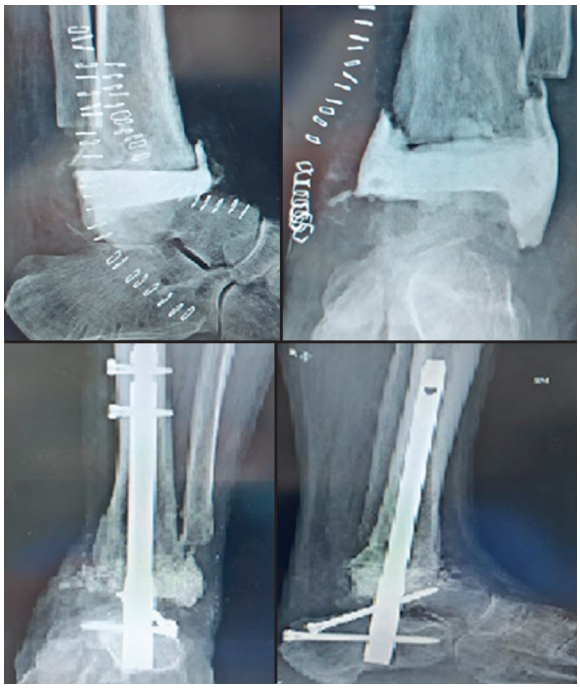

Figure 2. Postoperative radiographs.

Figure 3. Clinical examination at 48 months follow-up.

allografts (these grafts provide structural support–they often lack adequate vascularity, increasing the risk of nonunion and secondary collapse); bone cement (it serves as an effective temporary spacer); and trabecular metal interpositional spacers (it offers a porous scaffold for bone ingrowth)[1,2,3].

Additionally, allografts carry risks of disease transmission and immunogenic responses. Iliac crest grafting will result in a symptomatic donor site in < 48% of the patients, and bone cement as an artificial spacer is an inert foreign body that cannot integrate as well as a trabecular metal interpositional spacer[4]. Bone cement and trabecular metal spacers include difficulty in visualizing radiographic fusion and bone integration on plain radiograph or magnetic resonance imaging, as underlined by Frigg et al.[5] and Carlsson[6]. Trabecular metal, particularly tantalum, offers a porous scaffold for bone ingrowth but presents challenges in radiographic evaluation of fusion[5,6]. Ankle arthrodesis is a salvage procedure specifically aimed at preventing more proximal amputation. The goals of an ankle arthrodesis include realigning the ankle, alleviating pain by a solid union, and achieving a plantigrade foot. Multiple approaches have been described to achieve fusion, which remains a difficult goal with high nonunion rates.

In contrast, BAG has emerged as a superior alternative due to its dual function as a bone substitute and antimicrobial agent[7,8]. Its ability to chemically bond with bone facilitates osteogenesis, while its antibacterial properties, resulting from increased local pH and osmotic pressure, create an environment inhospitable to bacterial growth.

The use of a retrograde tibial nail with BAG as an osteoconductive scaffold for the treatment of chronic osteomyelitis is an excellent option to avoid recurrence of infection, leg-length dysmetria, with good clinical, functional, and radiological short-term results.

Specifically, research by De Giglio et al.[9] demonstrated that a significant decrease in the likelihood of requiring further antibiotic therapy in patients with diabetic foot infections treated with BAG, highlighting its role in improving osteomyelitis resolution rates.

Romanò et al.[10] reported an impressive 90% eradication rate with the use of BAG and confirmed the safety and efficacy of this biomaterial in a larger cohort, underscoring the safety and efficacy of this biomaterial in clinical applications. Despite the encouraging short-term results regarding clinical, functional, and radiological outcomes, the authors acknowledge the necessity for long-term studies to assess any potential delayed complications linked to BAG use in orthopedic procedures.

Conclusion

Ankle joint fusion using bioactive glass presents a viable and safe treatment option for chronic osteomyelitis, especially in cases with considerable bone defects.

Bioactive glass demonstrates excellent biocompatibility and serves as an osteoconductive scaffold with both osteogenic and osteoinductive properties, facilitating bone regeneration while mitigating infection risks. In our case, a multidisciplinary approach resulted in stable bone fusion without postoperative complications. We suggest BAG may be used as a structural scaffold for the second-step ankle arthrodesis in treating chronic osteomyelitis.

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