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Operative Techniques in
Orthopaedics

Treatment of Chronic Bone Infection

Heinz Winkler, MD,* and Peter Haiden, MD†

The treatment of chronic osteomyelitis depends on the obstinate persistence of the offending micro-organism(s) and often results in long-term patient disability causing remarkable costs to the health care system. Difficulties of treating chronic osteomyelitis derive from biofilm-forming pathogens that resist the host immunologic defense and antimicrobial substances, and the need to treat osseous defects that result from the disease itself and eventual previous interventions. Established surgical techniques require multiple costly operations with extended periods of disablement and impairment of the patients, sometimes making the therapy worse than the disease. This article suggests a new operative approach to address biofilm-adapted antimicrobial therapy and reconstruction of bony defects using antibiotic-impregnated allograft bone. The technique is applicable to all stages of the Cierny-Mader classification, and detailed description of specifications for the respective procedure is provided. Local use of high antibiotic concentrations enable simultaneous internal fixation with osteosynthetic material and minimize the need for using systemic antibiotics. This treatment results in short hospital stays, reduced pain, and faster rehabilitation for patients, markedly reducing their burden and the costs of treatment. Recurrences may occur in 10% of cases, but may be treated by repeating the procedure.

KEYWORDS bone, infection, osteomyelitis, osteitis, treatment, biofilm, bone defect, reconstruction, allograft, implant, internal fixation, one stage, antibiotic concentration

Introduction

Bacterial contamination of bone may occur via the blood stream or through open wounds (eg, fractures and ulcers). Orthopaedic infections may derive as sequelae of traumatic episodes or from surgery, especially when foreign material is implanted as in osteosynthesis. Damage to tissue leads to a decrease in blood supply and depression of the immune response, which can cause the formation of necrotic tissue and favor bacterial invasion. Bacteria, mostly *Staphylococci*, can then bind to damaged tissue and replicate, leading to an infection.

Unvascularized parts of bone may detach from vascularized bone and form a sequestrum. Clinical signs of infection persisting for longer than 10 days are associated with the development of necrotic bone and chronic osteomyelitis (COM). COM is characterized by the persistence of micro-organisms, low-grade inflammation, and the presence of dead bone (sequestrum) that may eventually develop into fistulous tracts. In most cases, there is poor local vascularization within a compromised soft tissue envelope. The infected foci within the bone are usually surrounded by sclerotic and poorly vascularized bone covered by a thickened periosteum, scarred muscle, and subcutaneous tissue (involucrum). The involucrum represents the body's attempt to wall off the offending material with reactive and inflammatory tissue, which is either bone or soft tissue. Antibiotics and the host's innate immune system cannot reach the avascular area inside; therefore, COM generally cannot be eradicated without surgical intervention.

The goal of surgery is to eliminate dead bone and achieve a viable vascularized environment. However, it should be noted that the involucrum is partially vascular and provides some structural support that should be taken into consideration during surgical treatment. During debridement, external fixators or spacers or both can be used to provide temporary stabilization, whereas systemic or local antibiotics are used to treat the infected site. There is no consensus on the time interval between debridement and definitive reconstruction, which is often performed when clinical findings and laboratory parameters have returned to normal. This time interval is

*Osteitis Centre, Privatklinik Döbling Wien, Wien, Austria.
†Department of Traumatology, Landesklinikum, Korneuburg Wiener Ring 3-52100, Korneuburg.
*Address reprint requests to Heinz Winkler, Osteitis Centre, Privatklinik Doebling, Heiligenstaedterstr 57-63, 1190 Wien, Austria. E-mail: h-winkler@aon.at, heinz.winkler@speed.at

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characterized by prolonged hospitalization and its associated costs, delayed mobilization, rehabilitation, and the risk of multiple surgeries. Given these drawbacks, which are especially prevalent in elderly patients, is it worth to wait?

The difficulties of treating COM derive from 2 distinct issues: (1) pathogen resistance against antimicrobials and immunologic defense and (2) osseous defects caused by osteolysis, sequestration, and surgical interventions. In this article, characters of COM would be described, including biofilm formation and classification, along with different surgical treatment options.

Biofilm

It has been believed that the development of COM results from inferior local blood supply and increased bacterial resistance. Infection treatment derived from the traditional conceptions of antimicrobial treatment in dealing with freely floating planktonic bacteria resulted in most failures. In the 1970s, Dr William Costerton elucidated the true reasons for bacterial resistance against conventional antimicrobial therapies. He showed that pathogens may change from the familiar planktonic (free floating) form into phenotypically different sessile forms after adhesion to poorly vascularized surfaces, forming an organized community of bacteria called biofilm. Biofilm-embedded bacteria require much higher concentrations of antibiotics for elimination compared with their planktonic forms for the following 2 reasons: (1) antimicrobial molecules must diffuse through the biofilm matrix to inactivate the encased cells, and (2) the extracellular polymeric substances constituting this matrix present a diffusional barrier for these molecules by influencing either the rate of transport of the molecule to the biofilm interior or the reaction of the antimicrobial material with the matrix material. Conditions that result in decreased growth, such as nutrient limitation or the presence of toxic substances (antibiotics), favor biofilm formation.

Gristina et al[1] have shown that the biofilm concept fully applies to COM (Fig. 1). In COM, our most obstinate opponents are not the familiar planktonic pathogens, but their phenotypically different sessile forms embedded in an extracellular matrix, the glycocalix.[2,3] The surface of devascularized bone and metal implants acts as a substratum for the attachment of bacteria and the formation of biofilms. Debridement may remove most of the bacteria, but even after a perfect debridement, some colonies that become detached from the biofilm during debridement may remain and are able to colonize niches of poorly vascularized surfaces and result in infection recurrence. This is the reason that most surgeons advocate for a 2-stage procedure, where one uses external fixators for temporary stabilization and avoids simultaneous insertion of osteosynthetic material at the freshly debrided site.

To more effectively treat the biofilm bacteria, others had previously proposed the idea of increasing antibiotic concentrations at the infection site by using local drug delivery systems. Buchholz and Engelbrecht[4] were the first to mix antibiotics and polymethylmethacrylate (PMMA) to create a

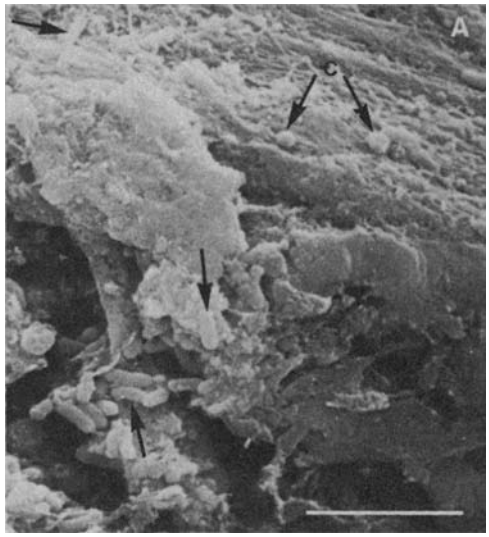

Figure 1 Polymicrobial biofilm community on bone. The film contains cocci (C) and rod-shaped bacteria (arrows); more bacteria are buried deeper within the biofilm. *Source*: Gristina AG, Oga M, Webb LX, Hobgood CD. Adherent bacterial colonization in the pathogenesis of osteomyelitis. Science 1985;228:990-993.

local carrier. From these findings, Klemm[5] developed techniques of using antibiotic-loaded bone cement in the form of beads to be placed into debrided bone defects. However, it became clear that antibiotic concentrations produced by antibiotic-loaded cement can kill planktonic bacteria, but may not be effective in eliminating remaining biofilm clusters. Between 90% and 95% of the antibiotic remains trapped in the cement, and the amounts released from the surface create only moderate antibiotic concentrations for the first few hours after implantation. This makes antibiotic-loaded cement rather ineffective as an antibiofilm tool, as 90% of implanted antibiotic bead chains and 50% of antibiotic spacers have been shown to be covered with biofilm at removal,[6,7] and may be associated with increased antibiotic resistance.[8,9] Treatment of small colony variants requires up to 100-fold of the minimum inhibiting concentrations (MIC) of antibiotics, and biofilm-embedded pathogens require up to 1000-fold MIC of antibiotics for elimination.[10] These concentrations are very difficult to reach using systemic antibiotic therapy and antibiotics released from PMMA.[11]

Classification

There are several systems available for classification of COM. For clinical practice, the Cierny-Mader classification[12] seems to be most valuable, as it is a clinical classification based on anatomic, clinical, and radiologic features. It divides COM into 4 anatomic stages (Fig. 2). Stage 1 or medullary osteomyelitis is confined to the medullary cavity of the bone. Stage 2 or superficial osteomyelitis involves only the outside of cortical bone and most often originates from a direct inoculation or a contiguous focus infection. Stage 3 or localized osteomyelitis usually involves both cortical and medullary bone. In this stage, the bone remains stable, and the infectious process does