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Biodegradable Antibiotic Delivery Systems in the treatment chronic osteomyelitis

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Abstract

An 82-year-old woman was referred to the orthopedic department with a three-month history of low-grade fever. She had a known past history of type 2 diabetes. She had been unwell for last 5-days, complaining of feeling hot and 'shivery' with general aches, particularly in her right shoulder. The staff in the residential home where she lived had called the general practitioner who had prescribed a three-day course of trimethoprim for a suspected urinary tract infection. On examination, she was pyrexia with a temperature of 39.5°C. She was drowsy but reusable. Pulse was 125 beats per minute and regular. Blood pressure was 90/55 mmHg. Heart sounds were normal with no added sounds or murmurs. The chest was clear. Her abdomen was soft and non-tender with no palpable masses or organs. The skin overlying the right shoulder was warm to touch and erythematous. She was unable to tolerate any passive movement of the joint. A plain x ray of her shoulder shows lucent defects in the head of the humerus with loss of the normally well-corticated surface. This is consistent with osteomyelitis. Two of 2-blood cultures and numerous operative cultures grew MRSA. His subsequent treatment consisted of intravenous vancomycin, achieving plasma drug levels approximating 24 µg/mL. This treatment was extended for 8 weeks, given the clinical concern for possible osteomyelitis in an area. Treatment was complicated by significant a decline in hearing. Biodegradable drug delivery systems provide a method for local delivery of drugs in deeper tissues, obviating parenteral or enteral usage; in some situations. A significant advantage is that much higher doses and/or strengths of the drug can be delivered locally than can be tolerated if the drug is delivered systemically. In this case report, we discussed the use of Biodegradable Antibiotic Delivery Systems in treatment chronic osteomyelitis.

Key words: Biodegradable Antibiotic Delivery Systems; MRSA; Osteomyelitis.

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Introduction

The treatment of chronic osteomyelitis includes debridement of the dead infected tissue, obliteration of dead space, osseous repair, adequate soft tissue coverage, and systemic antibiotics [1]. The delivery of antibiotics to bone varies considerably. Oral antibiotics are unpredictable with relatively low bone levels and are infrequently used. Intravenous antibiotics are used commonly in the treatment of chronic osteomyelitis [2]. Local antibiotic delivery has the

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advantage of high tissue concentrations with relatively low serum levels. This avoids some of the toxicity associated with systemic antibiotics, especially aminoglycosides [3]. Antibiotic-impregnated implants are particularly attractive because not only do they deliver high tissue levels of antibiotics but they also help obliterate the dead space that occurs after bone debridement [4, 5]. Antibiotic pumps do not achieve this desirable effect. The most common form of local antibiotic delivery by an implant is with the use of methylmethacrylate [6, 7] Various types of methylmethacrylate have been tested by elution studies [8]. The shape of the methylmethacrylate implant along with the type of methylmethacrylate has a significant effect on the amount of antibiotic delivery, as well as duration. Tobramycin, gentamicin, and vancomycin are the antibiotics that have been combined with methylmethacrylate [9].

Surgical management of chronic osteomyelitis has changed drastically in the past 25 years with the use of flaps and vascularized bone grafts. Because of the impaired blood supply to the affected regions, as well as decreased ability of the host immune system to clear infections, surgical intervention is almost always necessary. Thorough debridement of bone in chronic osteomyelitis is essential and is often the primary factor in eliminating infection. Such debridement often causes a large dead space that needs to be managed effectively to prevent recurrence of infection. The management of the dead space in this setting includes closed irrigation systems, local soft tissue flaps, vascularized free flaps, as well as a variety of methods for local antibiotic delivery. The local use of antibiotics to prevent skeletal infections was incorporated into general practice with the development of joint arthroplasty in Europe in the 1970s. Buchholz and Engelbrecht reported in a sentinel paper that penicillin, erythromycin, and gentamicin mixed into the cement used to affix prostheses to bone was found to provide high concentrations of antibiotics for extended periods of time, facilitating the use of antibiotics in infection prophylaxis for joint arthroplasty.7 In addition to this role, local antibiotic therapy has been instituted for treatment of arthroplasty infections, prophylaxis for open fractures, and treatment of chronic osteomyelitis. In 1979, Klemm created gentamicin-impregnated beads and used them to occupy dead space after debridement of infected bone. In more than 100\ patients, a cure rate of 91.4% was achieved.8

Case Report

An 82-year-old woman was referred to the orthopedic department with a three-month history of low-grade fever. She had a known past history of type 2 diabetes. She had been unwell for last 5-days, complaining of feeling hot and 'shivery' with general aches, particularly in her right shoulder. The staff in the residential home where she lived had called the general practitioner who had prescribed a three-day course of trimethoprim for a suspected urinary tract infection. On examination, she was pyrexia with a temperature of 39.5°C. She was drowsy but reusable. Pulse was 125 beats per minute and regular. Blood pressure was 90/55 mmHg. Heart sounds were normal with no added sounds or murmurs. The chest was clear. Her abdomen was soft and non-tender with no palpable masses or organs. The skin overlying the right shoulder was

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Discussion

The local delivery of antibiotics for chronic osteomyelitis is potentially an advantage over standard intravenous therapy. Not only does this biodegradable antibiotic implant obliterate the dead space, it delivers high doses of tissue antibiotics and aids in bone repair [10]. Furthermore, this implant does not need to be removed like methylmethacrylate. In the present study the patients showed evidence of excellent osseous repair, and none have required follow-up surgery such as autogenous iliac bone grafting despite the size of the defect and their location in weight-bearing bones. To date there have been no relapses of infection [11]. Most of the infections were due to S. aureus, and all but one of these were sensitive to tobramycin. The one mixed infection (E. coli, Klebsiella pneumoniae and methicillin resistant S. aureus) was treated with a combination of tobramycin and vancomycin implants [12]. These implants were selected based on the mixed flora and the fact that the staphylococcus present in this patient was methicillin resistant. It is interesting that this patient had the lowest bone repair score and the lowest functional outcome. Mixed bacterial bone infections are the most difficult to treat. This study is relatively small, although promising. Only six patients were reviewed, but the performance of the local antibiotic implants was quite consistent. Full degradation occurred, and bone repair occurred in an orderly manner. Two important questions remain unanswered. Can this technique be used without systemic antibiotics? If further studies prove successful without systemic antibiotics, there could potentially be significant cost savings [13]. Other [14, 15] showed in an animal model that calcium sulfate delivers adequate killing levels in tissue for up to six weeks with safe serum levels. If the same holds true in humans, then perhaps systemic antibiotics can be avoided. The cost savings would not only be in intravenous antibiotics but also in the venous catheter needed to deliver systemic drugs. Hospitalizations would be shortened and overall care easier. The second important question is late relapse. Chronic osteomyelitis is notorious for late

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relapse, even with aggressive systemic therapy and surgical treatment. At least in this small series with relatively short-term follow-up, the control of the infection was excellent.

Competing interests

The author declare that he has no competing interests.

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