Antibiotic-impregnated xenografts in the treatment of chronic osteomyelitic cavities

Seven cases followed for 3 to 5 years

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Summary. We describe seven patients with chronic osteomyelitis which developed in 3 following operation and in 4 after trauma. The treatment consisted of removal of dead tissue and filling the resulting cavities with gentamicin-impregnated xenografts. No antibiotics were used postoperatively. Urine gentamicin levels were above 0.5 µg/ml for 8 days. The patients were followed up for at least 3.5 years and neither clinical nor laboratory signs of infection were detected. These results lead us the conclusion that gentamicin-impregnated xenografts may have a place in the treatment of chronic osteomyelitis.

Résumé. Sept patients atteints d'ostéomyélite chronique dont l'origine est post-opératoire pour quatre et post-traumatique pour trois, ont eu le traitement chirurgical suivant: nettoyage avec ablation des tissus nécrosés et remplissage des espaces résiduels avec des xénogreffes imprégnées de Gentamycine (Unilab Surgibone). Il n'y a pas eu d'antibiothérapie post-opératoire. Le taux de Gentamycine dans les urines était au-dessus de 0,5 µg/ml pendant les 8 jours suivants. Tous les patients furent suivis au moins 3,5 ans sans qu'aucun signe clinique ou biologique d'infection ne soit détecté. Ces résultats nous conduisent à penser que les xénogreffes imprégnées de Gentamycine ont leur place dans le traitement de l'infection osseuse chronique.

Introduction

Despite advances in prophylaxis against infection, implant-related or traumatic chronic osteomyelitis remains a considerable problem [1]. Such infections are

often resistant to parenteral administration of antibiotics, and interest has focused on finding ways of delivering the antibiotic directly to the infected site. All the methods have some limitations, such as the need to remove the vehicle used and the uncontrolled delivery of the drugs [2, 10, 18, 20].

Xenografts have been reported to have a place in surgical practice, either to fill cavities [14] or to perform arthrodesis [4, 17]. Sennera was the first to describe the xenografts to fill the cavities in the presence of infection [14].

We have previously described the capacity of xenografts to deliver antibiotics [5], and we present our experience of this material in the treatment of chronic osteomyelitis.

Materials and methods

Seven patients, all with the clinical and radiological signs of chronic osteomyelitis, as well as skin sinuses, were treated. None had had antibiotics for at least one week before operation which involved radical excision of the sinuses, affected bony tissue and sequestra, if present, and implantation of gentamicin-impregnated xenografts into the resulting cavities.

The xenografts were prepared as previously described [5]: 5×5×5 mm blocks of Unilab Surgibone® were placed in gentamicin sulphate (Ibrahim Etem, Turkey). The amount of gentamicin was 25 mg for each block. The total number of the blocks used was different for each case, due to the volume of the expected cavity. The contact time of xenografts with gentamicin was 8 h.

Neither drains nor systemic antibiotics were used postoperatively. Gentamicin levels in urine were measured daily by the disc diffusion technique of Finegold and Baron [3], until the values were below 0.5 µg/ml. We preferred to measure the urinary levels of gentamicin, rather than serum levels, so as to estimate the antibiotic activity for 24 h, and not for a single instant in a day.

There were 6 males and one female, with a mean age of 36.4 years (range 18 to 61 years). The mean duration of symptoms was 36 months (range 5 to 96 months). The site of infec-

Table 1. Data on 7 patients treated for osteomyelitis

Patient no.	Sex-age	Location of infection	Duration of infection	Type of infection	Isolated bacteria
1	M-40	Tibial shaft	4 years	Postoperative	<i>S. aureus</i>
2	M-35	Distal femur	5 months	Posttraumatic	<i>S. aureus</i>
3	M-61	Proximal tibia	2 years	Posttraumatic	<i>E. coli</i>
4	F-18	Femoral shaft	8 months	Posttraumatic	<i>S. aureus</i>
5	M-25	Tibial shaft	4 years	Postoperative	<i>S. aureus</i>
6	M-33	Femoral shaft	8 years	Postoperative	<i>S. aureus</i>
7	M-43	Proximal tibia	2 years	Posttraumatic	<i>S. aureus</i>

M: Male, F: Female

tion was the tibia in 4 patients and the femur in 3. Three patients had infection following operation and four consequent to trauma. The organisms isolated were *Staphylococcus aureus* in six patients and *Escherichia coli* in one. Antibiotic sensitivity tests revealed that all the organisms isolated were sensitive to gentamicin sulphate. Data of the patients are shown in Table 1.

According to Cierny's classification [1], all the patients had anatomical type III lesions of localised osteomyelitis with full thickness cortical sequestration, a discrete lesion within a stable bony segment. Typically, the entire lesion can be completely excised with a cuff a viable tissue while preserving the integrity of the bony segment involved. All the patients were in physiological class A which means that they responded normally to stress and trauma [1].

Results

Mean urine levels of gentamicin are showed in Fig. 1. The level measured at 24 h was 4 µg/ml, 2 µg/ml on day 3, 4.5 µg/ml on day 5 (the peak), and 0.5 µg/ml on day 8. After this time, the levels were below the effective level of 0.5 µg/ml.

The following criteria were taken into consideration in evaluating the results of the operation:

- recurrence of the sinus
- recurrence of the signs of inflammation with a raised erythrocyte sedimentation rate and/or leucocytosis
- pathological fracture.

Fig. 1. Urinary excretion of gentamicin sulphate **Fig. 2.** a Case 4. Sinogram before operation. b Radiograph 3.5 years after operation

At an average follow-up of 3.5 years (range 3.5 to 5 years), none of the patients had clinical or laboratory signs of infection, no pathological fractures had occurred and the grafts were united (Fig. 2). Local or systemic adverse reactions to gentamicin were not observed during the study period. Nephrotoxicity was not detected by laboratory tests and no complaints of ototoxicity were recorded.

Discussion

The essential features of the treatment of chronic osteomyelitis are adequate debridement, obliteration of dead space and specific antibiotic therapy [1]. After debridement, obliteration of the remaining cavity is achieved by different methods, such as using the surrounding soft tissues [2], calcium hydroxyapatite [15], bone cement [8, 9, 11, 13], collagen sponge [10], plaster of Paris [2], lactic acid oligomer [18], or bone grafts, either autogenous [7] or heterogenous [14]. Although most of these techniques have been used in clinical practice to deliver antibiotics, they have some limitations mainly due to the need to re-

move the vehicles. Only autogenous bone grafts have been proved clinically to deliver antibiotics and stimulate osteogenesis. Although the osteogenic power of xenografts is inferior to that of autogenous bone [6], it is sometimes impossible to fill the large cavities with autografts, and morbidity from the donor site may follow [19]. Sennera was the first to use xenografts for this [14], and we have previously shown that xenografts can deliver antibiotics in vitro [5].

The only possible objection to the use of gentamicin-impregnated xenografts in the treatment of chronic osteomyelitis may be the relatively short duration of antibiotic release, but for patients with osteomyelitis, the duration of antibiotic administration is controversial and the standard 6 weeks has no documented superiority over treatment for one week [1, 12]. The benefit of prolonged high concentration of gentamicin is restricted for the first hour it is applied [16]. In the present study, we did not use additional systemic antibiotics, and so we have clearly demonstrated the effectiveness of our delivery system. Josefsson et al. had shown that local administration of antibiotics resulted in a significant decrease in the rate of infection compared with systemic administration in total hip arthroplasties [11].

We used gentamicin in our cases because all the organisms isolated were sensitive to it and this allowed us to compare our results with those of others, since gentamicin is the most commonly used antibiotic with different systems of delivery [2, 7, 8, 9, 10, 11, 15, 18]. Although we had shown that gentamicin, ciprofloxacin and penicillin G could be delivered by xenografts in vitro [5], other antibiotics must be evaluated in this manner, if the isolated organism is resistant to these antibiotics.

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