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Gentamicin-PMMA beads in the treatment of chronic osteomyelitis

Fifty cases of chronic osteomyelitis, associated with septic arthritis in five cases, were treated with radical surgery, systemic antibiotics, and insertion of gentamicin-PMMA beads. Seven cases were lost to follow-up. The remaining 43 cases were followed up for an average of 14 months. All but four cases healed.

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Klemm (1980) introduced the use of gentamicin-PMMA (polymethylmethacrylate) beads in bone and soft tissue infections in 1973. As in previously used methods, the most important part of the treatment is meticulous surgical debridement, i.e. removal of foreign material and sequestra and excision of all infected and necrotic tissues. Any procedure which falls short of achieving this will most probably fail to eradicate the infection, whatever method of antibiotic application is used. We have evaluated our treatment which combines radical excision of the infectious lesion, temporary insertion of gentamicin cement beads, and systemic antibiotics.

Patients and methods

Fifty patients were consecutively operated on with the use of gentamicin-PMMA beads (Septopal® chains, E. M. Merck Company, West Germany) for chronic bone infection of various aetiologies (Table 1), between March 1981 and December 1983. Septic arthritis adjacent to the chronic bone lesion was present in five patients.

The average age was 27 (5–90) years. The male-to-female ratio was 3:1. The mean interval between onset of symptoms and treatment was 4.6 years (range 1 month–20 years). Thirteen patients had had the disease for more than 7 years. Twenty-one patients had 1–6 previous operations for osteomyelitis. The femur was the commonest site for infection (24 cases), followed by the tibia (12 cases). Sixteen patients had the infection in the knee region. The rest were scattered among other bones (humerus 5, os calcis 3, radius 2, tarsal bones 2, below knee stump 1, and fibula 1). The average period for hospital stay was 38 (3–150) days.

Diagnosis

In all 50 cases, the diagnosis was established from the history, the clinical findings, and the radiographic picture. In 38, the diagnosis could be verified with positive bacterial culture from tissue biopsies or swabs taken from the lesion. Eight cases had negative cultures, and in four the culture reports were lost. *Staphylococcus aureus* was the most common microbe and was found in 25 of the lesions (Table 2).

Table 1. Aetiology of chronic osteomyelitis with or without septic arthritis.

	Chronic osteomyelitis	With septic arthritis	Average age (years)
Haematogenous	25	3	24
Open fracture	7	–	30
Internal fixation*	15	1	28
Operation on soft tissue	1	1**	70
Burn	1	–	35
Amputation stump	1		20
Total	50		27

* Done for closed fractures in 9 cases, for open fractures in 5, and complicating shoulder arthrodesis with screw fixation in 1.

** Complicating repair of the medial collateral ligament.

Table 2. Microbiological findings in 38 cases with positive cultures, and their sensitivity to gentamicin, and ampicillin and/or cloxacillin (S = sensitive, R = resistant)

Pathogen	No. of pathogens	Gentamicin sensitivity			Ampicillin and/or Cloxacillin sensitivity	
		S	R	Unknown	S	R
Staph. aureus	25	20	3	2	23	2
Proteus	6	4	2	–	3	3
Pseudomonas	6	6	–	–	3	3
Salmonella typhii	2	2	–	–	–	2
Klebsiella	1	1	–	–	–	1
Strept. faecalis	1	–	–	1	1	–
Staph. epidermidis	1	1	–	–	–	1
Total*	42	34	5	3	30	12

* Mono-infection was noted in 33 patients, and mixed infection in 5 patients.

Surgery

In each of the 50 cases a radical operation aimed at the removal of as much as possible of the infected tissue was planned. The pre-operative extent of the lesion was assessed with the aid of standard radiograms, tomography, and sinography when appropriate. The operation was then done under general anaesthesia, and a tourniquet was used whenever possible. The aim was radical excision of all necrotic and infected tissues, including sinuses. The cavities were then irrigated with saline and hydrogen peroxide, and filled with gentamicin-PMMA beads. One or two beads were left outside the skin to facilitate removal, except in two cases where bone grafting was planned and performed 6 weeks later. In 22 patients a drain was inserted and removed after 24–48 h. On average 16 beads were inserted, and removed after an average of 19 (8–53) days. Twenty-six patients needed general anaesthesia for the removal.

Systemic antibiotics

Any antibiotic, if given, was stopped 7 days before the operation, in the hope of obtaining a positive culture from the operation specimens. Systemic antibiotic treatment was then started immediately after the specimens were taken. Ampicillin and cloxacillin in combination (Ampiclox®, 500 mg Ampicillin and 500 mg Cloxacillin) was injected intravenously or intramuscularly every 6 h for the first 48 h, after which the peroral route was used. This was continued until the sensitivity test on the microbes was available, after which the appropriate antibiotic was either started or continued. The average duration of systemic antibiotic was 3 (2–12) months.

Follow-up

Seven patients were lost to follow-up. The remaining 43 patients were followed up for an average of 14 (3–30) months. The observation period after cessation of systemic antibiotic averaged 6 (1–24) months. The results were classified as either success or failure. The criteria for success were:

a. Wound healing within 4 weeks.
b. Freedom from pain and toxic symptoms.
c. Absence of progressing radiographic changes.
d. Closure of sinuses.

If a case did not fulfil these criteria, it classified as failure.

Results

Thirty-nine of 43 patients were classified as successful (including the two cases which had bone grafting). Four cases were failures; the sinus failed to close in two, while infection failed to subside, as evidenced by pain and toxic symptoms in one, and by pain and a residual sequestrum in the other case. Of these failures, two grew *staphylococcus aureus,* one *proteus* and one *pseudomonas*. Yet all these organisms were found sensitive to gentamicin. In two failures, the infection was very widespread and aggressive.

Discussion

In eight of the 46 available bacterial cultures, the result was negative. This might be explained by the fact that pre-operative antibiotic treatment had reduced the bacteria significantly, so that the culture technique was not sensitive enough to pick up low-grade chronic infections, or that the specimens were not taken from an active part of the lesion. Other authors have had similar experience (Vécsei & Barquet 1981). The majority of the infections in our study were caused by *staphylococcus aureus;* of these, 20 were sensitive to gentamicin. Four-fifths of the organisms in this study were sensitive to gentamicin. This agrees with other reports (Hedström et al. 1980, Vécsei & Starlinger 1982). When we correlated this finding with the clinical outcome, we found that five of the 39 successful cases grew organisms resistant to gentamicin (Table 2). On the other hand, all our four failures grew organisms found sensitive to gentamicin. The explanation for this is two-fold. Firstly, a microorganism affected only by gentamicin concentrations above 16 mg/l is usually characterized as resistant. These microbes are, however, often affected by the extremely high local concentrations, up to 100 mg/l or more, achieved with the beads in the wound haematoma and secretion (Dingeldein & Wahlig 1976, Wahlig et al. 1978). Secondly, a failure is most probably due to insufficient surgical eradication of the bacteria-bearing tissues, rather than to the presence of organisms resistant to gentamicin. However, provided that bacterial residue is kept to a minimum, a high success rate may be anticipated with the local use of gentamicin-PMMA beads.

The recommended period for leaving the gentamicin beads in a bone cavity is 10–14 days (Klemm 1980). If the beads are left longer, they are often difficult to remove, which also is our own experience (26 of our 50 cases needed general anaesthesia for removal of the beads). Studies have shown a gradual decrease in the release of gentamicin from the beads, but after 70 days therapeutically active concentrations can still be found in the connective tissues surrounding the beads (Wahlig & Dingeldein 1983).

Our choice of ampicillin and cloxacillin as "the best blind guess", proved fairly successful as three quarters of the positive cultures were sensitive to this combination (Table 2).

Systemic antibiotics were used for an average of 3 months, which might contribute to the somewhat better results than those where no or only short-term systemic antibiotics were given (De Groote et al. 1980). Moreover, no recurrence was observed during the follow-up period after cessation of the antibiotics.

The somewhat long hospitalization periods, on average 38 days, reflect the social conditions in Kuwait. Many labourer-patients could not be discharged early for the simple reason that their accomodation was inadequate for convalescence.

In contrast to hospitalization, the follow-up periods were often short. This again reflects the fact that the majority of the inhabitants of Kuwait are non-Kuwaitis, who return to their home country shortly after finishing their treatment or their work contracts. Thus, the average follow-up period in our study was too short for us to make a reliable prognosis.

However, the results are promising. An over-all 90 per cent success rate, (we avoid the term cure-rate), compares well with other studies (Jenny & Taglang 1980, Weise & Weller 1980). The most valuable advantage with the method is that the wound can be closed primarily, and the patient mobilized early. It is also a simple method, in contrast to earlier methods with either lengthy suction-irrigation drains, which often leaked or became blocked, or where secondary healing was awaited.

We suggest that gentamicin-PMMA beads should be included in the armamentarium for the treatment of chronic osteomyelitis.

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