Allograft bone in two-stage revision of the hip for infection

IS IT SAFE?

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A two-stage procedure was carried out on 57 patients with confirmed infection in a hip replacement. Allograft bone was used in the second stage. Pathogenic organisms were identified in all patients. In stage 1, the prosthesis was removed together with infected tissue. Antibiotics were added to customised cement beads. Systemic antibiotics were not used. At the second stage, 45 of the patients had either acetabular impaction grafting, femoral impaction grafting or a combination; 12 had a massive allograft.

Eight patients suffered recurrent infection (14%), in six with the original infecting organism. The risk factors for re-infection were multiple previous procedures and highly resistant organisms. We believe that systemic antibiotic therapy should be considered for these patients. Allograft bone is shown to be a useful adjunct in most infected hip replacements with considerable loss of bone stock.

Infection is perhaps the most serious complication of replacement of the hip. The consequent loss of bone stock is an added challenge. While single-stage exchange has had good results,1-3 two-stage revision appears to offer a better prospect of eradicating the infection.4,5 The use of allograft bone for reconstruction at the second stage is controversial. There have been a number of favourable reports on the use of massive allograft or morsellised allograft within larger series of revisions.6-11 We describe the use of both massive and morsellised allograft in two-stage revision for infected hip replacements in a series of 57 consecutive patients who underwent surgery according to a set protocol.

Patients and Methods

From our database we identified 67 patients who had undergone two-stage revision for infection between 1989 and 1999. The inclusion criteria were confirmed infection with positive microbiology, the use of allograft bone in the second stage and a minimum follow-up of two years from the second stage. Four patients had died from unrelated causes within that period. Six had been lost to follow-up or their notes had been destroyed but none had shown evidence of infection at their most recent review. This left 57 patients available for study. There were 29 men and 28 women with a mean age of 62 years (28 to 82). Only 11 had infected primary replacements; the remainder had infected revisions. The mean number of previous operations was three (1 to 7). In 34 the original diagnosis had been osteoarthritis (Table I).

A needle aspiration of every affected hip was carried out before the first stage to confirm infection and to determine the appropriate antibiotics to be used in the cement. During the first stage a minimum of five tissue specimens was taken. Only those patients in whom infection was confirmed in tissue biopsies were included in the study.

At the first stage, a radical debridement was performed along with removal of all components before inserting customised antibiotic cement beads tailored to the microbiological findings. The dose of antibiotic added to the cement at this stage was much greater than that to be used in the subsequent second stage.

Table I. Diagnosis in the 57 patients

<table>
<thead>
<tr>
<th>Original diagnosis</th>
<th>Number of cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Osteoarthritis</td>
<td>34</td>
</tr>
<tr>
<td>Developmental hip dysplasia</td>
<td>6</td>
</tr>
<tr>
<td>Trauma</td>
<td>6</td>
</tr>
<tr>
<td>Rheumatoid arthritis</td>
<td>4</td>
</tr>
<tr>
<td>Perthes’ disease</td>
<td>2</td>
</tr>
<tr>
<td>Septic arthritis</td>
<td>1</td>
</tr>
<tr>
<td>Avascular necrosis</td>
<td>1</td>
</tr>
<tr>
<td>Ankylosing spondylitis</td>
<td>1</td>
</tr>
<tr>
<td>Tumour</td>
<td>1</td>
</tr>
<tr>
<td>Slipped upper femoral epiphysis</td>
<td>1</td>
</tr>
</tbody>
</table>
When vancomycin or gentamicin was indicated, 2.0 g of vancomycin per 40 g pack of Palacos R cement (Schering Plough Ltd, Welwyn Garden City, UK) or 1.0 g of gentamicin per 40 g pack were used. Systemic antibiotics were not given except as prophylactic doses of cefuroxime to cover the operative procedure (750 mg tds for 48 hours).

The timing of the second stage was based on clinical, radiological and laboratory (ESR <20 mm/hr) evidence that infection had been overcome. The interval between stages was variable, ranging from one to 79 months (median 6). Repeat procedures for debridement were required in two cases, but long delays were usually due to uncertain resolution of infection.

At the second stage, the debridement was repeated. The antibiotics to be added to the cement were changed when indicated by the culture results obtained at the first stage. Most patients had a single organism, most commonly coagulase-negative Staphylococcus (CNS). More than half of the organisms were highly resistant (Table II). Again five tissue specimens were taken before re-implantation.

In both the first and second stages the cement used in all cases was Palacos R (Schering Plough Ltd) to which various antibiotics had been added, most commonly vancomycin, gentamicin or a combination. At the second stage the amount of antibiotic added to the cement was less than that at the first stage because of concerns about mechanical strength, 0.5g of gentamicin being added to a 40 g pack and 1 g of vancomycin when required. One patient was infected with Candida albicans against which fluconazole was used successfully in the cement. The patients received routine intravenous cefuroxime (750 mg tds for 48 hours) to cover reimplantation but did not have further systemic antibiotics for the infecting organism.

The patients had either impaction grafting of the acetabulum and/or the femur, sometimes with a cortical strut graft (45), or a massive allograft to either the femur or acetabulum with or without added impaction grafting (12) (Table III). Allograft was obtained from our tissue bank which was established in 1989 and set up according to the guidelines of the Musculoskeletal Council of the American Association of Tissue Banks. Bone obtained between 1989 and 1991 was fresh-frozen allograft. All bone used for grafting subsequent to this was irradiated with 2.5 mega rads and pieces were sent for culture at the time of use.

Femoral impaction grafting was performed according to the Exeter technique11-13 using an Exeter stem (Stryker-Howmedica-Osteonics, Newbury, UK) in 25 cases. Acetabular impaction grafting was done using standard impaction tools (Stryker-Howmedica-Osteonics). Most of the acetabular implants were the Charnley Elite (Depuy, Leeds, UK) flanged socket (29 of 33 cases). In ten cases an acetabular support ring was added and in 21 stainless-steel rim or floor mesh (Stryker-Howmedica-Osteonics) was used to contain the grafted bone within the defect. Proximal femoral allografts were inserted using the Huckstep interlocking stem (B. Braun Medical Ltd, Sheffield, UK) in four cases and a long-stem titanium grit-blasted prosthesis (Johnson & Johnson Orthopaedics Inc, Raynham, Massachusetts) in six. Reconstruction with a proximal femoral allograft was done according to the technique previously described by Allan et al.14

The patients were reviewed at irregular intervals over a mean period of 4.5 years (2 to 10.5).

Results
This study concentrated essentially on the incidence of reinfection after bone allografting. No attempt was made to assess radiologically the performance of the allograft. Eight patients redeveloped infection (14%) in six with the original infecting organism (Table IV). In one patient, (case 55), the responsible organism was Staphylococcus aureus sensitive to gentamicin. It was cultured at the time of the second stage and also at the repeat debridement. The other seven patients had aggressive bacterial infections with gentamicin-resistant CNS and/or gentamicin-resistant enterobacteria.

Table II. Details of the infecting organisms in the 57 patients

<table>
<thead>
<tr>
<th>Organism identification</th>
<th>Number of cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Coagulate-negative Staphylococcus</td>
<td>33</td>
</tr>
<tr>
<td>(18 resistant, 15 sensitive)</td>
<td></td>
</tr>
<tr>
<td>Polymicrobial organisms</td>
<td>8</td>
</tr>
<tr>
<td>Staphylococcus aureus</td>
<td>4</td>
</tr>
<tr>
<td>Streptococcus</td>
<td>3</td>
</tr>
<tr>
<td>MRSA*</td>
<td>2</td>
</tr>
<tr>
<td>Enterococcus</td>
<td>2</td>
</tr>
<tr>
<td>Pseudomonas</td>
<td>2</td>
</tr>
<tr>
<td>Escherichia coli</td>
<td>1</td>
</tr>
<tr>
<td>Candida</td>
<td>1</td>
</tr>
<tr>
<td>Bacteroides</td>
<td>1</td>
</tr>
</tbody>
</table>

* methicillin-resistant Staphylococcus aureus

Table III. Details of the type of allograft used in the 57 patients

<table>
<thead>
<tr>
<th>Type of allograft</th>
<th>Number of cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Impacted acetabular, morsellised graft alone</td>
<td>22</td>
</tr>
<tr>
<td>Impacted femoral, morsellised graft alone</td>
<td>6</td>
</tr>
<tr>
<td>Both femoral and acetabular impacted graft</td>
<td>11</td>
</tr>
<tr>
<td>Impacted femoral, morsellised and cortical strut graft</td>
<td>6</td>
</tr>
<tr>
<td>Massive femoral allograft, plus impacted acetabular allograft</td>
<td>8</td>
</tr>
<tr>
<td>Massive femoral allograft, plus massive acetabular allograft</td>
<td>2</td>
</tr>
<tr>
<td>Massive acetabular allograft, plus impacted femoral graft</td>
<td>2</td>
</tr>
</tbody>
</table>
These bacteria were identified at the time of aspiration and the appropriate antibiotics were added to the cement at both stages. The remaining patient (case 22) was reinfected with \textit{Streptococcus viridans}, a mouth commensal organism.

Seven of the eight infected patients had morsellised grafts impacted into the acetabulum; the other had a block acetabular allograft. On the femoral side five had no grafts, one had impaction grafting plus a cortical strut, and two had massive femoral allografts. All allograft bone, cultured at the time of use at the second stage, remained sterile. There were no catastrophic graft failures. Sixteen patients developed non-infective complications (Table V) the incidence of which (28\%) was comparable with that of other series dealing with complex reconstructions.

Of the eight patients who became reinfected, only two were successfully treated at a second two-stage procedure (cases 7 and 22). Of the remaining six, three (cases 14, 45 and 55) required excisional arthroplasty to eradicate the infection and of those, one remains infected (case 14). One patient died from an unrelated cause (case 20) before revision, one is still infected despite a repeat two-stage procedure (case 18) and another (case 14) is awaiting further surgery. Eleven patients had positive cultures from tissue removed at the time of the second stage; five of these patients subsequently became clinically infected.

Discussion

Eradication of infection and restoration of bone stock remain a challenge in hip replacement surgery. The use of allograft bone in infected cases has been questioned in the past.\textsuperscript{15} Nestor \textit{et al}\textsuperscript{16} suggested a three-stage protocol for reimplantation using bone graft. In their series using allograft bone, in most cases with an uncemented prosthesis, the infection rate was 18\%. Berry \textit{et al}\textsuperscript{6} had two cases of reinfection (11\%) in 18 patients who had received either morsellised or massive allografts. Alexeef \textit{et al}\textsuperscript{7} had no further infection in 11 patients with massive allografts. English \textit{et al}\textsuperscript{11} reported four cases of infection (7.5\%) in 53 patients when femoral impaction grafting was used at the second stage.

In our series the rate of reinfection of 14\% was higher than that in other series for two-stage exchange. Even in this relatively large series the small number of recurrent infections makes statistical analysis meaningless. A number of factors known to be influential\textsuperscript{17} need to be examined if

\begin{table}[ht]
\centering
\caption{Details of the eight patients who developed re-infection}
\begin{tabular}{|c|c|c|c|c|c|c|}
\hline
\textbf{Case} & \textbf{Organism}\textsuperscript{*} & \textbf{Positive culture at second stage} & \textbf{Reinfecting organism} & \textbf{Number of previous operations} & \textbf{Acetabular allograft} & \textbf{Femoral allograft} & \textbf{Outcome} & \textbf{Comment} \\
\hline
7 & CNS, \textit{enterococcus} (resistant) & CNS & Same & 4 & Morsellised & None & Successful revision & Required two 1\textsuperscript{st} stage debridements \\
14 & CNS (resistant) & CNS (resistant) & Same & 3 & Morsellised & None & Waiting revision & \\
18 & CNS (resistant) & Negative & Same & 5 & Massive & Massive & Re-infected & Repeat two-stage unsuccessful \\
19 & CNS (resistant), \textit{enterobacter} & Negative & Same & 3 & Morsellised & None & Re-infected & Still infected after \\
20 & \textit{Enterococcus} (resistant) & Negative & Same & 3 & Morsellised & None & Died before revision & Girdlestone excision \\
22 & CNS (resistant) & CNS & \textit{S. viridans} & 5 & Morsellised & None & Successful revision & Likely haematogenous infection \\
45 & CNS (resistant) & CNS (resistant) & Same & 2 & Morsellised & Cortical strut & Girdlestone excision & Required two first-stage debridements. Morbidly obese. Poor skin. \\
55 & \textit{Staph. aureus} (sensitive) & \textit{Staph. aureus} & CNS (sensitive) & 4 & Morsellised & Massive & Girdlestone excision & No abductors, therefore not reimplanted \\
\hline
\end{tabular}
\textsuperscript{* CNS, coagulase-negative \textit{Staphylococcus}. Text in parentheses represents gentamicin sensitivity}
\end{table}

\begin{table}[ht]
\centering
\caption{Details of the non-infective complications}
\begin{tabular}{|c|c|c|}
\hline
\textbf{Complication} & \textbf{Number} & \textbf{Outcome} \\
\hline
Broken stem of femoral implant & 1 & Revised \\
Dislocation & 6 & Three revised. Others stabilised \\
Aseptic loosening & 3 & All revised \\
Substantial haematoma & 1 & Drained. No infection \\
Femoral nerve palsy & 1 & Recovered \\
Symptomatic trochanteric nonunion & 3 & Two reattached to unite. One treated conservatively \\
Pulmonary embolus & 1 & Recovered \\
\hline
\end{tabular}
\end{table}
we are to explain the apparent high rate of infection in our series, for example the virulence of the organism, the use of local depot antibiotic only and the patient population.

While gentamicin-resistant CNS are not classified as virulent organisms there is no doubt that these are more difficult to eradicate than most.18 Two patients required repeat first-stage debridements to control infection; one was still infected despite two-stage exchange performed twice and another remained infected after two exchanges and an excisional arthroplasty. These cases demonstrate the tenacity of the infection and the difficulty in eradicating it in some patients.

One difference between our series and others, in which two-stage exchanges were performed, is the absence of systemic antibiotic therapy. A number of papers have established the capability of antibiotic-loaded cement to deliver a much greater local concentration of antibiotic than is possible by systemic therapy.19-22 and to be effective in eliminating infection.3,23 In six of the eight infected cases in our series, the bone cement was loaded with vancomycin. On the other hand there were 26 patients in whom infection was eliminated with this vancomycin regime. While vancomycin has been shown to elute in high levels during the early days after implantation, the concentration falls off steadily.24,25 If organisms are sensitive only to vancomycin this may not give sufficient time to eradicate the infection. The addition of systemic therapy may have improved the results.

Previous reports have recorded the results of cultures at the time of reimplantation of a prosthesis;6,10,11,22,26 11 patients in our series had positive cultures. The significance of this is uncertain. English et al11 recommended a perioperative frozen section to predict the risk of subsequent infection. Banit, Kaufer and Hartford28 found the use of frozen sections to give satisfactory results. Prolonged systemic antibiotic therapy may perhaps be considered in patients infected with organisms sensitive only to vancomycin, in addition to the use of antibiotic-loaded cement. Patients with highly-resistant organisms, and a history of multiple procedures, should be warned that the outcome remains uncertain.

References