Cross-linked polyethylene and bisphosphonate therapy for osteolysis in total hip arthroplasty: A case report

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ABSTRACT

A 39-year-old woman underwent bilateral total hip arthroplasty with conventional, ethylene oxide-sterilised liners when she was a subject in a radiostereometric analysis study. Within 2 years she had rapid polyethylene wear with aggressive, asymptomatic, and periprosthetic osteolysis on both sides. Oral alendronate therapy halted the progression of osteolysis over a year and revision to cross-linked polyethylene liners was then undertaken while one stem was curettaged and the other revised. Radiostereometric analysis revealed a 96% reduction in wear rate over 2 years with the cross-linked liners. On stopping alendronate treatment, aggressive osteolysis recurred on the curettaged but not on the revised femur.

Key words: bisphosphonates; hip arthroplasty; osteolysis

INTRODUCTION

Periprosthetic osteolysis is the dominant problem in total hip arthroplasty (THA). It is generally accepted that osteolysis is mainly due to particulate wear debris from the bearing surface leading to macrophage-induced osteoclastic bone resorption. Recently, 2 potentially major improvements have been reported: the reduction in wear debris volume by cross-linked polyethylene and bisphosphonate inhibition.
of bone resorption \textit{in vitro}\textsuperscript{5} and in animal models of particle-induced osteolysis.\textsuperscript{6} We present a case of periprosthetic osteolysis, followed meticulously for 5 years, in which both of these new strategies were utilised.

**CASE REPORT**

In 1997 a very active 39-year-old woman underwent staged bilateral THA for osteoarthritis. Implants consisted of Spectron EF femoral stems (Smith & Nephew, Memphis, United States) with 28 mm zirconium oxide (ZrO) heads, and cemented with Palacos-G (Schering-Plough, Brussels, Belgium). The uncemented cups were both Reflexion 1 (Smith & Nephew, Memphis, United States) sealed with a central hole cover and used with 20° angulated polyethylene liners made of GUR 1050 sterilised with ethylene oxide (EtO).

**Figure 1** Initial postoperative anteroposterior radiographs of (a) right and (b) left hips.
The patient participated in a radiostereometric analysis (RSA) study of cup fixation. Porous-coated shells were used on each acetabulum, with an additional hydroxyapatite (HA) coating on the right side. With the 20° elevated liners in a proximal position, the cups had satisfactory orientation and the stems were well cemented and positioned (Fig. 1).

At one year postoperatively, she had an excellent clinical outcome and was very active. Radiographs appeared satisfactory.

At 2 years postoperatively, she encountered no problems and was able to continue to lead a full and very active lifestyle. However, radiographs revealed a rapidly progressing periprosthetic osteolysis of

![Radiographs of (a) right and (b) left hips at 2 years postoperatively, showing bilateral femoral periprosthetic osteolysis. Note the absence of osteolysis on the acetabular side.](image)
both femurs (Fig. 2). The left stem (femoral head) had subsided by 0.8 mm while the right stem had subsided by 0.2 mm (mean value for Spectron stems, 0.1 mm). A stress test of 3 times of bodyweight applied at 2 months showed a subsidence of 0.17 mm (mean value for Spectron stems, 0.05 mm). RSA measurements indicated that the cups remained stable and the interfaces were in good condition. Proximal femoral head penetration (wear) on the left and right sides measured 0.64 mm and 0.72 mm, respectively. The patient was advised to reduce her activity level, and treatment with the oral bisphosphonate—alendronate (10 mg once daily)—was commenced.

Investigations conducted 3 years postoperatively revealed that progressive osteolysis had halted and that a more sclerotic line had surrounded the lyses (Fig. 3). Stem subsidence remained at 0.80 mm on the left side and measured 0.40 mm on the right side.
Acetabular wear had worsened on both the left (0.85 mm) and right (0.96 mm) sides. The patient remained asymptomatic and, although having reduced her activities, she was still more active than most THA patients. The EtO-sterilised liners were exchanged for 5-Mrad cross-linked polyethylene and the ZrO heads were replaced with new ones.

A synovectomy was performed bilaterally. The right proximal femur was curettaged and cement packed in to seal off the cavity. The left stem was extracted with the proximal cement mantle and a new stem cemented in place. Air bubbles from the narrow cement canal and sclerotic bone prevented the formation of an optimal cement mantle (Fig. 4). Alendronate was discontinued after 3 months at the patient’s request.

At 4 years postoperatively, the cup interfaces remained in excellent condition with stable acetabular components. The patient was satisfied with the result. Head penetration was very low at 0.10 mm

Figure 4  Postoperative radiographs of (a) right and (b) left hips following exchange of the left femoral stem and curettage of right femoral granulomata.
bilaterally (creep plus wear). As expected, the stem-cement interface did not look optimal on the revised side, however, no active lysis was apparent. On the right side the osteolysis had probably increased a little but she remained asymptomatic. Subsidence of the right stem was now 0.70 mm after initial surgery and was 0.30 mm after revision for the left side.

At 5 years postoperatively, the cups remained very stable. No migration could be detected and the interfaces were still free from radiolucent lines. Wear remained very low at 0.10 mm and was too low to be measured even with RSA. No evidence of osteolysis progression was seen in the left femur. However, there was a subsidence of 0.5 mm since revision with a $1.7^\circ$ of retroversion. The right side, in contrast, showed extensive femoral osteolysis with only the recemented proximal cement and the distal 3 cm remaining fixed to the femur (Fig. 5). The distal cement has been stable over the 5 years of follow-up. The

Figure 5 Radiographs of (a) right and (b) left hips at 5 years postoperatively. Osteolysis has returned in the right femur. The left femur remains in satisfactory condition.
stem itself had subsided 1.1 mm since the initial surgery and had rotated 4º posteriorly.

The patient had reduced her activities by this time. She also experienced mild thigh discomfort on the left side but without functional limitations. She has been recommenced on bisphosphonates and was awaiting revision at the time of writing this report.

DISCUSSION

In this case rapid early osteolysis occurred in bilateral THA with a high polyethylene wear rate of 0.30 mm/year bilaterally. This is much more than the regarded 'safe' level of 0.10 mm/year and is probably a major reason for the early onset of bilateral osteolysis. Although the patient reduced her activities in the later years following conversion to cross-linked polyethylene liners, her activity level is still very high compared with that of those in her age group.

The reduction in proximal wear rate with cross-linked polyethylene is dramatic: 0.05 mm (left)/0.15 mm (right) compared to 0.64 mm/0.72 mm over 2 years. This reduction is even more impressive given that the head penetration in the first 2 months was high (0.05 mm and 0.06 mm for the conventional and cross-linked liners, respectively) and was almost entirely due to creep. Therefore the average proximal wear between 2 and 24 months was 0.63 mm for the conventional liners and 0.04 mm for the cross-linked liners.

The level of wear of the cross-linked polyethylene liners, however, was unable to be measured accurately since it was below the sensitivity of RSA technique, which has a limit of approximately 0.07 mm. The patient did however participate in an RSA study (n=15) of the same 5-Mrad cross-linked liners which found an average annual wear of 0.01 mm representing a 96% wear reduction compared to EtO-sterilised liners.

A hip simulator study revealed that 5-Mrad cross-linked polyethylene reduces volumetric wear although the number of particles is actually increased. To achieve a reduction of both the number and volume, 10 Mrad was required. The macrophage response to particles is complex and is dependent upon number, size, and material of particles. Osteolysis, which occurred prior to revision, was not observed following the procedure despite the presence of a poor interface. This indicates that cross-linked polyethylene triggers osteolysis to a lesser degree than normal polyethylene.

The pathogenesis of periprosthetic osteolysis has recently been challenged. Implant instability, and an increase in the periprosthetic fluid pressure and osteolysis to a lesser degree than normal polyethylene. This indicates that cross-linked polyethylene triggers the procedure despite the presence of a poor interface. The reasons for this may be a better stability or a superior compatibility of the uncemented interfaces. Since particles and osteolytic triggers seem to penetrate more readily through holes in the acetabular shell than the periphery in osseointegrated implants, the use of hole covers to seal the shell, and the fact that screws were not employed, were deemed to be important in this case.

Although the wear rate in this patient was high, it was no greater than that observed in many patients in the same study who did not develop osteolysis. These patients, however, had more stable stems. Implant instability may have implications in the biological effect of wear particles. Our findings suggest that a stable and tight interface can resist particle penetration well.

To prevent osteolytic progression, we initiated bisphosphonate treatment since studies both in vitro and in animal models of wear-mediated osteolysis have shown that it has inhibitory effects on particle-stimulated macrophages and on bone resorption. Bisphosphonates can also reduce serum markers of human periprosthetic osteolysis. The aggressive osteolysis that developed between one and 2 years in this patient had ceased on both sides at 3 years and the earlier infiltrating lesion became less active and had more sclerotic margins. When alendronate therapy was later discontinued, the osteolysis returned rapidly and progressively but only on the right side where there had been a subtotal removal of the membranes. This suggests that bisphosphonate treatment had a protective effect but that its administration may have to be continued until a full revision with total removal of particle-laden membranes is performed. The outcome of the left side, which had undergone a full revision, was much better than that of the right side despite the re-cemented interface being of poor quality.

The very early development of osteolysis in this patient suggests that she may be a compromised host. A broad clinical spectrum of osteolytic responses exists between individuals. A recent cell culture study has shown that smaller polyethylene particles, as from 5-Mrad cross-linked polyethylene, produce bone-resorbing activity at lower volumetric doses than larger particles do. In this case we have a control hip which did not develop osteolysis with the cross-linked polyethylene, despite resulting in a poorer interface than conventional EtO-sterilised liners. This suggests that aggressive tissue response may be due to
suboptimal curettage of the right hip and/or residual stem instability and not because of hypersensitisation or a response to cross-linked polyethylene.

We treated this patient with alendronate and then exchanged liners as soon as the cross-linked polyethylene liners became available. Although hard-on-hard bearings may convey theoretical advantages, we believe that revision of her well-established cups was not justified. A longer time-frame is necessary to determine whether this patient will show a reaction to the new polyethylene liners.

On reflection, a bilateral stem revision with impaction grafting may have achieved a better outcome for this case. Furthermore, the possibility of rapid deterioration after stopping bisphosphonate therapy should have been taken into consideration.

At the time of writing this report, this patient was receiving zoledronate treatment and she was awaiting stem revision with impaction grafting. We also plan to revise the acetabular cup to allow a ceramic-on-ceramic bearing surface, which would help to keep wear to a minimum.

CONCLUSION

Promising results were found with cross-linked polyethylene and, to some extent, with bisphosphonate treatment of aseptic loosening. If such results are confirmed in large and well-controlled clinical trials, it will have enormous implications on implant longevity, patient morbidity, and cost of treatment.

REFERENCES