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Presence of macrophages at the bone-cement interface of stable hip arthroplasty components

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The bone cement interface of four clinically stable hip-joint prosthetic components was examined histologically for the presence of macrophages using routine staining and a histochemical technique for acid phosphatase. Macrophages were found in the absence of wear debris in all four cases. Because these cells are capable of bone resorption, their presence at a well-fixed interface must give cause for concern.

Introduction

Macrophages as precursors of the osteoclast (Chambers 1980) are capable of resorbing bone (Mundy et al. 1977), so that it may be that "their presence at the interface represents a tissue reaction no implant surgeon can safely ignore" (Charnley 1976). Macrophages are known to accumulate at the bone-PMMA interface in response to polyethylene-wear debris and particulate cement (Revell 1982, Vernon- Roberts & Freeman 1976, Willert 1973, Willert et al. 1974). We (Freeman et al. 1982) and others (Linder & Hansson 1985) have recently observed the presence of macrophages at clinically well-fixed cemented components. These observations stimulated us to review the histologic appearance at a series of clinically stable well-fixed components that came to revision in an attempt to define the significance of the presence of macrophages at the clinically stable interface.

Patients and methods

Tissue was obtained from the bone-PMMA interface at the time of revision hip surgery in 4 patients. The samples studied were obtained from clinically well-fixed components requiring revision surgery because of pain of unknown origin (Case 4) or loosening of the reciprocal component. One femoral and all the acetabular components were rigidly fixed at the time of replacement surgery.

Case 1. A 70-year-old lady with arthrosis who 13 years previously had undergone left hip replacement with a Charnley prosthesis. This had functioned satisfactorily for 10 years, but eventually she had pain, which necessitated a revision. At the time of surgery, the acetabular component was noted to be well fixed, but the femoral component was loose within the shaft. Histologic preparations were available from both the well-fixed acetabular and the loose femoral components.

Case 2. A 50-year-old man who had undergone ICLH double-cup hip replacement 4 years previ-

Figure 1. Case 2. Double-cup prosthesis in situ. The hip had been painful, but there are no obvious radiographic features to suggest loosening. At surgery the femoral component was loose, but the acetabular component was well fixed.

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ously (Figure 1). The hip was never completely painless and eventually came to revision. Radiographs of the hip prior to revision were thought to show no abnormality. At surgery the femoral component was loose, but the acetabular component was well fixed. Both components were removed and the hip was revised to a stemmed arthroplasty. Histologic preparations were available from the membranes at the well-fixed acetabular side and the loose femoral side.

Case 3. A 68-year-old man with arthrosis of the hip who underwent left ICLH double-cup replacement in 1979. The hip became symptomatic and required revision in 1984. Radiographs prior to revision showed no abnormality on the femoral side and a lucent line, 1 cm in width in one zone of the acetabular side. At the time of surgery the acetabular component was well fixed, but the femoral component was loose. The hip was revised to a stemmed arthroplasty so that histologic preparations were available from both the membranes on the acetabular and femoral sides.

Case 4. A 51-year-old man with arthrosis of the hip who had undergone Müller hip replacement 3 years previously. This had become increasingly painful and successive radiographs showed the presence of lucent lines around both components, measuring 2 mm in width around the femoral component and 1 mm around the acetabular component, suggesting that they were loose. At surgery, despite the appearance of the x-ray film, both femoral and acetabular components were found to be extremely well fixed. However, the decision was taken to revise the components and hence histologic preparations became available of tissue from two well-fixed bone-cement interfaces.

Tissue from the femoral side was obtained by hammering the prosthesis out of the cement bed. The cement was then broken up to expose any membrane present in the proximal 5 cm of the implant bed, but not more distally. Obtaining adequate samples from a firmly implanted acetabular component was more difficult. In order to do so, the acetabular component was cut into four quadrants in a cruciate manner using a Tuke saw. The segments were then removed using a curved osteotome. The underlying cement was then broken up and removed piecemeal. This allowed exposure of the membrane at the interface between acetabular bone and cement. Since the membrane peeled off the bone with ease and because we were concerned to preserve as much bone as possible, no bone was removed with the membrane.

Tissue from the interfaces was examined using frozen sections and histochemical staining to demonstrate acid-phosphatase activity, as a marker of macrophages, together with routine paraffin wax-embedded hematoxylin-eosin stained sections. In addition, paraffin-embedded sections were stained with the peroxidase-antiperoxidase immunohistochemical method for lysozyme, which is a marker of macrophages. The histologic examination was performed by one of us (P.A.R.) without knowledge of the clinical details, reasons for revision surgery, or whether there was loosening of the relevant prosthetic component. Tissue from the loosened component in the same joint was also examined blindly to lessen possible bias in observation.

Results

There was no difficulty in recognizing the presence of macrophages and giant cells in response to birefringent polyethylene or particulate metal debris in samples obtained from the loosened prosthetic components.

The well-fixed bone-cement interface in the 4 cases described above showed an infiltrate of macrophages (Figure 2) with no giant cells and no birefringent polyethylene or fine granular metal debris visible by high-power light microscopy (Figures 3 and 4). No individual beads of cement polymer were detected in the material examined by frozen section. Staining for acid phosphatase and lysozyme confirmed the presence of macrophages (Figures 2 and 5) and demonstrated that the infiltrate was frequently heavier than could be detected in routine hematoxylin-eosin sections. A large piece of cement remained attached to the surface of the specimen from the acetabulum in case 3, and this was preserved in frozen sections so that it was possible to demonstrate acid phosphatase- containing macrophages immediately adjacent to this cement (Figure 5). It is to be emphasized that the macrophage infiltrate was present at indisputably well-fixed interfaces and in the absence of separated cement particles or wear debris.

Figure 2. Case 1. Low-power view of the fibrous tissue between bone and cement of a well-fixed acetabular component. The tissue has been stained to demonstrate lysozyme in macrophages that appear black in this photograph. PAP method, lysozyme, x 80.

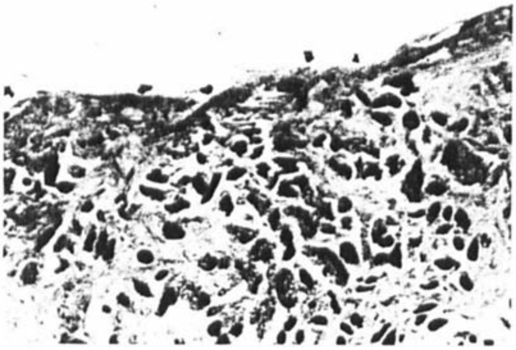

Figure 3. Case 3. Cellular infiltrate composed of macrophages in the fibrous membrane immediately adjacent to a well-fixed acetabular component. HE, x 800.

Figure 4. Case 3. High-power view of macrophage infiltrate at cement interface of a well-fixed acetabular component. HE, x 400.

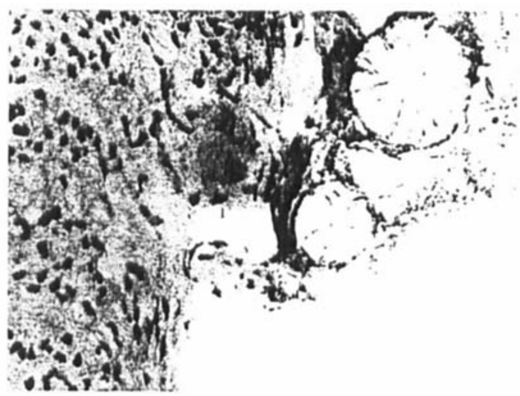

Figure 5. Case 3. High-power view of acid-phosphatase stained macrophages (left) adjacent to bone cement (right). Beads of bone cement polymer that were incorporated in the block of cement are visible in this frozen section. Acid phosphatase, x 400.

Discussion

The presence of wear debris with an accompanying macrophage and giant cell reaction is well described in the tissues adjacent to loosened joint prostheses (Willert 1973, Willert et al. 1974, Vernon-Roberts & Freeman 1976, Revell 1982). Other authors (Goldring et al. 1983) have studied the histology and histochemistry at loose bone-cement interfaces and demonstrated its synovial nature, being rich in macrophages and being able to generate collagenase and prostaglandins that are capable of causing bone lysis. The lytic enzymes in this tissue may be activated by loosening of the component. Wear debris with an accompanying cellular reaction is also occasionally seen in the fibrous membrane between bone and cement of surgically well-fixed specimens. Our present results suggest, however, that macrophages may be recruited to the bone-PMMA interface even in the absence of wear debris or any other apparent stimulus. Particles of bone cement that have become detached and residual beads of unpolymerized cement excite a giant- cell response. We have demonstrated, however, that large numbers of macrophages may be seen immediately next to the main cement mass in the absence of giant cells. These findings confirm our earlier observation (Freeman et al. 1982) and those of Linder & Hansson (1983) that the presence of nonparticulate PMMA cement at a surgically immobile bone-cement interface may induce a macrophage response.

The presence of these macrophages, though visible by hematoxylin-eosin staining, is made much more obvious when acid phosphatase staining of frozen sections is used. Macrophages are seen to be much more abundant than might have been suspected by hematoxylin-eosin staining, and this raises the question whether routine histopathologic processing is adequate in the assessment of the bone-cement interface.

The significance of the presence of macrophages at the well-fixed interface seemingly in response to nonparticulate cement is open to question. Charnley (1976) took the view that "their presence must give cause for alarm" due to their ability to undergo transformation into cells capable of bone lysis. However, the more recent literature (Johnston & Crowninshield 1983) reports lower rates of loosening of the femoral components than in earlier studies, and it is likely, but unproven, that the interfaces in their series are equally infiltrated with macrophages. There are three possible theories that may account for this seeming disparity. The first is that macrophages are benign bystanders whose presence is purely fortuitous and of no consequence. This is unlikely in view of their proven osteolytic potential. The second is that recent advance in cement techniques, i.e., pressure injection, vacuum preparation, and lower viscosity, in some way obviate macrophage accumulation. This hypothesis is unproven until well-fixed prostheses cemented with these techniques are available for study at postmortem. The third possibility is that macrophages per se are of no consequence and only assume a role of importance when they are activated or become osteoclasts.

Because more recent series report good results with cemented prostheses (Older 1984, Johnston & Crowninshield 1983), it may be that Charnley's "cause for alarm" should be modified to "possible cause for concern." However, we still have reasons to develop a second-generation acrylic cement that has properties resulting in less tissue damage at implantation (Mjöberg 1986) and which causes minimal macrophage recruitment.

References

Chambers T J. The cellular basis of bone resorption. Clin Orthop 1980 Sep(151):283–93.

Charnley J. Cement bone interface. In: Low friction arthroplasty of the hip. Springer Verlag, Heidelberg, 1976, Chapter 4:25–39.

Freeman M A, Bradley G W, Revell P A. Observations upon the interface between bone and polymethylmethacrylate cement. J Bone Joint Surg (Br) 1982;64(4):489–93.

Goldring S R, Schiller A L, Roelke M, Rourke C M, O Neil D A, Harris W H. The synovial-like membrane at the bone cement interface in loose total hip replacements and its proposed role in bone lysis. J Bone Joint Surg (Am) 1983 Jun;65(5):575–84.

Johnston R C, Crowninshield R D. Roentgenologic results of total hip arthroplasty. A ten year follow-up study. Clin Orthop 1983 Dec;(181):92–8.

Linder L, Hansson H A. Ultrastructural aspects of the interface between bone and cement in man. Report of three cases. J Bone Joint Surg (Br) 1983 Nov;65(5):646–9.

Mjöberg B. Loosening of the cemented hip prosthesis. The importance of heat injury. Acta Orthop Scand 1986;57 (Suppl 221).

Mundy C R, Altman A J, Gondek M D, Bandelin J G. Direct resorption of bone by human monocytes. Science 1977 Jun 3;196:1109–11.

Older M W J. A ten to twelve year follow up study of Charnley arthroplasty of the hip. J Bone Joint Surg (Br) 1984;66:299–300.

Revell P A. Tissue reactions to joint prostheses and the products of wear and corrosion. Curr Top Pathol 1982;71:73–101.

Vernon-Roberts B, Freeman M A R. Morphological and analytical studies of the tissues adjacent to joint prostheses: investigations into the causes of loosening of prostheses. In: Schaldach, M and Hohmann, D(eds) Advances in artificial hip and knee joint technology. Springer Verlag, Heidelberg, 1976:148–86.

Willert H G. Tissue reactions around joint implants and bone cement. In: Chapchal, G(ed) Arthroplasty of the hip. Thieme, Stuttgart, 1973:11–21.

Willert H G, Ludwig J, Semlitsch M. Reaction of bone to methacrylate after hip arthroplasty: a long term gross, light microscopic, and scanning electron microscopic study. J Bone Joint Surg (Am) 1974 Oct;56(7):1368–82.