Case reports

Infection following total hip arthroplasty with a hydroxyapatite-coated prosthesis

Histology and histomorphometry 6 years after implantation and infection—a case report

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A primary total hip replacement was performed on the right hip of a 72-year-old male (Caucasian) because of osteoarthrosis. He had no history of sepsis or surgical treatment of the hip. He was included in a prospective study of the ABG total hip prosthesis (Anatomique Benoist Gérard, Howmedica, Staines, England). The stem and the acetabular shell were made of a titanium alloy (Ti6Al4V). The femoral component had a hydroxyapatite coating (thickness 60 ± 30 μm) on its proximal third. The back of the acetabular component was entirely covered with HA (Tonino et al. 1995). The femoral head was made of a cobalt-chromium alloy and had a diameter of 28 mm. Surgery was performed by a senior staff member via an anterolateral approach and was uneventful. The patient received a single dose of prophylactic antibiotics (a second generation cephalosporin), just before induction of analgesia. Thrombosis prophylaxis consisted of administration of subcutaneous heparin from the day before surgery and acenocoumarol, which was started on the day of surgery. After 5 days of bedrest, the patient was mobilized, and he was walking with two crutches, when a hematoma developed. During the following days, the wound became swollen, warm and painful and his temperature rose to 40 °C. The ESR was 95 mm and C-reactive protein (CRP) > 200. On day 10 postoperatively, the hip joint was re-opened: a deep infection was found extending to the implants. An extensive debridement of the joint and its surroundings was performed and gentamicin beads were left behind in the joint space. Microbiology showed growth of Enterobacter cloacae and Streptococcus hemolyticus group C. This infection was treated with vancomycin intravenously. On day 21, we made a second debridement of the joint and implanted a new set of gentamicin beads in the joint space. These beads were removed 2 weeks later; thereafter the wound healed. Antibiotic therapy was continued intravenously for 2 months after the hip replacement followed by another 2 months of oral antibiotics (ofloxacin and feneticillin). Parameters of infection had been normal (ESR less than 10 mm, CRP less than 5) for more than 4 weeks when the therapy was discontinued. At 3 months, the Merle d'Aubigné score was 18, the maximal score. This score remained constant during the entire follow-up and the hip performed well until the patient's death 6 years later. The radiographs showed no signs of loosening (Figure 1). From the second year onwards cancellous densities were noted in Gruen regions 2 and 6 and later also in regions 3 and 5. In Gruen region 4 (at the tip of the femoral prosthesis), an area of sclerosis was seen after the third postoperative year. Bone resorption was first noted in Gruen region 1 at the 5-year follow-up visit. The bone around the acetabular component showed a reactive line in the DeLee and Charnley (1976) region 1 at the 6-month follow-up, which slowly spread to region 2 at 5 years, but never reached region 3. No other bone changes were seen in the acetabular region. Technetium scintigraphy was performed at 6 and 12 months after the hip

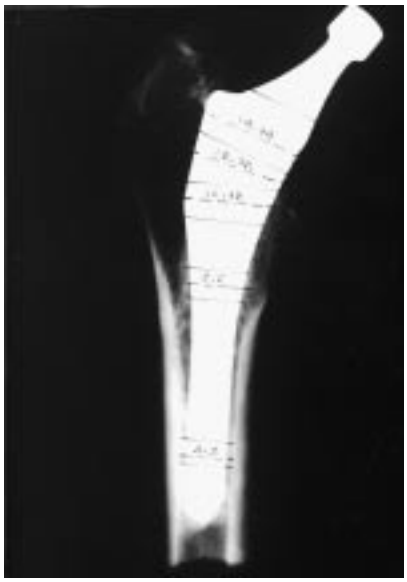

Figure 1. Postmortem radiograph of proximal femur showing osseointegration of the implant (see text) and the levels of the sections.

replacement and yearly thereafter. After 6 months, the 3-phase scintigraphy already showed normal blood flow and blood pool values suggesting that the infection was cured. The bone scan showed slightly elevated uptake, as in most of the uneventful ABG hip replacements. At 5 years, the scintigraphic pattern was normal. The patient sustained an intracerebral hemorrage and died 6 years and 6 weeks after the total hip replacement. At the time of the hip operation, written consent was given to remove the prosthesis after death.

Specimen acquisition and preparation

The prosthetic components were collected en bloc with the surrounding bone. On removal, the acetabular bone fractured, causing the cup to loosen. Bone and implant were immersed in buffered formalin for 7 days and then in 70% ethanol for 24 hours. Photographs and radiographs of the specimens were taken, which were then embedded in a PMMA resin. With a diamond, microtome sections were cut 20 µm thick. The sections corresponded to the DeLee and Charnley regions on the acetabular side and the Gruen regions on the femoral side (Figure 1). They were stained for qualitative histology (paragon staining, a combination of basic fuchsin and toluidine blue) and quantitative histomorphometry. We used a Polyvar microscope

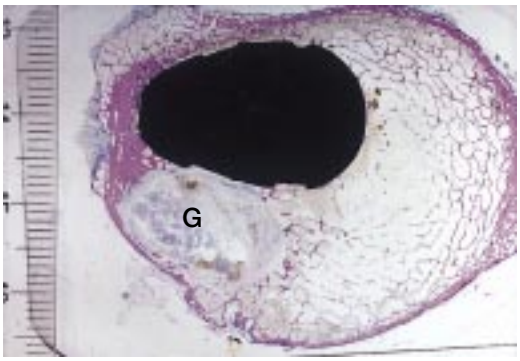

Figure 2. Histologic section through Gruen zones 1C and 7B of the proximal femur. black = implant, G = granuloma.

(Reichert-Jung, Vienna, Austria) for the qualitative analysis. Quantitative measurements were done, using an Axioskop microscope (Carl Zeiss, Munich, Germany), which was equipped with a color-image-analyzing system (Samba; Samba Technologies, Grenoble, France). Bone contact was measured as the percentage of the circumference of the implant that was in direct, close contact with bone. Bone density was measured in several preselected areas around the components. This was expressed as a percentage of the area covered with bone. Residual HA coating was measured as a percentage of the circumference of the implant that was still covered with HA. Only fragments of coating > 5–10 µm could be seen. Thus, the values presented do not take into account very small particles or a thin film of HA coating.

Qualitative histological findings

Due to the fracturing of the pelvis and the subsequent loosening of the cup, we could not make a reliable assessment of the bone-prosthesis contact on the acetabular side. Therefore the cup findings are not discussed further. Macroscopic examination of the specimen revealed a substantial granuloma (11 × 19 mm) with a large central necrotic cavity surrounding the posteromedial half of the proximal part of the femoral prosthesis. Microscopy of the sections through Gruen regions 1 and 7 confirmed the presence of a chronic fibronecrotic reaction, which extended up to the interface between the prosthesis and the surrounding tissue, with an acute and active inflammatory response directly adjacent to it (Figure 2). The cells present were mainly lymphocytes, macrophages and giant cells. There were

Figure 3. Detail of section through Gruen regions 1C-7B showing cancellous bone apposition onto the implant (black). The arrow points to a residual part of the hydroxyapatite coating.

a few plasma cells and polymorphonuclear cells. Numerous particles of both metallic and polymeric origin were seen in the granuloma. The metallic particles were mainly found close to the implant and the polyethylene debris in the central necrotic cavity. On the lateral side, there was a high ratio of direct contact between bone and implant with trabecular bone apposition (Figure 3). On the medial side, we also found apposition of bone, but here it did not extend beyond the grooves in the femoral component. The cellularity of the bone marrow was normal, with no signs of fibroinflammatory infiltrate. Bone density in this area seemed normal. The HA coating was relatively unaffected in the area close to the granuloma. We saw evidence of residual coating all around the prosthesis. In Gruen regions 2 and 6, the stem was surrounded by a thick fibrous membrane medially and laterally, with a discrete inflammatory reaction. Here, there were no signs of granuloma. On the anterior side, there was direct contact between bone and implant while on the posterior aspect, there was a thin fibrous layer (Figure 4). Normal cancellous bone with low remodeling was seen. No polyethylene or metallic particles were found in this section. More distally, in Gruen regions 3 and 5, we saw only a thin fibrous membrane on the anteromedial side, which showed no inflammation. The anterolateral, lateral and posterior sides had numerous areas of close contact between bone and implant. Bone density appeared normal.

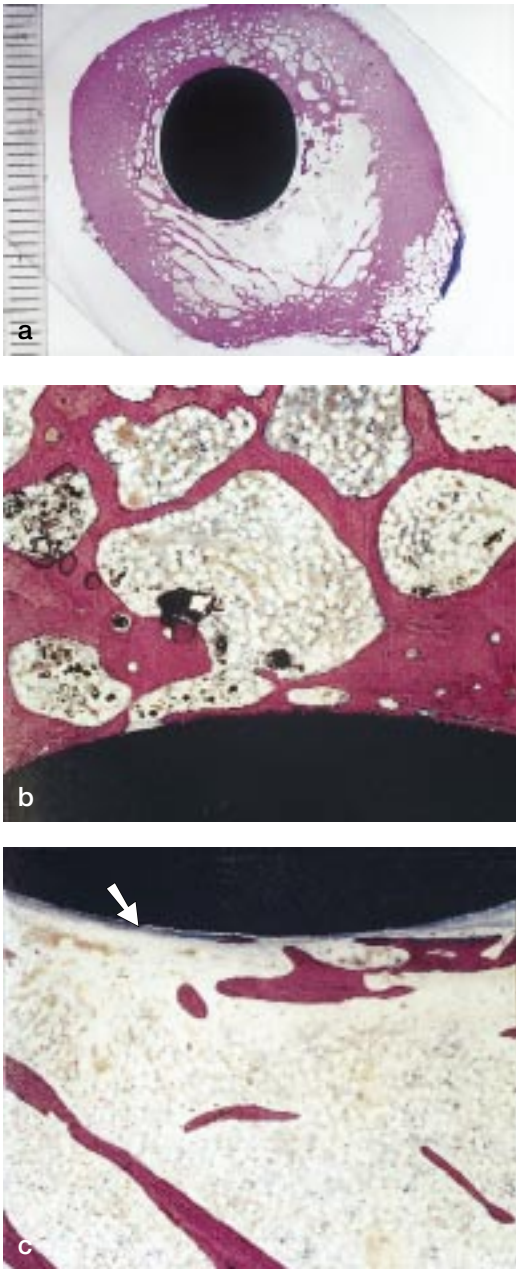

Figure 4.
a. Section through Gruen regions 2–6.
b. Detail of section from figure a showing direct contact between cancellous bone and implant (black) on the anterior side.
c. Detail of figure a showing fibrous layer (arrow) on the posterior side. Black = implant.

Histomorphometry

In the proximal part of the femur, the bone-contact values were similar regardless of the level of the

Table 1. Bone-implant contact in femur (%)

Section level	Anterior	Posterior	Lateral	Medial	Mean value (SD)
1A–7A	22	28	47	67	37 (27), n = 7
1B–7B	45	29	12	75	35 (30), n = 7
1C–7B	25	51	33	41	37 (14), n = 7
Metaphysis	31	36	31	61	37 (24), n = 21
Diaphysis 2–6	92	1	0	0	23 (46), n = 4
Diaphysis 3–5	50	73	45	47	54 (13), n = 4

Table 2. Bone density in femur (%)

Section level	Anterior	Posterior	Lateral	Medial	Mean value (SD)
1A–7A	16	1	21	5	12 (13), n = 7
1B–7B	19	1	4	24	10 (10), n = 7
1C –7B	26	7	4	69	20 (24), n = 7
Metaphysis	20	3	10	32	14 (17), n = 21
Diaphysis 2–6	39	11	18	50	29 (18), n = 4
Diaphysis 3–5	25	61	76	33	49 (24), n = 4

Table 3. Residual HA coating of the femoral component in %. Mean residual thickness in μm (SD)

Section level		Anterior	Posterior	Lateral	Medial	Mean value
1A–7A	%	4	31	5	4	11 (13)
	μm (SD)	20 (8)	28 (9)	24 (5)	34 (21)	27 (6)
1B –7B	%	5	38	15	13	18
	μm (SD)	14 (8)	22 (7)	22 (6)	22 (9)	20 (4)
1C–7B	%	8	35	3	10	14
	μm (SD)	19 (7)	31 (11)	19 (4)	20 (7)	22 (6)
Metaphysis	%	6	35	8	9	14
	μm	18	27	22	25	23

section (Table 1). The highest values were seen on the medial side due to the bone apposition of bone in the medial grooves of the stem. The highest percentages of bone contact were measured in the sections through Gruen regions 3 and 5. The bone density gradually increased from proximal to distal (Table 2). Hardly any residual coating (Table 3) was seen on all sections, except on the posterior side, where about 35% of the coating remained. The mean thickness of the coating was 23 μm.

Discussion

The patient's hip prosthesis performed well clinically for more than 6 years and the consecutive radiographs of the pelvis taken on the annual follow-up visits showed no change in the position, migration or subsidence of the components. The stem was well fixed in the femoral shaft. We found an overall bone-implant contact of 37% which is consistent with earlier findings in uninfected THAs with HA-coated hip implants (Tonino et al. 1999). One case report describes 69–91% proximal bone-implant contact (10 months after initial hip replacement) (Lintner et al. 1994). In our case, a large cystic granuloma containing a considerable amount of polyethylene and metallic particles along with lymphocytes, macrophages and giant cells was present in the metaphysis. Only a few

plasma cells and neutrophils could be identified and no bacterial debris. We therefore assume that the granuloma formation was mainly due to a foreign body reaction to wear debris. Since no polyethylene particles were seen distal to the proximal Gruen regions, we conclude that the osseointegration was circumferential and complete, sealing off the proximal femur and limiting the joint space. This is also consistent with earlier findings (Tonino et al. 1999) and confirms that bone ongrowth to the stem followed a normal pattern in this patient, notwithstanding the infection. Experimental studies in miniature pigs also have shown good osseous ingrowth of bone with HA-coated implants despite a local infection (Wilke et al. 1993). Rabbit studies have shown that local infection can affect histomorphometric parameters: in severe infections, the bone-implant contact ratio has been found to be smaller in HA implants than in uninfected HA implants and uncoated implants (Oosterbos et al. 2002). The presence of the granuloma in the proximal femur of our patient showed another interesting phenomenon. The location of the granuloma corresponded exactly to the area of a higher amount (30%) of residual HA coating while all other proximal surfaces of the stem were covered with less than 10% HA. This can not be explained by higher dissolution of the coating at lower pH levels, as may occur in an infection, nor can it be explained by higher phagocytic activity, like that present in the formation of a PE wear-induced granuloma. It can, however, be explained by the lack of bone-remodeling activity at the site of the granuloma: in normal bone remodeling, osteoclastic-like cells desintegrate the HA coating with time (Dhert et al. 1993, Frayssinet et al. 1993). Our observation supports the theory that resorption of the HA coating depends mainly on the rate of bone remodeling (Tonino et al. 2001).

This case report indicates that it is possible to eradicate an infection after total hip replacement without removing the prosthesis. Despite an infection, our HA-coated prosthesis showed a normal pattern of osseointegration.

No competing interests declared.

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