

AVASCULAR NECROSIS OF THE FEMORAL HEAD AFTER ALLOGENIC BONE-MARROW TRANSPLANTATION

A RETROSPECTIVE STUDY OF 27 CONSECUTIVE THAs WITH A MINIMAL TWO-YEAR FOLLOW-UP

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After an allogenic bone-marrow transplant, avascular necrosis of the femoral head may affect young adults, producing destructive lesions which require hip replacement. We have reviewed 27 consecutive such total hip arthroplasties (THA) at a minimal follow-up of two years. Of these, 20 were primary operations for Ficat (1985) stage-III and stage-IV lesions, and seven were revisions after the failure of previous surgery. The median age at operation was 30 years (17.5 to 44). The prostheses had a cemented, collared titanium-alloy stem, an alumina-alumina joint, and a press-fit socket. Seven had a titanium-alloy metal back and 20 had all-alumina cups of which six had to be cemented.

At an average follow-up of five years, no patient had been lost to follow-up. One had died from septicaemia after two years and another with chronic graft-versus-host disease developed a deep infection 2.5 years postoperatively and had a successful revision. There were no revisions for aseptic loosening. The clinical results on the Merle d'Aubigné and Postel (1954) scale were very good or excellent in 23 hips (88%), good in one and fair in two. Ten hips showed incomplete acetabular radiolucencies less than 1 mm thick, but there were no radiolucent lines around the stems.

We conclude that for these difficult patients THA with ceramic joints and careful technique provides the best short- and medium-term option after the failure of medical treatment.

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Since the 1980s, allogenic bone-marrow transplantation has been a relatively successful treatment for some haematological malignancies in young patients. Survival has improved so that more than 60% of patients are free from haematological disease after five years (Gratwohl et al 1988; Bortin et al 1992). The two main causes of persistent morbidity and mortality are late infection and graft-versus-host disease (Atkinson 1990; Deeg 1990). Another complication is avascular necrosis which has been reported to affect over 10% of transplanted patients (Atkinson, Cohen and Biggs 1987; Russell et al 1989; Enright, Haake and Weisdorf 1990; Mascarin et al 1991; Socié et al 1994; Sixou et al 1995). The hip was involved in 60% of these, usually with advanced and bilateral lesions, requiring replacement arthroplasty.

Total hip arthroplasty (THA) is the most effective treatment when the femoral head has collapsed, but the results of THA for avascular necrosis are much worse than those for primary osteoarthritis. There is a higher rate of infection (Acurio and Friedman 1992) and of loosening (Ritter and Meding 1986; Salvati and Cornell 1988; Saito et al 1989). Thus, hip replacement after a bone-marrow transplant is a very challenging procedure. We report our early experience with 27 such arthroplasties using an alumina-on-alumina prosthesis. The minimum follow-up was two years, and our aim is to draw attention to the characteristics of the disease and to warn against certain risk factors in these patients.

PATIENTS AND METHODS

From January 1980 to April 1994, 23 patients with bilateral avascular necrosis of the femoral head after a bone-marrow transplant had been referred to the Department of Traumatology and Orthopaedic Surgery of Lariboisière Hospital. We performed 32 consecutive THAs, but we report only those with at least two years of follow-up, giving 27 procedures in 16 patients (Table I).

A marrow transplant had been performed for leukaemia in 11 patients (17 THAs), for aplastic anaemia in four (9 THAs) and for lymphoma in one (1 THA). The average age at transplantation was 29 ± 8 years (15.5 to 40.5). For the marrow graft, all the patients had been given intensive chemotherapy with alkylating agents and irradiation; those requiring THA had developed graft-versus-host disease

Table I. Details and results of treatment in 16 patients

Case	Initial disease*	Age at bone-marrow transplant (yr)	Side	Previous surgery	Age at THA (yr)	Preoperative Merle d'Aubigné and Postel score	Socket type†	Latest follow-up		Lucent lines	
								Duration (mth)	Merle d'Aubigné and Postel score	Socket	Stem
1	AA	20.5	R	Core decompression	24	12 (4-5-3)	b	33‡	-	-	-
			L	Core decompression	26	2 (0-1-1)	c	55	14 (6-3-5)	0	0
			R	THA	27	10 (3-3-4)	c	42	14 (6-3-5)	II	0
2	CML	15.5	L	0	17.5	15 (4-6-5)	b	37	18 (6-6-6)	I+II	0
3	CML	30	L	0	32.5	13 (2-6-5)	a	34	18 (6-6-6)	0	0
			R	0	33	13 (2-6-5)	b	27	17 (5-6-6)	0	0
4	AA	28.5	R	0	32	11 (4-3-4)	b	68	18 (6-6-6)	0	0
			L	0	35	12 (2-6-4)	a	37	18 (6-6-6)	0	0
5§	CML	20.5	R	0	22	10 (4-3-3)	b	24	18 (6-6-6)	III	0
			L	0	22	10 (4-3-3)	b	24	18 (6-6-6)	II	0
6	ALL	28	R	Core decompression	30	5 (1-3-1)	b	55	17 (5-6-6)	II+III	0
			L	Core decompression	30	5 (1-3-1)	b	55	18 (6-6-6)	II	0
7	CML	39	R	0	44	12 (3-6-3)	b	60	18 (6-6-6)	I	0
8	Lymphoma	20	R	0	24	10 (2-3-5)	b	65	18 (6-6-6)	0	0
9	CML	40.5	R	0	44	15 (4-6-5)	b	60	17 (5-6-6)	II	0
10	AML	29.5	R	0	32	13 (4-6-3)	b	70	18 (6-6-6)	0	0
			L	0	32	12 (3-6-3)	b	72	18 (6-6-6)	0	0
11	AA	23.5	R	0	26.5	3 (1-1-1)	c	156	18 (6-6-6)	0	0
			L	0	26.5	3 (1-1-1)	c	156	18 (6-6-6)	II+III	0
12	AA	31.5	L	0	35	14 (3-6-5)	a	40	18 (6-6-6)	0	0
			R	0	35	14 (3-6-5)	a	41	18 (6-6-6)	0	0
13	CML	40	L	0	44	11 (2-6-3)	b	38	17 (5-6-6)	III	0
			R	0	44	12 (4-5-3)	a	35	18 (6-6-6)	0	0
14	AML	22	R	Cup arthroplasty	26	10 (2-4-4)	c	100	18 (6-6-6)	0	0
			L	Cup arthroplasty	26	11 (3-4-4)	c	97	18 (6-6-6)	0	0
15	CML	43	R	0	47	15 (4-6-5)	a	24	18 (6-6-6)	0	0
16	ALL	25	L	0	28.5	6 (1-4-1)	a	24	16 (5-6-5)	0	0

* AA, aplastic anaemia; CML, chronic myelogenous leukaemia; ALL, acute lymphocytic leukaemia; AML, acute myelogenous leukaemia

† a, Cerafit; b, Cerapress; c, cemented alumina cup (see text)

‡ revised by another THA for late infection

§ died from septicaemia

Table II. History of infections in the series and isolated organisms

Bacterial*	Viral*	Opportunist
Meningoencephalopathy (1) (P)	HV (5) (2B, 3C) Zoster (4)	<i>Pneumocystis carinii</i> (2)
Septicaemia (2) (S, P)	Varicella (1)	<i>Aspergillus</i> (2)
Pulmonary infections (6) (P, BG)	CMV (2) HSV (2)	<i>Toxoplasma</i> (1)

* P, *Pneumococcus*; S, *Staphylococcus aureus*; BG, Gram-negative bacillus; CMV, cytomegalovirus; HV, viral hepatitis B or C; HSV, herpes simplex virus

necessitating steroid therapy. Most had suffered from infections related to their state of immunosuppression (Table II), but none had a documented history of osteomyelitis or septic arthritis.

Hip replacement was a primary procedure for advanced radiological lesions (Ficat (1985) stages III and IV) in 20 hips. In six it was required after early failure of four core decompressions and two cup arthroplasties (Fig. 1), and one was a revision after late deep infection (case 1; Table I).

The average age at hip replacement was 31 ± 8 years (17.5 to 44); the average height of the patients was 170 ± 11 cm (153 to 193) and their average weight was 64 ± 16 kg (49 to 109). Six patients had unilateral replacement; bilateral procedures were carried out in ten, in two of whom the operations were done at the same time.

All the arthroplasties were undertaken by one of the authors (LS), using the posterolateral approach. The prostheses were the Ceraver type (Ceraver Osteal, Roissy, France) with a cemented, collared, anodised stem of titanium alloy and an alumina head of 32 mm diameter (Sedel et al 1990). Two types of acetabular component were used: seven patients had a press-fit titanium alloy metal-back with an alumina core (Cerafit), with or without the use of screws. The other 20 patients had bulky alumina cups (Cerapress) impacted into an acetabulum under-reamed by 2 mm (74%), but six of these required cementing because of poor bone quality or because they were revisions. In all cases we used high-viscosity gentamicin-loaded cement with finger packing.

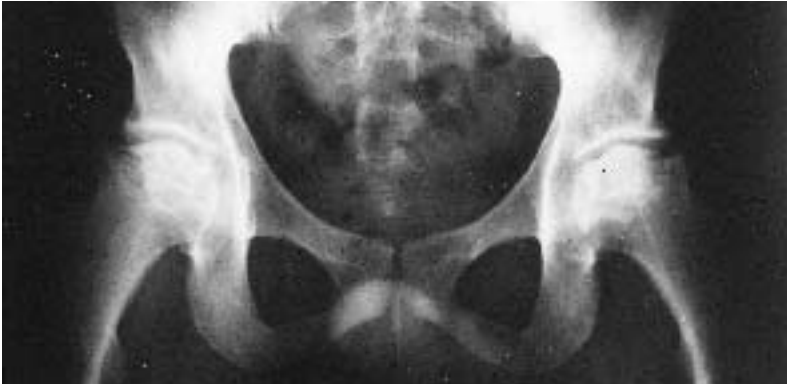


Fig. 1a



Fig. 1b



Fig. 1c



Fig. 1d

Radiograph of a 26-year-old man after allogenic bone-marrow transplantation for acute myelogenous leukaemia. Figure 1a – Bilateral avascular necrosis in Ficat stage III. Figure 1b – Bilateral cup arthroplasties. Figure 1c – Revision at two years by bilateral THA using press-fit alumina sockets with cement. Figure 1d – At eight years there is an excellent clinical result on both sides and no radiological abnormalities.



Fig. 2a



Fig. 2b



Fig. 2c



Fig. 2d

A 44-year-old man, after allogenic bone-marrow transplantation for chronic myelogenous leukaemia. Figure 2a – Avascular necrosis stage III on the right. Figure 2b – THA using a press-fit alumina socket; there was an immediate complete radiolucent line around the acetabular component. Figures 2c and 2d – At five years there is a very good clinical result although the opposite hip is occasionally painful. The radiolucent line has partially disappeared and except for moderate calcar resorption there are no abnormalities on the femoral side.

Patients were reviewed independently by the first author by clinical examination and radiography. The clinical results were assessed on the Merle d'Aubigné and Postel system (1954), and considered to be excellent or very good for scores of 18 or 17, good for 16, fair for 15 or 14 and poor for 13 or less. Radiolucent lines were recorded according to DeLee and Charnley (1976) for the socket and Gruen, McNeice and Amstutz (1979) for the stem. Clear resorption, osteolysis and any migration of the components were also noted.

RESULTS

No patient was lost to follow-up, but one with bilateral THAs (case 5) died from septicaemia two years after

operation. She had had acute graft-versus-host disease which had been treated with steroids for six months and had also had a splenectomy as part of her treatment for leukaemia. The septicaemia followed a severe pulmonary infection. At her last follow-up, she had excellent results on both sides.

The average follow-up of the other 25 hips was 59 ± 35 months (24 to 156); median 55 months. There had been no revisions for aseptic loosening or osteolysis and the results are shown in Table I.

On the Merle d'Aubigné and Postel grading system, 23 hips were excellent or very good (88%), one was good (4%) and two were fair (8%). Excluding the patient with severe infection described below, the average score had increased from 10.3 ± 3.8 (2 to 15) before operation to

17.5 ± 1.1 (14 to 18) at the latest follow-up.

The radiological results are shown in Table I. There were radiolucent lines around ten acetabula (Fig. 2), but all were less than 1 mm thick and non-progressive. Seven involved only one DeLee-Charnley zone and three involved two. There was no detectable socket migration. No femoral component showed a radiolucent line, osteolysis or subsidence. There was moderate calcar resorption in eight hips (30%; mean 2.6 ± 1.4 mm) (Fig. 2).

Complications. One patient with bilateral replacements (case 13) had a unilateral traumatic dislocation at seven months, which was reduced and did not recur. He now has excellent function on both sides. Another with bilateral THAs (case 1) had immediate palsy of the femoral nerve on the right side which partially recovered, and a late deep infection which was treated by revision to another THA. She had extensive chronic graft-versus host disease requiring steroid therapy, multiple pulmonary infections and neuromuscular involvement, including sclerodermatous changes, fasciitis of the hip and polyneuropathy. At her latest follow-up, the nerve palsy had partially recovered and infection had not recurred. She had no pain and satisfactory radiographs, but the functional result was only fair because of stiffness of the hip.

DISCUSSION

There are few reports of the results of hip replacement for avascular necrosis of the femoral head after allogenic bone-marrow transplantation. Enright et al (1990) mentions 16 cases with a revision rate of 37% but did not give details of the types of prosthesis or of follow-up.

A specific feature of the problem is related to the occurrence of graft-versus-host disease. This is a multiorgan syndrome, rather similar to a collagen-vascular disease. It results from a systemic immune reaction by the donor cells against host cells (Atkinson 1990; Kolb and Bender-Götze 1990), and Sixou et al (1995) have drawn attention to the role of a vasculitis which may add to the other factors affecting the occurrence of avascular necrosis such as steroids, other drugs, irradiation and serum lipid abnormalities. Atkinson (1990) considers that graft-versus-host disease treated with continuous steroid is the principal risk factor for late infections. It may also be an important cause of functional impairment by causing sclerodermatous skin changes, joint stiffness, muscular dystrophy and polyneuropathies (Kolb and Bender-Götze 1990). In our series, the postoperative nerve palsy was possibly due to preoperative neuropathy and nerve entrapment in fibrous tissue. Similarly, the single result in the 'fair' category showed no radiological abnormalities; stiffness appeared to be due to soft-tissue involvement.

The treatment of avascular necrosis of the femoral head, particularly in young patients, remains controversial as regards conservative procedures and arthroplasty, but it is known that steroid-induced necrosis gives poor results after

conservative surgery such as core decompression. In our series of patients THA seemed to be the best option; it enabled the patient to return rapidly to pain-free functional activity. We found that core decompression or cup arthroplasty did not delay the time at which THA became essential. The decision for primary THA was challenging, but the early results were satisfactory.

The risk of infection was high in our series, mainly because of the underlying disease processes. After a marrow transplant, the immunosuppressive state of the patient is constant for one year and may be prolonged by drugs, splenectomy or the onset of chronic graft-versus-host disease, which is considered to be the main cause of late infection (Atkinson 1990). Radical measures are necessary, including a multidisciplinary approach to eradicate seats of infection, carefully adjusted antibiotic prophylaxis, and the latest operative techniques including laminar air flow, and cement with antibiotics. Any local conditions require urgent acute evaluation. Our only deep infection was in a patient with extensive chronic graft-versus-host disease who had several operations before THA; this led us to recommend primary THA, using a limited and non-devitalising approach, especially in patients with local sclerodermatous changes.

Both avascular necrosis and youth are considered to be risk factors for loosening (Saito et al 1989; Chandler et al 1981; Dorr, Luckett and Conaty 1990), and it is accepted that patients with a known aetiological basis for avascular necrosis, such as steroid therapy or transplantation, have an even worse prognosis than those in whom there is no obvious cause.

To improve the long-term results of THA in young patients, use has been made of new techniques of bone anchorage, with or without cement, and new materials for bearing surfaces. We consider that an important cause of loosening may be foreign-body reaction against wear debris, especially polyethylene particles; for this reason we have used hybrid alumina-alumina hip prostheses since 1977.

In contrast with other reports, we have had satisfactory results in younger patients, with a survivorship of 89.4% at ten years in a series of 131 patients under 50 years of age, although 22% of them had steroid-induced necrosis (Sedel et al 1990, 1994; Nizard et al 1992). Both the number of patients and the follow-up of our current series are relatively small, but our results help to support the conclusion that minimal production of wear debris may be important.

The high incidence of radiolucent lines around the sockets is a cause for concern; this supports the view that acetabular fixation is still the weak link of THA. Most of the lucencies were limited and were present on post-operative radiographs (Fig. 2). The lack of socket migration leads us to consider this to be a problem of adjustment rather than a true sign of loosening. The advantages of using a press-fit technique include a reduction in bone removal, a decrease in the duration of surgery and a

potential for easier revision. We used acetabular cement only when the quality of the pelvic bone was poor, primary stability was inadequate, or for revision cases (Fig. 1).

Avascular necrosis of the femoral head after an allogeneic bone-marrow transplant is a very severe condition in young adults. We have shown that early conservative surgery does not delay the time to THA, but actually increases the morbidity and the risk of infection. Careful primary THA seems to be a safe and effective treatment, but chronic graft-versus-host disease is a major risk factor, especially in patients with preoperative soft-tissue involvement and good results cannot be guaranteed in these cases. In patients who are expected to survive for more than the life-span of the chosen prosthesis, the use of new materials may reduce wear, but further long-term clinical studies are needed.

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