Vascular transplantation

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Introduction

Allograft aortic replacement, as studied experimentally by Carrel[1] at the turn of the last century, was introduced for clinical use in the early years of vascular surgery[2,3]. Although clinical results were encouraging, several complications were soon recognized. Secondary dilation and calcification caused by allograft degeneration were observed in a significant number of patients[4,5].

Aortic reconstruction with Dacron prostheses has had satisfactory results for more than 30 years. Prosthetic infection soon appeared, however, as a rare but devastating complication. Although there has been a steady improvement in results over the last decade, prosthetic infection is still associated with high mortality and amputation rates, and its management remains a matter of controversy.

Excellent results reported by heart surgeons after allograft replacement for management of infections of the ascending aorta, have suggested the use of arterial homografts in prosthetic infections[6-8].

We report our experience with 31 patients who received *in situ* fresh homograft transplantation of infected infrarenal aortic prosthetic grafts.

Methods

In a prospective study, 31 patients (30 men, 1 woman, mean age 66.4 – 7.2 years) underwent fresh homograft transplantation for high-grade aorto-iliac graft infection. Aorto-enteric fistulas complicated the infection in 13 patients (42%). Treatment included total removal of the infected graft followed by fresh homograft replacement. Blood group compatibility (AB0) and negative cross-match (absence of preformed antibodies in serum recipient) were respected in all patients.

Postoperatively, the first consecutive 14 patients received low-dose cyclosporine (1-3 mg/kg/die) (Group 1); the following 17 patients did not receive immunosuppressive therapy (Group 2).

Clinical examination and abdominal computed tomography scans were performed at 1, 6, 12, 18, and 24 months after surgery. Immunological studies (anti-human leukocyte antigen - HLA - antibody production and antibody specificity) were performed by immunoenzymatic techniques (PRA-STAT ELISA) preoperatively and at early and late follow-up (1, 3, 7 days and 1, 3, 6, 12, 18, 24 months, respectively).

Results

Overall perioperative mortality rate was 35.5% (11/31). In Group 1 (treated with cyclosporine) 5 patients died (35.7%), all from recurrent aorto-enteric fistulas; in Group 2 (without cyclosporine), 6 patients died (35.3%), 2 from myocardial infarction, 2 from recurrent aorto-enteric fistula and 2 from bleeding caused by anastomotic rupture. No difference in mortality between the two groups was observed.

At late follow-up, in Group 1 (mean period 45 months, range 34-52 months), 1 patient died from an intestinal infarction; the surviving patients (n = 8) had no clinical signs of recurrent infection or complications related to immunosuppressive therapy. At late follow-up in Group 2 (mean period 14 months, range 2-28 months) 2 patients died, 1 from rupture of an aortic anastomotic aneurysm and 1 from myocardial infarction; 1 patient exhibited a late occlusive lesion of

the homograft in the iliac segment treated with transluminal angioplasty and covered stent; none of the surviving patients (n = 9) had clinical signs of recurrent infection. Abdominal computed tomography scans revealed an increased aortic wall, without signs of aneurysmatic dilation in either group.

Immunological studies showed a progressive increase in percent panel reactive antibodies in all patients from the first month up to 18 months post-transplant.

A statistically significant difference ($p = 0.01$) in antibody production was observed between the two groups. The patients treated with cyclosporine (Group 1) produced fewer anti-HLA antibodies later than untreated patients (Group 2).

Discussion

Prosthetic infection still carries a high mortality rate even in cases of *in situ* fresh homograft transplantation. The advantage of removing the infecting graft and undertaking aortic reconstruction in the same sitting does not offset the problems entailed by high risk factors: advanced age, septic state, emergency surgery and aorto-enteric fistulas. In fact, fistulas were present in 42% of our series and strongly influenced the outcome, being the prime cause of perioperative mortality.

Few clinical reports have investigated the immune response in these patients either because arterial homografts are deemed to have a low antigenicity, or because graft rejection is not thought to play a major role in clinical outcome. Therefore, arterial homografts are usually transplanted without matching donor and recipient for blood group (AB0) or HLA. In addition, immunosuppressive therapy has been considered unsafe for use in patients with infection.

Some clinical studies have reported late complications due to graft rejection[7,9] which have been confirmed in experimental models. Many animal studies have demonstrated strong homograft antigenicity triggering an immune response similar to the rejection process which develops in solid organ transplant recipients[10,11].

In previous studies we showed that human fresh arterial homografts are immunogenic and trigger a strong donor-specific anti-HLA antibody response[12,13]. The most significant findings in these studies were the antibody activity against HLA indicating a donor-specific rejection.

Immunosuppressive therapy with low dose of cyclosporine does not seem to influence clinical outcome in patients treated for graft infections with fresh arterial homografts. Immunosuppression reduces the humoral immune response, but the clinical significance of antibody production remains unsettled.

Our data suggest that arterial homografts continue to maintain biological activity for a long time after implantation. They should be regarded as biologically active true vascular transplants rather than mechanical tissue implants. The correlation between antibody production and late homograft failure warrants further investigation. Efforts should be made to curb the immune response by prospective cross-matching, immunosuppressive therapy and preoperative manipulation of homografts to reduce their antigenicity.

References

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