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PAPER OF INTEREST TO BOTH SPECIALITIES

Successful abdominal aortic aneurysm resection in long-term survivors of cardiac transplantation

J. O. Defraigne, N. Sakalihasan, J. C. Demoulin* and R. Limet
*Departments of Cardiovascular Surgery and *Cardiology, Centre Hospitalier Universitaire de Liège, Sart–Tilman University Hospital, 4000 Liège, Belgium*

With the improvement of survival rates following cardiac transplantation, the probability of recipients developing extracardiac disease is increased. Three cases are reported of abdominal aortic aneurysm successfully operated on in cardiac allograft recipients 1 to 4 years after transplantation. Indications for transplantation were valvular, idiopathic and ischaemic cardiomyopathy. Post-transplant hypertension and hyperlipidaemia may have played a role in the rapid growth of the aneurysms. Cardiac function and the incidence of graft atherosclerosis were assessed before surgery by coronary angiography. All three patients were discharged from hospital. Abdominal aortic aneurysm resection may be a safe procedure in cardiac transplant patients. In view of the rapid increase in the size of the aneurysms in transplanted patients, careful screening should be performed during follow-up.

Keywords: abdominal aortic aneurysm, resection, cardiac transplantation, survival

Cardiac transplantation has become a successful form of treatment for selected patients with end-stage cardiac disease. Satisfactory long-term survival is now achieved, with overall 1- and 3-year survival rates exceeding 80% and 60%[1]. Consequently, the probability that transplanted patients may suffer from non-cardiac diseases during the follow-up has also increased[2–9].

From January 1984 to January 1993, 111 orthotopic cardiac transplantations were performed in the authors' department, in 109 recipients. Among these, 60% had transplants for advanced ischaemic cardiomyopathy. These patients may be at risk of other localized atherosclerotic lesions and eventually development of an abdominal aortic aneurysm during the post-transplant period[2–6,9]. Moreoever, immunosuppressive therapy is associated with various side effects predisposing to atherosclerosis[10–21]. In a recent series, Bull *et al.*[6] reported the occurrence of peripheral vascular disease within 3 years in 23 (10%) of 232 recipients. Of these patients, seven presented with an abdominal aortic aneurysm.

The rapid growth of a true atherosclerotic aneurysm of the ascending aorta within the first year after transplant has been previously reported[20]. Surgical repair of abdominal aortic aneurysms in cardiac transplant patients has been infrequently reported[2–6,9]. The present report reviews three cases of abdominal aortic aneurysm which were successfully operated on within 1 to 4 years after transplantation.

Correspondence to: Dr J. O. Defraigne

Case reports

Case 1

In 1988, a 59-year-old man underwent an orthotopic heart transplantation for end-stage cardiac failure 16 years after an aortic valve replacement. Coronary angiography was normal and the valvular prosthesis was performing well. Immunosuppression consisted of cyclosporin A, methylprednisolone and azathioprine. During the first year post-transplantation, two rejection episodes were treated with a bolus administration of corticoids. During follow-up, some side effects of immunosuppression developed. Systolic (170 mmHg) and diastolic (90 mmHg) hypertension required intake of calcium-channel blockers (nifedipine) and angiotensin-converting enzyme inhibitor (enalapril). The serum lipid profiles were abnormal with hypercholesterolaemia (7.3 mmol/l; normal range 3.9–5.5 mmol/l) and hypertriglyceridaemia (5.4 mmol/l; normal range 0.56–1.8 mmol/l). A slight improvement was obtained with Simvastatin. Some 2 years after transplantation, routine abdominal examination and echocardiography showed

an increase in the transverse diameter of the infrarenal aorta which measured 30 mm. Coronary angiography performed after 3 years was normal, with a left ventricular ejection fraction of 70%. The corticoids were tapered off and the patient maintained on a single therapy of cyclosporin. Annual echocardiographic check-ups performed after 3 and 4 years showed the transverse diameter of the abdominal aorta reaching 40, then 53 mm. Considering the rapid growth of the aneurysm and the patient's good health status, treatment of the aneurysm was proposed. The patient was operated on through an extraperitoneal approach. A bifurcated graft was interposed between the infrarenal aorta and the left iliac artery and the right common femoral artery. During surgery, intracardiac pressures were monitored with a Swan–Ganz catheter. The patient was extubated on day 1. After 1 week, he presented with hyperthermia (39°C). Blood and urinary cultures positively identified *Pseudomonas aeruginosa*. Treatment consisted of amikacine and glazidim. Renal function worsened, with an elevation of serum creatinine to 550 μmol/l (normal range 70–106 μmol/l) and of blood urea to 25 mmol/l (normal range 7.5–16.7 mmol/l). As diuresis was conserved (2 l/24 h), no dialysis was considered necessary. Antibiotic therapy was converted to ciprofloxacin and the cyclosporin dose reduced. The patient was hydrated and low-dose dopamine (5 μg/kg per min) administered. The renal function improved progressively and the patient was discharged 1 month after the operation; 2 years later, he is alive and well.

Case 2

A 62-year-old man was transplanted in 1990 for end-stage idiopathic dilated cardiomyopathy. Pretransplant coronary angiography was normal. Preoperative physical and ultrasonography showed an infrarenal aortic aneurysm with a transverse diameter of 4 cm. The immediate post-transplantation period was uneventful. Immunosuppression consisted of cyclosporin, prednisone and azathioprine. One rejection episode (stage IIb) was observed after 6 months and successfully treated with oral prednisone (100 mg/day for 5 days). At this time the patient was hypertensive with systolic and diastolic blood pressures reaching 180 and 90 mmHg respectively. The lipid profile was normal. At 1 year after transplantation, abdominal computed tomogaphy showed a rapid increase in the transverse diameter of the aneurysm which reached 65 mm. Surgery was rapidly planned. Preoperative coronary angiography was normal and the left ventricular ejection fraction was good (65%). Preoperative immunosuppressive treatment included cyclosporin and prednisone (8 mg/day). After a midline laparotomy, a bifurcated graft was interposed between the infrarenal aorta and the primitive iliac arteries. The postoperative course was uneventful except for transient segmental atelectasis. The patient was discharged after 15 days; 18 months after the operation, the patient is alive and well.

Case 3

A 62-year-old man was transplanted in 1990 for cardiac failure related to ischaemic disease. On preoperative ultrasonographic examination, the transverse diameter of the aorta was measured at 30 mm. After 2 weeks, a rejection episode required an intravenous bolus of corticoids (1 g of intravenous prednisone/day during 3 days). No complications were noted during the postoperative course. After 1 year, routine coronary angiography showed a 70% stenosis of a diagonal branch which was successfully dilated. The ejection fraction was measured at 68%. At this time the corticoids were tapered off and the patient maintained solely on cyclosporin immunosuppressive therapy. No hypertension occurred but hypercholesterolaemia was present (6.2 mmol/l). The transverse diameter of the abdominal aorta was measured by echocardiography at regular intervals; after 2 years, this reached 53 mm. Coronary angiography was normal. Because of the rapid growth of the aneurysm, surgery was considered. A bifurcated graft was implanted, through a midline laparotomy, between the infrarenal aorta and the common iliac arteries. The postoperative course was uneventful and the patient was discharged on day 10 after operation.

Discussion

With the improvement of long-term survival after cardiac transplantation, the number of abdominal aneurysms encountered in the population of transplant patients will probably increase. Moreover, the upper age limit for transplantation has been extended and 60 or 65-year-old patients are now routinely considered[1] and abdominal aortic aneurysms may be present in as much as 2% of the elderly population[22]. Most of these older recipients have transplants for end-stage ischaemic cardiopathy. This increases the probability of coexistent manifestations of atherosclerosis at an early stage and of a subsequent higher risk of later developing extracardiac vascular disease, such as stroke, peripheral vascular disease or an aortic aneurysm. Nevertheless, the true incidence of aortic aneurysms in cardiac transplant recipients is difficult to ascertain from the literature because of the lack of a prospective study based on preoperative ultrasonographic screening. Reichman *et al.*[2] observed two aneurysms in a subgroup of patients having transplants for ischaemic heart failure, which represents an incidence of 2%. In 93 recipients who underwent routine preoperative abdominal ultrasonography, Piotrowski and colleagues[9] found four aneurysms, all in the subgroup transplanted for ischaemic heart disease. They concluded that the occurrence of aneurysms might be limited to patients with ischaemic cardiopathy. This is not the case in the authors' experience since in cases 1 and 2 the heart

failure was related to valvular and idiopathic cardiomyopathies.

Risk factors commonly associated with the development of atherosclerosis are frequently identified in recipients of heart grafts, which may explain both early onset and rapid growth of the aneurysm. As emphasized by Reitz *et al.*[3], transplant patients who develop an abdominal aortic aneurysm are generally younger than usually expected.

As shown by many studies, systemic hypertension, which was seen in the present three recipients after transplantation, plays a significant role in the development of abdominal aortic aneurysms. Hypertension is reported in 50–90% of patients treated with cyclosporin and has generally a poor response to medical therapy, although calcium-channel blockers may have some effect[18,19]. This hypertension, which is largely multifactorial, increases the shear stress of the aortic wall, especially in the context of the increased ejection fraction after transplantation[17,23].

Nevertheless, as shown by Reitz *et al.*[3] before the advent of cyclosporin, factors other than cyclosporin therapy alone could be important. Corticosteroids further increase the potential for the development of hypertension, because of salt retention and the eventual worsening of diabetes and may accelerate the progression of atherosclerosis, with increased incidences of stroke or myocardial infarction[15]. Experimental models support a role for corticoids in the development and rupture of aortic aneurysms[24]. Glucocorticoids impair wound healing and decrease collagen synthesis and aortic aneurysms occur in various diseases treated with corticosteroids[24]. In this context, regular prospective ultrasonographic screening in patients treated by corticosteroids may be of interest[6].

After transplantation, hyperlipidaemia is a well recognized factor contributing to the development of atherosclerosis. Hypertriglyceridaemia is a classic feature of cyclosporin therapy. Its severity is related to various causes such as immunosuppressive and antihypertensive medication, reduced creatinine clearance, diet, and possibly diabetes. In the study of Higgins and Ratcliffe[16], female patients and patients with a genetic predisposition are subgroups at risk where hyperlipidaemia is exacerbated by immunosuppressive drugs. If hyperlipidaemia is discovered, Bull *et al.*[6] recommend a programme of diet and exercise and an effort to reduce the steroid dose, with restriction of lipid-lowering drugs to highly selected patients.

In the logistic regression analysis performed by Bull and co-workers[6], a pretransplant history of ischaemic cardiomyopathy, the presence of hypertension and an elevation of serum triglycerides after transplantation are the most significant risk factors separating the transplant patients with peripheral vascular disease from the unaffected transplant population. The occurrence of accelerated coronary atherosclerosis was also significantly associated with the development of peripheral vascular disease, although the histopathological aspects of accelerated coronaritis differ from those of classical atherosclerotic coronary artery disease.

The growth rate of aneurysms in cardiac transplant patients may be rapid. Piotrowski *et al.*[9] reported a mean(s.d.) expansion rate of 0.74(0.15) cm/year. For the present patients, the mean(s.d.) expansion rate was higher (1.75(0.35) cm/year). This is considerably higher than that reported in a previous study in non-transplanted abdominal aortic patients[22]. The present patients had to be operated upon within 1 to 4 years after transplantation. This emphasizes the need for careful aortic screening after transplantation and possibly resorting to early surgical intervention. Because of rapid aneurysm expansion in several heart transplant recipients, Bull *et al.*[6] routinely screen all candidates for heart transplantation with abdominal ultrasonography and recommend early operation. For patients with significant aneurysms diagnosed before transplantation, these authors recommend, if possible, repair before transplantation.

Some perioperative aspects should be adapted to cardiac transplant patients undergoing abdominal aortic surgery[3,6–8]. Preoperative assessment includes evaluation for rejection. Routine preoperative biopsy is not absolutely essential provided that no signs of cardiac failure or rhythm disturbances are present and that echocardiography shows satisfactory ventricular function. In the general population, operative mortality after elective abdominal aortic aneurysm resection is mainly related to perioperative myocardial infarction[25,26]. As in the present patients, cardiac catheterization and coronary angiography before operation may be indicated in order to exclude graft coronary atherosclerosis which may increase the risk of perioperative infarction. In fact, the lesions of graft coronaritis are more subject to platelet aggregation and to occlusion than classical atherosclerotic lesions, even in the absence of ulceration.

Adaptation of the denervated heart to increased demand relies on filling volumes and pressures, in accordance with the Frank–Starling relation. The denervated heart supports the haemodynamic changes related to infrarenal aortic cross-clamping and declamping, if adequate preload and intravascular volume are maintained throughout the operation, and if the myocardial contractility is good[3,5]. In this respect, monitoring of pulmonary wedge with a Swan–Ganz catheter and of intracardiac filling with transoesophageal echocardiography may be helpful. After surgery, precise management of immunosuppressive therapy is mandatory. The impaired postoperative gastrointestinal resorption suggests that intravenous drug administration is the more reliable route.

Infection is the major source of morbidity and mortality in these patients. Except for emergency cases, operation should be delayed until the end of the first post-transplant year, when rejection episodes tend to be less frequent and when the patient is maintained solely

on cyclosporin therapy. Nevertheless, a small augmentation of the corticoids dosages may be required in the postoperative period to avoid adrenal insufficiency in patients who have been maintained on long-term corticoid therapy. Prophylactic measures for prevention of infection are of prime concern and include antibiotic prophylaxis, early removal of indwelling catheters and vigorous pulmonary physiotherapy.

In conclusion aneurysm expansion appears to be rapid in the population undergoing transplantation. Some factors promote aneurysm expansion such as pre-existent atherosclerosis, increased haemodynamic stress caused by improved cardiac output, and the effect of the immunosuppressive regimen. Close physical abdominal examination and routine periodic ultrasonographic screening of the recipient is indicated during follow-up after transplant. Any increase in diameter requires prompt intervention because of the risk of rupture. Elective surgery is well tolerated.

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