Successful Combined Heart and Kidney Transplantation in a Patient With Sickle-cell Anemia

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Little is known about the management of dual-organ transplantation for sickle-cell disease (SCD)-related complications. In this case study, we report the successful outcome of combined heart and kidney transplantation in a patient with SCD. The recipient was a 33-year-old man with homozygous SCD, who developed end-stage heart and renal failure requiring combined heart and kidney transplantation. The patient was managed with pre-operative blood transfusion and moderate hypothermic cardiopulmonary bypass, with limited peri-operative complications. During the first 6 months there was one episode of acute heart rejection without concomitant renal rejection. Eighteen months after surgery, the patient is at home without vaso-occlusive crises or septic complications. Heart and renal allograft function is preserved, without coronary artery vasculopathy, but with asymptomatic moderate transplant renal artery stenosis. SCD is managed by periodic transfusion. This case study demonstrates that combined heart and kidney transplantation is feasible in patients with SCD. Careful attention to peri- and post-operative management is required. J Heart Lung Transplant 2006;25:993–6. Copyright © 2006 by the International Society for Heart and Lung Transplantation.

Sickle-cell disease (SCD) is an autosomal-recessive disorder due to abnormal hemoglobin (Hb), called HbS, which polymerizes on de-oxygenation, leading to chronic hemolytic anemia, vaso-occlusion characterized by painful vaso-occlusive crises, acute chest syndrome, and increased susceptibility to infection caused by asplenia.[1] Characteristic widespread vascular occlusions in SCD may involve every organ, with chronic damage and dysfunction that reduces quality of life and life expectancy.[1]

Although cardiac involvement in SCD is not uncommon,[2,3] end-stage heart failure is rare, whereas renal involvement has been shown to progress to end-stage renal disease in up to 5% of the total population of SCD patients.[4] We describe, for the first time, one patient with SCD who developed end-stage heart failure and end-stage renal disease requiring combined heart and kidney transplantation.

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CASE REPORT

The patient, a 33-year-old black man from the French West Indies, with homozygous SCD, was referred to our department in January 2004 for evaluation of the possibility of combined heart and kidney transplantation. SCD was diagnosed quite late at age 17 years in 1988, because of chronic anemia and delayed growth and puberty. Stuttering priapism occurred in 1989, and lasted 3 years. The patient was then lost to follow-up until 1998, when chronic renal failure related to focal segmental glomerulosclerosis (confirmed by kidney biopsy histologic examination) was diagnosed. Despite angiotensin-converting enzyme inhibitor treatment, renal function progressively deteriorated requiring intermittent hemodialysis since July 2002. Dilated cardiomyopathy with significant mitral insufficiency but without coronary artery disease was diagnosed in 2000. Despite mitral annulus repair in 2000, the patient developed progressive dyspnea (New York Heart Association [NYHA] Stage IV), with many admissions for acute heart failure. Echocardiography revealed a dilated left ventricle (75 mm) with diffuse hypokinesia (ejection fraction 30% with a massive mitral insufficiency).

Medical treatment was very limited because beta-blockers and angiotensin-converting enzyme inhibitors were not tolerated. The right ventricle was very hypokinetic and dilated, with severe tricuspid insufficiency. Right heart catheterization revealed moderate pulmonary hypertension (mean pulmonary artery pressure 34 mm Hg) with normal pulmonary vascular resistance (1.6 Wood units) and transpulmonary gradient (6 mm

Hg). Pulmonary capillary pressure was high (29 mm Hg) with a V wave and a low cardiac index (1.73 liters/min/m^2). Asymptomatic gall-bladder lithiasis was noted. Despite repeated blood transfusion every month to maintain Hb >9 g/dl and sickle-cell HbS <40%, liver function tests were normal and the patient did not developed anti-HLA antibodies. Liver biopsy in February 2002 revealed marked hemosiderosis, within hepatocytes and Kupffer cells, but an absence of cirrhosis. Extensive pre-operative examination revealed no contraindication to combined transplantation and the patient was listed for heart and kidney transplantation in March 2004. An orthotopic heart transplant combined with a heterotopic kidney transplant was performed on April 15, 2004. Before surgery, the patient did not receive exchange transfusion (because of a low HbS concentration of 6%), but a blood transfusion was done to maintain Hb >9 g/dl. Intra-operatively the patient was placed on cardiopulmonary bypass and blood temperature was lowered to 34.9°C. The donor was a 49-year-old man who died from a cerebral hemorrhage. Donor and recipient shared 3 HLA mismatches (1A, 1B and 1DR).

Standard cardiac transplantation immunosuppression was used, consisting of induction with anti-thymocyte globulin (Thymoglobulin, Mérieux) for 5 days combined with methylprednisolone during (1,000 mg) and after (500 mg at 24 and 48 hours) the operation. Prednisone was started after extubation with an oral dose of 1 mg/kg/day and progressively tapered to 0.2 mg/kg/day at 2 months. Mycophenolate mofetil was administered on Day 5 at 2 g/day, which was then adjusted according to clinical safety. Tacrolimus was initiated on Day 3 to maintain serum tacrolimus trough concentration at 5 to 10 ng/ml. Anti-microbial prophylaxis included cefotaxim for 48 hours and trimethoprim–sulfamethoxazole for 6 months. Because of a functional spleen, no specific penicillin prophylaxis was given in our patient but should be discussed in cases of abnormal splenic function. According to the cytomegalovirus (CMV) IgG serostatus of the recipient (R^+) and donor (D^+) at the time of transplantation, the patient was preventively treated with oral valganciclovir (dose adjusted according creatinine clearance) during the first 12 weeks after transplantation. Macroscopic and microscopic examination of the explanted heart revealed a bi-ventricular dilation with a myocardial fibrosis and a hypertrophic right ventricle. No cardiac hemosiderosis was detected.

The post-operative course was eventful with two bleeding complications. First, at Day 2, early acute renal dysfunction occurred, associated with abdominal pain. Doppler ultrasonography revealed a hematoma surrounding the kidney while compressing the renal parenchyma. The patient was taken to the operating room for emergent evacuation of the hematoma. Renal function progressively improved after one dialysis. Second, at Day 10, pleural effusion following the first endomyocardial biopsy, without cardiac perforation, required chest tube drainage followed by sternotomy for hemostasis.

At 26 days post-transplant, the patient presented with biopsy-proven acute heart rejection (Grade 3A), without hemodynamic compromise or echocardiographic modification and without concomitant kidney rejection on kidney allograft biopsy. Intravenous methylprednisolone 500 mg was given on 3 consecutive days and endomyocardial biopsy was Grade 0 after 10 days. The patient developed diabetes mellitus from the time of surgery, which was treated with insulin. The patient was discharged on post-transplant Day 33. In September 2004, 2 months after discontinuation of CMV preventive treatment, the patient developed CMV reactivation without CMV disease, which was treated successfully with oral valganciclovir for 12 weeks. Asymptomatic transplant renal artery stenosis (TRAS) was diagnosed by routine Doppler ultrasonography (peak systolic velocity 235 cm/s, resistive index 0.62) in October 2004, confirmed by magnetic resonance angiography, which revealed proximal anastomosis stenosis with an estimated mean diameter of 40%.

Because it was not hemodynamically significant, this renal vascular complication did not require any specific treatment (percutaneous transluminal angioplasty). SCD was managed by periodic transfusion (once a month) to keep Hb ≥9 g/dl. Presently, 18 months after the procedure, no complication related to the original disease (vaso-occlusive crisis) has occurred. Interestingly, despite immunosuppressive treatment in this patient with a specific risk factor for bacterial complication (asplenia), no septic complications have occurred. No new episodes of acute heart or renal rejection have been observed, and coronary angiography performed in April 2005 was normal and confirmed by multi-slice computed tomography. Echocardiography showed excellent graft function and kidney function is good (creatinine clearance calculated as 60 ml/min with the Cockroft–Gault equation), with urinary protein excretion at 0.1 g/day. The patient is currently at home and expected to return to work shortly.

DISCUSSION

We have reported the first successful experience of combined heart and kidney transplantation in a patient with SCD. The kidneys and heart are the two major organs classically involved in SCD. Renal failure occurs in 4% to 18% of SCD patients.[4] Renal injury, including renal tubular disease, papillary necrosis and glomerulonephritis, is a major risk factor for early death in these patients.[4,5] Focal segmental glomerulosclerosis is the