

First Combined Heart-Kidney Transplantation in Israel

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Combined heart and kidney transplantation from the same donor is an acceptable but rarely performed therapeutic option for selected patients with end-stage heart and renal failure. The first case was reported in 1978 in a patient with stone heart syndrome. The patient died 15 days after the operation from sepsis with no evidence of cardiac or renal allograft rejection. The first successful heart and kidney transplantation with long-term survival was reported 8 years later in 1986. In the last few years combined organ transplantation has become more common as selection criteria for transplantation have broadened secondary to improvement in immunosuppression and surgical techniques. In 2000 the first Israeli experience with combined pancreas-kidney transplantation was reported [1]. We present the first case in Israel of a heart-kidney transplantation from the same donor in a young patient with end-stage congestive heart failure with secondary end-stage chronic renal failure.

Patient Description

A 21 year old 45 kg man underwent heart-kidney transplantation for adriamycin-induced dilated cardiomyopathy and secondary end-stage renal failure. Past medical history revealed a diagnosis of Wilm's tumor of the left kidney at age 12 years, which was treated by left nephrectomy followed by chemotherapy with adriamycin. Seven years after completion of treatment, cardiomyopathy developed with subsequent right heart failure, ascitis and anasarca. The disease course was characterized by several hospitalizations for exacerbation of the congestive heart

failure. At age 20 years his renal function deteriorated due to low cardiac output syndrome; patient ejection fraction was 15%. Renal failure was manifested by oliguria, followed by anuria and an increase in creatinine level from 1.3 to 3.3 mg/dl. The patient was placed on hemodialysis and was listed for combined heart and kidney transplantation.

Five weeks before transplantation he was hospitalized in the intensive cardiac care unit and dobutamine infusion was started. The patient was referred to our cardiac surgical department with severe biventricular heart failure, tension ascitis, anasarca, hypo-albuminemia and uremia. Liver function and coagulation profile were normal.

Orthotopic heart transplantation and simultaneous tricuspid valve De Vega anuloplasty was performed. The heart was harvested from a 29 year old 56 kg female donor after a motor vehicle accident. The cause of brain death was a large intracerebral hematoma with herniation.

Donor-recipient matching was performed according to blood group ABO. Human leukocyte antigen matching was not attempted.

Cardiopulmonary bypass time was 116 minutes; total ischemic time of the heart was 119 minutes. After weaning the patient from the cardiopulmonary bypass, neutralization of heparin and hemodynamic stabilization, the left donor kidney was transplanted retroperitoneally into the right recipient iliac fossa. Tension ascites fluid was not evacuated during the kidney surgery. Total operative time was 240 minutes. The beginning of urination was observed in the operating room.

During the immediate postoperative period the patient was given an infusion of isoproterenol, epinephrine and dopamine. The heart rate was maintained at > 100 beats per minute, cardiac index at > 2.8/L/min/m² and hourly urine output > 100 ml.

Immunosuppression was induced with 1 g mycophenolate 1 hour before operation, 1 g methylprednisolone upon release of the aortic cross-clamp and maintained by daily administration of intravenous antithymocyte globulin, 10 mg/kg, and oral prednisone 1.2 mg/kg in a divided dose, oral mycophenolate 1 g twice daily, and oral tacrolimus according to blood level. Antithymocyte globulin and prednisone were gradually tapered and the antithymocyte globulin was discontinued 7 days postoperatively. Blood tacrolimus level was maintained at 8–12 ng/ml.

Extubation was performed 14 hours after transplantation. The patient's condition remained stable for 3 postoperative days, after which inotropic support was discontinued. On postoperative day 4, however, sudden severe respiratory distress with decreasing oxygen saturation < 80%, pO₂ < 50 mmHg and pCO₂ > 95 mmHg was observed and intubation was performed. Rupture of the diaphragm with flooding of the chest cavity by ascitic fluids was suspected. Chest X-ray examination revealed massive bilateral pleural effusion. The mechanism of diaphragmatic rupture was probably connected to the sudden increase of intra-abdominal pressure during respiratory physiotherapy. Bilateral chest tubes were inserted and a large amount (6 L) of serotic fluid was drained, leading to rapid improvement

of respiratory function. The patient was weaned from the ventilator and extubated. Chest tubes were removed after 4 days.

The postoperative course was complicated by a very slow decrease in the interstitial edema, requiring aggressive diuretic treatment, high caloric nutrition, and aggressive physiotherapy with permanent use of the compression therapy systems on the legs (Lympha Press®, Mega Afek, Israel). Heart function was evaluated by weekly ultrasound examination during hospitalization. There were no episodes of heart or kidney rejection. Serum creatinine level was normalized 1 month after operation.

The patient was discharged home on postoperative day 43. Maintenance therapy consisted of oral tacrolimus for a target blood level of approximately 8–12 ng/ml and oral prednisone 20 mg daily; mycophenolate was substitute to oral azathioprine 25 mg twice daily because of leukopenia. Rejection surveillance was performed by endomyocardial biopsies. Kidney biopsies were not performed 12 months after transplantation. Heart and renal allograft function is normal.

Comment

In end-stage cardiomyopathy where concomitant chronic renal failure is a contraindication for cardiac transplantation, simultaneous heart and kidney transplantation from a single donor may be the only feasible therapeutic option. The more frequently reported complications are diabetic and/or hypertensive nephropathy concomitant with ischemic or dilated cardiomyopathy, or renal failure secondary

to end-stage heart failure. Narula et al. [2] analyzed 84 patients who underwent 84 heart-kidney transplantations and reported that dilatation (38%) and ischemia (22%) were the main causes of heart failure. The reasons listed for simultaneous renal transplantation included a variety of renal diseases exacerbated by end-stage heart failure, with the most common diagnoses being juvenile diabetes mellitus (17%) and glomerulonephritis (11%). In a study by Lesser and co-authors [3], the main causes of heart failure in their series of 13 patients who underwent 14 heart-kidney transplantations were ischemic (43%) and dilated (22%) cardiomyopathies. The main causes of renal failure were hypertensive (29%) and diabetic (21%) nephropathies.

Adriamycin is standard chemotherapy for patients with Wilms' tumor and a well-recognized cause of cardiomyopathy and end-stage heart failure. Worsening renal function in most patients with advanced heart failure usually indicates severe end-organ compromise. The incidence of end-stage renal disease for patients with unilateral Wilm's tumor was quite low, less than 1%. However, patients with Wilms' tumor, aniridia, major genitourinary malformations, and mental retardation (the so-called WAGR syndrome) have a 50% chance of developing end-stage renal disease. This small group of patients represents only 0.75% of the overall Wilms' tumor population [4].

Groetzner and colleagues [5] suggest that tacrolimus-based immunosuppression yields promising long-term results in heart-kidney and heart transplantations. The incidence of transplant vasculopathy

seems to be lower after heart-kidney than after heart transplantation. If these results are secondary to a protective effect of tacrolimus-induced tolerance or of tolerance-associated co-transplantation, they will need to be investigated in prospective multicenter trials. In conclusion, the good results of heart-kidney transplantation make this procedure an effective therapeutic option in selected patients.

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