Outcome of renal transplantation from a donor with polycystic kidney disease

Resultado do transplante renal com doador portador de doença renal policística

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Abstract

Faced with the long waiting list for a kidney transplant, the use of donors with expanded criteria, like polycystic kidneys, is an option that aims to increase in a short time the supply of kidneys for transplant. This report of two cases of transplants performed from a donor with polycystic kidneys showed promising results, and the receptors evolved with good renal function, serum creatinine measurements within the normal range and with adequate glomerular filtration rate, evaluated over a period of four years post transplant. This fact confirms that the option of using donors with polycystic kidneys is safe and gives good results.

Keywords: autosomal dominant; kidney transplantation; polycystic kidney, tissue donors.

Resumo

Diante da longa fila de espera por um transplante renal, a utilização de doadores com critério expandido, a exemplo de rins policísticos, torna-se uma opção que visa aumentar a oferta de rins para transplante a curto prazo. O presente relato de dois casos de transplantes realizados a partir de um doador com rins policísticos apresentou resultado promissor, tendo os receptores evoluído com boa função renal, dosagens de creatinina sérica dentro da faixa de normalidade e com taxa de filtração glomerular adequada, avaliados num período de quatro anos pós-transplante. Isto confirma que a opção da utilização de doadores com rins policísticos é segura e apresenta bons resultados.

Palavras-chave: doadores de tecidos; rim policístico autossômico dominante; transplante de rim.

Introduction

Kidney transplantation provides individuals with end-stage renal disease with adequate levels of renal function from the clinical standpoint and a chance for recipients to return to their social and professional lives.[1]

Data from the Brazilian Organ Transplant Registry managed by the Brazilian Organ Transplant Association (ABTO)[2] show that just over 40% (5,433 of 11,445) of the individuals waiting for an organ were offered a transplant procedure in 2013. In the northern state of Pará, only 53 renal transplant procedures were performed for 455 patients in the waiting list in 2013. Individuals in need of kidney transplantation have to endure long waits for an organ.

Expanded criteria donors account for a considerable portion of transplant procedures and have been instrumental in increasing the supply of kidneys in the short term.[3]

Polycystic kidney disease (PKD) is a genetic disorder contemplated by the expanded criteria of the Brazilian Ministry of Health.[4] The condition manifests in two forms: autosomal dominant polycystic kidney disease (ADPKD) or autosomal recessive polycystic kidney disease (ARPKD). PKD causes chronic kidney failure and large cysts to form in the kidneys. By the time they are detected, the cysts are usually large and numerous, and will have invaded the spaces once occupied by normal renal tissue while compressing and obliterating it, leading to the onset of end-stage renal disease.[5,6]

Submitted on: 08/14/2015.
Approved on: 12/11/2015.

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DOI: 10.5935/0101-2800.20160059

Case presentation

The donor

A 12-year-old brown male child weighing 70 kg and measuring 170 cm in height, with O positive blood and no previous diseases according to his relatives, was taken to a hospital after suffering from sudden-onset headaches for seven days, along with incoercible vomiting, systemic hypertension, and sleepiness. The patient developed polyuria and sensory depression, and was referred to an intensive care unit (ICU) where he was intubated (FiO_2 at 40%) and offered mechanical ventilation.

His urine output was 340 ml/24h and he had a blood pressure (BP) of 110/60 mmHg. A head computed tomography scan taken on day 7 of his ICU stay revealed he had a meningeal bleeding caused by a ruptured cerebral aneurysm. No cerebral blood flow was detected from the carotid or vertebral arteries.

Workup performed on the day of the patient's death showed the following values: hematocrit 22%; hemoglobin 7.5 mg/dL; BUN 36 mg/dL; serum creatinine 0.7 mg/dL; potassium 4.3 mEq/l; sodium 152 mEq/l; glucose 95 mg/dl; SGOT 15; GPT 14; pH 7.38; pO_2 154; pCO_2 54; SaO_2 49%; positive IgG serology for cytomegalovirus (CMV) and negative serology for hepatitis B and C. HLA (human leukocyte antigen) testing performed in the histocompatibility lab revealed A02;02, B39;48 and DRB1 08;09.

Multiple small cysts were seen in the donor's kidneys during the organ procurement procedure.

The recipients

One of the recipients was a 24-year-old brown woman on hemodialysis for three years diagnosed with chronic glomerulonephritis. Her preoperative tests showed she had O positive blood, negative serology for HIV (human immunodeficiency virus) and hepatitis B and C, and positive IgG serology for CMV and toxoplasmosis. Immune tests showed HLA A31;68, B39;53, DRB1 01;08, negative cross match, and 40% and 0% panel reactive antibodies (PRA) in classes I and II, respectively.

The graft was on cold ischemia for 24 hours and four minutes. The immunosuppression scheme included induction therapy with thymoglobulin (6 mg/kg in four doses); mycophenolate sodium (360 mg twice a day from the first day after surgery); prednisone (30 mg/day from the first day after surgery); and tacrolimus (12 mg/day) starting seven days after surgery. Her urine output values one, three, and five days after transplantation were 20 ml, 23 ml, and 35 ml, respectively.

The patient required hemodialysis until ten days after the procedure. She was discharged 38 days after surgery. Nine months after transplantation, tacrolimus was replaced with everolimus (4 mg/day). Initial ultrasound examination showed a kidney measuring 11.8 x 5.6 x 6.4 cm, with a volume of 227 cm^3 and multiple cysts, the larger measuring 1.4 cm.

Four years after the transplant procedure her mean serum creatinine level was 1.0 mg/dl. The most recent ultrasound image showed a kidney measuring 13.3 x 6.4 x 6.3 cm with a volume of 288.2 cm^3; two anechogenic cysts were observed, the larger measuring 1.7 cm in the lower third of the kidney; no other alterations were seen. She was kept on immunosuppressants with minor dose adjustments: mycophenolate sodium (1.08 g/day), prednisone (5 mg/day), and everolimus (3.5 mg/day).

The second recipient was a 47-year-old brown woman on hemodialysis for four years diagnosed with chronic glomerulonephritis. Her preoperative tests showed she had O positive blood, negative serology for HIV (human immunodeficiency virus) and hepatitis B and C, and positive IgG serology for CMV and toxoplasmosis. Immune tests showed HLA A24;24, B39;44, DRB1 4;8, negative cross match, and 50% and 0% panel reactive antibodies (PRA) in classes I and II, respectively.

The graft was on cold ischemia for 23 hours. The immunosuppression scheme included induction therapy with thymoglobulin (6 mg/kg in four doses); mycophenolate sodium (720 mg a day from the first day after surgery); prednisone (30 mg/day from the first day after surgery); and tacrolimus (10 mg/day) starting seven days after surgery. Her urine output values one, three, and five days after transplantation were 682 ml, 680 ml, and 80 ml/24hs, respectively. The patient required hemodialysis until eight days after surgery.

She was discharged 22 days after surgery. Nine months after transplantation, tacrolimus was replaced with everolimus (2 mg/day). Initial ultrasound examination showed a kidney measuring 11.8 x 5.6 x 6.4 cm with a volume of 227 cm^3 and multiple cortical cysts, the larger measuring 1.4 cm; no other alterations were seen.

Four years after the transplant procedure her serum creatinine level ranged from 0.72 mg/dl to 1.4 mg/dl. The most recent ultrasound image showed a kidney measuring 12 x 6.9 x 5.6 cm; multiple cysts measuring up to 2.6 cm; and mild pyelocaliceal dilation. She was kept on immunosuppressants with dose adjustments: mycophenolate sodium (720 mg/dl), prednisone (5 mg/day), and everolimus (2 mg/day).

The time distribution of creatinine serum levels observed in both recipients are shown on Table 1 and Figure 1.

Table 1 Four-year follow-up serum creatinine levels of recipients of grafts from donors with polycystic kidney disease

	24-year-old recipient	47-year-old recipient
Immediate postop	12.30	7.00
1 month	1.40	1.40
2 months	1.29	1.20
3 months	1.60	1.00
1 year	1.10	0.94
2 years	1.20	0.90
3 years	1.10	1.00
4 years	1.00	1.10

Source: research protocol, 2014.

Discussion

According to the Brazilian Society of Nephrology and the Brazilian Society of Urology,[7] polycystic kidney disease should be treated as a relative indication for kidney transplantation. Kidneys with early-stage PKD may be considered viable for donation, as they do not cause the onset of adverse effects and increase recipient survival.[8]

Canaud *et al*.[9] reported that finding ADPKD in donor kidneys after transplantation is a rare, but not exceptional event.

Eng *et al*.[8] reported no complications in the 15-year follow-up of a patient given a graft from a donor with PKD. The recipient developed good renal function with a serum creatinine level of 1.2 mg/dl and cystic disease with slow progression.

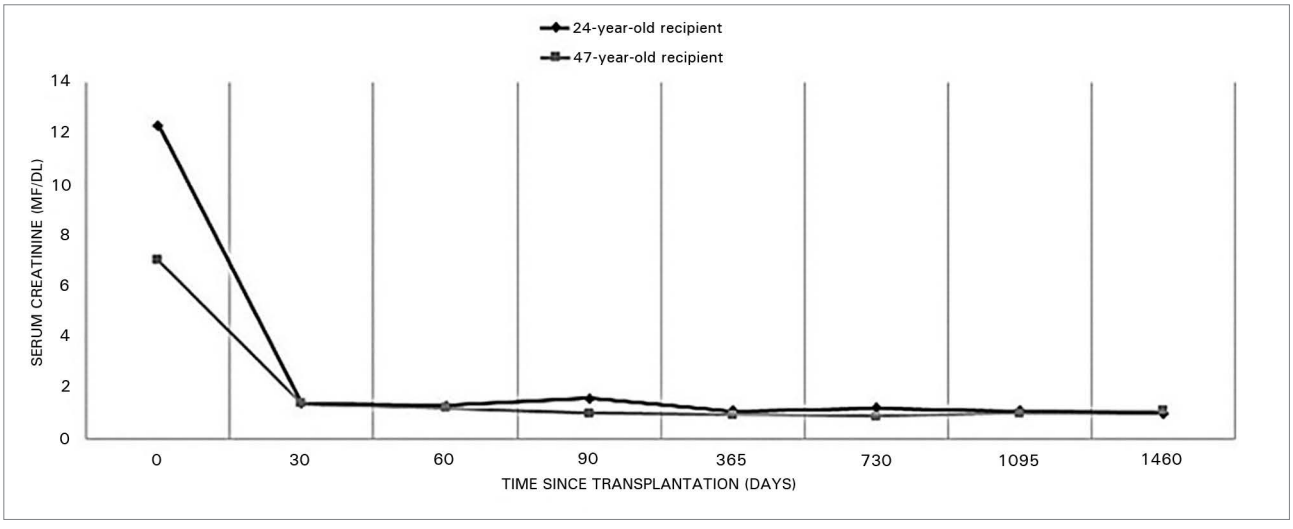
The pathophysiology of ADPKD is rather complex and largely unknown. The appearance of cysts has been correlated with the deregulation of several molecular pathways, such as the mTOR (mammalian target of rapamycin) pathway, unusually activated in this situation.[9-11]

Significant delays in cyst growth have been described in experimental studies with rodents given mTOR inhibitors.[12] However, when used to treat the native kidneys of individuals with ADPKD, sirolimus failed to reduce the growth rate of renal cysts while everolimus, although effective in decreasing the growth rate of cysts, could not prevent progression to renal failure.[13,14]

Furthermore, recent data from prospective studies following renal transplant patients with ADPKD have described significant decreases in cyst volumes after treatment with sirolimus *versus* calcineurin inhibitors.[11]

Finding the critical serum levels of everolimus and sirolimus is of crucial importance, once the ideal dosages of these drugs to inhibit the mTOR

Figure 1. Four-year follow-up serum creatinine levels of recipients of grafts from donors with polycystic kidney disease.



pathway without producing severe side effects are still unknown.[9,15]

The recipients of grafts from donors with PKD observed in this study developed good renal function and levels of serum creatinine within the range of normality, good glomerular filtration rates and mild kidney and cyst enlargement. These outcomes confirm the safety of using expanded criteria donors as a viable option to increase the supply of organs for donation and provide recipients with good functional outcomes and increased survival.

Immunosuppression therapy schemes vary depending on the needs of each recipient. Although the dosages to suppress the growth of renal cysts have not been standardized, adequate workup screening and periodic assessment of patients allow the identification of the adjustments needed in each case and the development of functional grafts without greater complications.

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