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Clinical Report

Reuse of a previously transplanted kidney: does success come with a price?

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Abstract

Longer wait times for deceased donor kidney transplant have prompted newer initiatives to expedite the process. Reuse of a previously transplanted kidney might be appropriate in certain circumstances. However, one must also consider the unique issues that may arise after such transplants. We describe our experience in one such case where the donor kidney had lesions of focal and segmental glomerulosclerosis and signs of alloreactivity (positive C4d staining) prior to transplantation and the recipient developed ganciclovir-resistant cytomegalovirus (CMV) infection, which was perhaps transmitted from the donor. Despite the challenges, the allograft function remained stable 5 years after reuse.

Keywords: cytomegalovirus (CMV); ganciclovir resistance; organ reuse; rejection

Case description

The recipient

A 42-year-old African American male, whose reported cause of end-stage renal disease (ESRD) was hypertension, received a one-antigen-matched deceased donor kidney transplant in June 2005.

The donor(s)

A 38-year Caucasian female (donor B), who developed ESRD due to type 1 diabetes mellitus, received a living donor kidney transplant in 1997, and a pancreas transplant in 2002. Both organs failed and she subsequently received a simultaneous kidney-pancreas (SPK) transplant in April 2005. She was at intermediate risk for cytomegalovirus (CMV) infection at the time of the SPK transplant (D−/R+) and her maintenance immunosuppression consisted of tacrolimus, mycophenolate mofetil (MMF) and prednisone. Her records indicated that she was treated for CMV infection based on symptomatology (fever and diarrhea) with intravenous ganciclovir about a month after SPK transplant for an undetermined period of time followed by prophylaxis with oral valganciclovir at 450 mg/day. Her cause of death was a spontaneous intracranial bleed, and at the time of recovery of her transplanted kidney, CMV IgM was not detected in serum. A frozen section of donor B's kidney revealed normal renal parenchyma with only one obsolescent glomerulus of 100 in the sample. However, the final interpretation, communicated 2 days after the transplant, revealed focal and segmental glomerulosclerosis (FSGS), with collapsing features, diffuse C4d staining in the peritubular capillaries (Figure 2D) and acute tubular necrosis suggestive of acute humoral rejection. Electron microscopy (EM) revealed diffuse podocyte foot process effacement.

The original donor (donor A) was an 18-year-old African American male who had died due to blunt force trauma to the head causing an intracranial bleed.

We proceeded with the transplant based on the frozen section findings, terminal creatinine value (1.2 mg/dL) and the total cold ischemia time (27 h and 22 min). Our patient received induction therapy with anti-rabbit thymocyte globulin (ATG) and methylprednisolone; intravenous ganciclovir was used as prophylaxis against the CMV since he had delayed graft function and was receiving ATG. Since the renal allograft had lesions of FSGS, the urine protein-to-creatinine ratio (U P/Cr) was monitored, and the initial ratio was 2.8. ATG was continued for 2 weeks and ganciclovir for 3 weeks (0.625 mg/kg three times a week for 2 weeks followed by 0.625 mg/kg/day for 1 week) after which he received oral valganciclovir 450 mg/day (adjusted to glomerular filtration rate, GFR). Serum creatinine decreased from 13.9 to 3.5 mg/dL on day 13 post transplant, at which point dialysis treatments were stopped and immunosuppression was maintained with tacrolimus, MMF and prednisone.

On day 24 post transplant, his white blood cell count decreased to 2400 cells/mm^3, which led to the lowering of the MMF (from 2000 mg to 1000 mg/day). The leukopenia persisted for another week and his blood tested positive for CMV DNA by PCR (307 000 copies/mL) at which point MMF was discontinued and intravenous ganciclovir at 2.5 mg/kg/day was substituted for oral valganciclovir. He then became symptomatic with fever and malaise and the CMV levels in the blood rose to 1 199 000 copies/mL over a 2-week period despite adequate doses of ganciclovir. The possibility of mutant CMV strain resistant to ganciclovir was considered and intravenous foscarnet 3 g every 12 h (50 mg/kg every 12 h for estimated GFR of 58 mL/min) was started. His symptoms improved quickly and as depicted in Figure 1, CMV decreased dramatically over the next 2 weeks to 3000 copies/mL. A mutation for ganciclovir resistance tested positive at the UL-97 location. On day 75 post transplant, CMV was no longer detectable in his blood. Foscarnet was continued for a total of 3 months, his tacrolimus level during this episode was 5–8 ng/mL and the U P/Cr ranged between 1.25 and 2.5. His maintenance immunosuppression was changed to tacrolimus, leflunomide and prednisone.

A biopsy performed on day 110 post transplant revealed persistent lesions of FSGS (EM revealed only focal foot process effacement) and diffuse C4d staining in the peritubular capillaries (Figure 2A and E). Since the donor-specific antibodies (DSA) tested negative, no treatment was initiated. A second allograft biopsy at 5.5 months post transplant still revealed FSGS and only focal C4d staining.

Over the next year, CMV DNA was monitored monthly and was not detected. Another biopsy performed 13 months post transplant still revealed FSGS lesions (Figure 2C), but C4d staining was negative. However, tubular atrophy increased to ~40%. The U P/Cr was 0.6–0.8 and the serum creatinine level was 1.6–2.0 mg/dL. At last follow-up, 5 years after transplant, his serum creatinine level was 2.1 mg/dL, with a U P/Cr (obtained several months earlier) of 0.12. The clinical course of our patient is depicted in Figure 1.

Discussion

The average wait time to receive a deceased donor kidney transplant in the USA is 4–5 years [1, 2]. Under appropriate circumstances, expanded criteria donors [3], donation after cardiac death donors [4], donors with hepatitis C [5] and CDC (Centers for Disease Control and Prevention) high-risk donors [6] are considered. Today, the most common cause of loss of the renal allograft is death of the patient with a functioning graft. Ojo *et al*. analyzed data registered with the Scientific Registry of Transplant Recipients between 1987 and 1996 and found that 43% of the kidney transplant recipients at the time of death had a creatinine value of 1.9 ± 0.8 mg/dL, which compared favorably with recipients that were alive with a functioning graft and had a creatinine value of 1.7 ± 0.7 mg/dL [7].

Three case reports of kidney reuse are reported in the literature [8–10], without any major issues. Recently, a fourth report regarding the reuse of the kidney allograft was described where the EM lesions of FSGS in the primary recipient disappeared after it was transplanted into another recipient without underlying FSGS [11]. Both allograft function and EM changes improved after the second transplant. It is important to note that the glomeruli did not reveal light microscopic changes of FSGS.

Our case is exceptional in that the patient, despite receiving a reused organ, overcame all odds to eventually have a great outcome. Although our case was a success story, it came at a price. It not only presented us with unique challenges but also added additional costs to the health system.

First, CMV infection was encountered early after transplantation and increase in CMV viremia in the presence of adequate doses of ganciclovir led us to consider

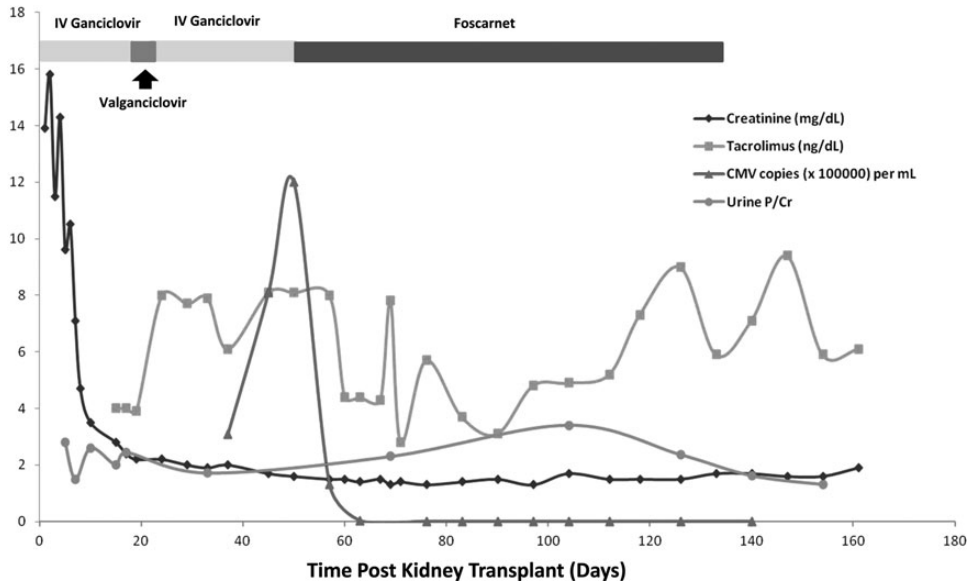

Fig. 1. Timeline of clinical events after transplantation. As noted in the figure, CMV decreased dramatically after starting foscarnet. Also noted in the figure are the serum creatinine values, tacrolimus levels and urine protein-to-creatinine ratios.

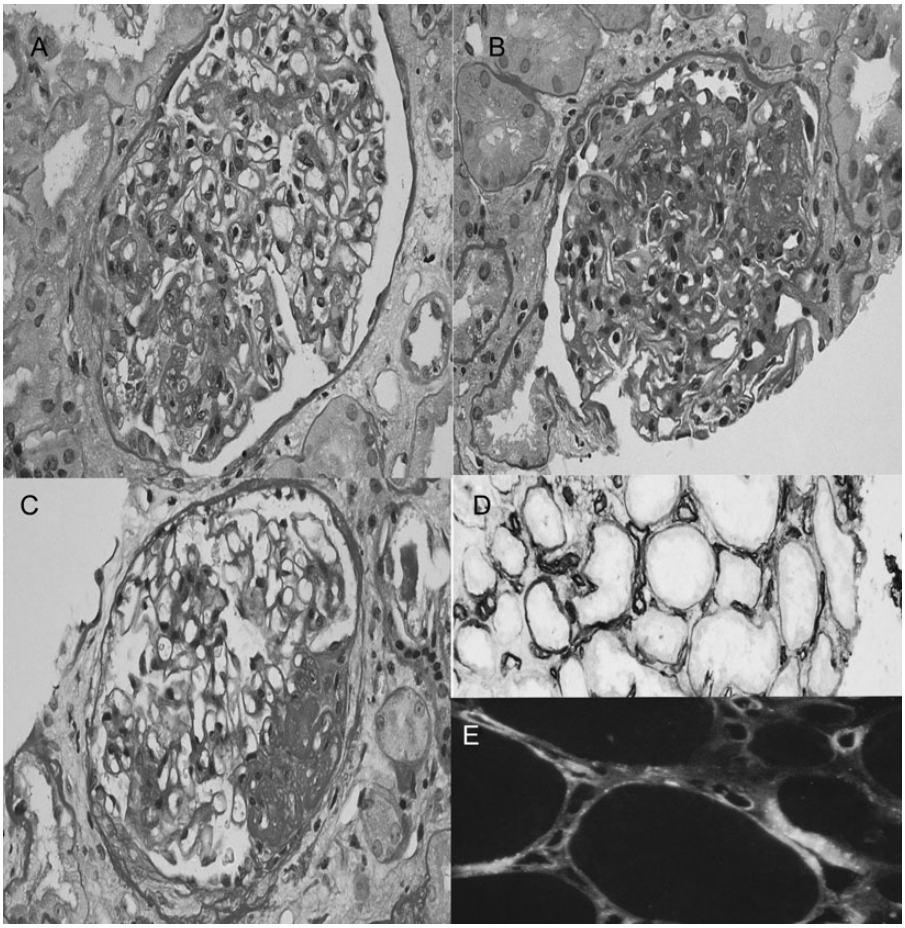

Fig. 2. (**A**) Glomerulus showing FSGS in the allograft biopsy 3.5 months post transplant. (**B**) FSGS in the biopsy from 5.5 months post transplant. (**C**) FSGS in the biopsy at 13 months. (**D**) The pre-implantation biopsy showing diffuse peritubular capillary C4d staining on immunoperoxidase staining. (**E**) Focal peritubular capillary C4d in the biopsy at 3.5 months.

ganciclovir resistance [12]. It was mentioned that donor B was treated for CMV infection with intravenous ganciclovir after the SPK transplant and was then placed on a prophylactic dose of valganciclovir 450 mg/day in the presence of normal allograft function. Our conjecture is that sub-therapeutic valganciclovir dose in the presence of sub-clinical CMV infection or low levels of viremia might have predisposed to ganciclovir resistance. The mutant CMV strain was transmitted to our patient through donor B as our patient was never exposed to ganciclovir.

Next, the C4d staining in the donor kidney was most likely due to humoral alloreactivity in donor B against donor A alloantigens. Our patient was not sensitized prior to transplantation and the crossmatch testing was negative, and there were no light microscopic features of antibody-mediated rejection or the presence of donor-specific antibodies. Also, data from protocol biopsies in sensitized transplant recipients [13] and other longitudinal renal allograft biopsy studies [14] suggest that C4d staining could persist for several months. This could explain the possibility that in our patient, C4d was detected when the biopsy was performed on day 110 post transplant and at 5.5 months, but was not detected after 13 months.

Lastly, the lesions of FSGS with foot process effacement came from the donor kidney (donor B). It is unknown whether these lesions could have been transmitted through donor A as there was no pre-implantation biopsy. To the best of our knowledge, our patient had ESRD due to hypertension. After transplantation, we carefully monitored the U P/Cr and while the repeat biopsies revealed persistence of the FSGS lesions, there was some resolution of the foot process effacement (diffuse to focal). The key difference in our case compared with the recent report [11] was the presence of established light microscopic lesions of FSGS at the time of transplantation and hence, we are unsure whether these lesions would resolve.

In conclusion, organ reuse seems worth the effort. Perhaps, with caution, it could be explored on a larger scale. However, such an effort needs coordination amongst transplant centers, organ-procuring organizations and regulatory bodies to come up with a plan. While the task certainly seems daunting, a discussion seems worthwhile.

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Conflict of interest statement. None declared.

References

1. Leichtman AB, Cohen D, O' Connor K *et al*. Kidney and Pancreas transplantation in the United States, 1997–2006; the HRSA Breakthrough Collaboratives and the 58 DSA Challenge. *Am J Transplant* 2008; 8: 946–957

2. Port FK. Organ donation and transplantation trends in the United States, 2001. *Am J Transplant* 2003; 3: 7–12
3. Metzger RA, Delmonico FL, Feng S *et al*. Expanded criteria donors for kidney transplantation. *Am J Transplant* 2003; 3: 114–125
4. Ojo AO, Hanson JA, Meier-Kriesche H *et al*. Survival in recipients of marginal cadaveric donor kidneys compared with other recipients and wait-listed transplant candidates. *J Am Soc Nephrol* 2001; 12: 589–597
5. Abbott KC, Lentine KL, Bucci JR *et al*. The impact of transplantation with deceased donor hepatitis C-positive kidneys on survival in wait-listed long-term dialysis patients. *Am J Transplant* 2004; 4: 2032–2037
6. Kucirka LM, Namuyinga R, Hanrahan C *et al*. Provider utilization of high-Risk donor organs and nucleic acid testing: results of two national surveys. *Am J Transplant* 2009; 9: 1197–1204
7. Ojo AO, Hanson JA, Wolfe RA *et al*. Long-term survival in renal transplant recipients with graft function. *Kidney Int* 2000; 57: 307–313
8. Al-Hasani MK, Saltissi D, Chang R *et al*. Successful regrafting of an explanted transplant kidney. *Transplantation* 1987; 43: 916–917
9. Bowman JS III, Jaffers G, Waymack JP. Reutilization of a transplanted kidney—a case report. *Transplantation* 1991; 51: 1124–1125
10. Goralczyk AD, Obed A, Lorf T. Fourteen-year survival of a renal graft reused 2 years after initial transplantation: a case report. *Transplant Int* 2010; 23: e15–e17
11. Gallon L, Leventhal J, Skaro A *et al*. Resolution of recurrent focal segmental glomerulosclerosis after retransplantation. *N Engl J Med* 2012; 366: 1648–1649
12. Limaye AP, Corey L, Koelle DM *et al*. Emergence of ganciclovir-resistant cytomegalovirus disease among recipients of solid-organ transplants. *Lancet* 2000; 356: 645–649
13. Loupy A, Hill GS, Suberbielle C *et al*. Significance of C4d banff scores in early protocol biopsies of kidney transplant recipients with preformed donor-specific antibodies (DSA). *Am J Transplant* 2011; 11: 56–65
14. Kieran N, Wang X, Perkins J *et al*. Combination of peritubular C4d and transplant glomerulopathy predicts late renal allograft failure. *J Am Soc Nephrol* 2009; 20: 2260–2268

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