



EXCEPTIONAL CASE

First UK case report of kidney transplantation from an HIV-infected deceased donor to two HIV-infected recipients

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Abstract

Kidney transplantation is now considered the treatment of choice for many human immunodeficiency virus (HIV)-infected patients with end-stage renal disease (ESRD). Graft survival rates using HIV-negative donors and carefully selected HIV-positive ESRD patients are similar to those observed in HIV-uninfected kidney transplant recipients. To address the relative shortfall in donated organs it has been proposed that organs from HIV-infected deceased donors might be allocated to HIV-infected patients on the transplant waiting list. Preliminary experience in South Africa reports promising short-term outcomes in a small number of HIV-infected recipients of kidney transplants from HIV-infected donors. We sought to replicate this experience in the UK by accepting kidney offers from HIV infected deceased donors for patients with HIV-infection on the kidney transplant waiting list. Here we report the UK's first cases of kidney transplantation between HIV-positive donors and recipients.

Key words: acute rejection, delayed graft function, ESRD, HIV, kidney transplantation

Introduction

Kidney transplantation is now the standard of care for many human immunodeficiency virus (HIV)-infected patients with end-stage renal disease (ESRD). Early outcomes using HIV-negative donors and carefully selected HIV-positive ESRD patients are favourable, with rates of graft survival similar to those observed in HIV-uninfected kidney transplant recipients [1]. However, there is a relative shortfall in donated organs that affects all transplant candidates, including those with HIV. One way to help alleviate this shortage would be to enable the allocation of organs from HIV-infected deceased donors to HIV-infected patients on the transplant waiting list. These organs would otherwise be discarded. The precedent for this approach

was set in South Africa, where promising short-term outcomes have been reported in a small number of HIV-infected recipients of kidney transplants from HIV-infected donors [2]. We sought to replicate this experience in the UK, and here we report the UK's first cases of kidney transplantation between HIV-positive donors and recipients.

Materials and methods

Donor and recipient selection criteria were as follows: for the donor, stable and well-characterized HIV infection (HIV viral load <50 copies/mL; CD4 count >200 cells/mm³) for at least 6 months prior to brain injury; no history of virological failure or drug resistance; preferably where information about the donor

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Table 1. Clinical and evolutionary data of the kidney transplant recipients

Clinical data	Recipient 1		Recipient 2	
Age (years)	60		45	
Gender	Male		Male	
Immunosuppressive treatment	Ciclosporin		Ciclosporin	
	Mycophenolate mofetil		Mycophenolate mofetil	
	Steroids		Steroids	
	Lamivudine		Lamivudine	
Antiretroviral treatment	Abacavir		Dolutegravir	
	Darunavir		Darunavir	
	Ritonavir		Ritonavir	
Episodes of acute rejection	1		0	
CD4 and CD8 counts (cells/mm ³)	CD4	CD8	CD4	CD8
At baseline	203	386	398	312
At 6 months	351	1126	330	276
At 12 months	306	1030	202	235
At 24 months	Not available	Not available	597	497
Plasma HIV viral load (copies/mL)				
At baseline	21		33	
At 6 months	Not detected		<20	
At 12 months	Not detected		37	
At 24 months	34		Not detected	
eGFR (mL/min/1.73 m ²)				
At baseline	13		7	
At 6 months	49		39	
At 12 months	51		37	
At 24 months	39		35	
Serum creatinine (µmol/L)				
At baseline	507		869	
At 6 months	161		206	
At 12 months	156		218	
At 24 months	194		228	
Proteinuria (mg/mmol)				
At baseline	1+ on dipstick		1+ on dipstick	
At 6 months	1+ on dipstick		1+ on dipstick	
At 12 months	38		27	
At 24 months	13		1+ on dipstick	

virus (such as historical genotype patterns and current viral load) could be obtained. The potential for donor coinfection with hepatitis C virus (HCV) was considered, and, given that HIV/HCV-coinfected kidney transplant recipients have poorer graft outcomes than HIV mono-infected recipients [3], HIV/HCV coinfected donors were excluded. Potential transplant recipients were identified as those with a history of compliance with HIV treatment and well-controlled HIV infection (HIV viral load <50 copies/mL; CD4 count >200 cells/mm³) for at least 6 months prior to admission to the transplant waiting list. This is in accordance with current UK guidance [4]. Candidates for transplantation were counselled about the potential risks of HIV-infected organ donation, including risks of superinfection with a recombinant virus with loss of virological control or transmission of viral resistance, higher rejection rates, interaction between donor antiretroviral medications and recipient immunosuppression and transmission of other (opportunistic) infections from the donor, in comparison with the risks of remaining on the transplant waiting list. Suitable candidates gave informed consent both at the time of listing and prior to transplantation. The study was approved internally by the departmental governance and strategy group and externally by the Kidney Advisory Group of NHS Blood and Transplant.

Results

The donor was a 55-year-old white male. The cause of death was brain death following a subarachnoid haemorrhage. The patient was known to have had HIV infection for the preceding 7 years. Following an episode of pneumocystis pneumonia 6 years previously the patient had commenced antiretroviral treatment with tenofovir, emtricitabine and efavirenz and this remained unchanged thereafter. The HIV viral load was <50 copies/mL for the preceding 3 years; the CD4 count had been >200 cells/mm³ for the preceding 6 years. The patient's HIV physician reported them to be adherent with medication and well for the preceding 6 years. There was no history of opportunistic infection or malignancy. Coinfection with HCV was excluded. Pre-mortem kidney function was normal and there was no dipstick proteinuria. Both kidneys were accepted and implanted into two local recipients with informed consent: a 60-year-old Black Caribbean male active 563 days on the deceased donor waiting list (Recipient 1) and a 45-year-old Black Caribbean male active 306 days on the deceased donor waiting list (Recipient 2). The cold ischaemic times were 18 h and 22 h 40 min, respectively. Induction immunosuppression was with basiliximab and methylprednisolone, and maintenance immunosuppression with ciclosporin (target levels 200–300 µg/L for the first month post-transplant),

mycophenolate mofetil and corticosteroids. Pre-implantation biopsies were taken from both kidneys and showed mild acute tubular injury but were otherwise normal.

Recipient 1 had ESRD secondary to diabetic nephropathy. His preoperative antiretroviral regimen was lamivudine, abacavir, darunavir and ritonavir. His preoperative CD4 count was 203 cells/mm³ and his HIV viral load was 21 copies/mL. Postoperatively, the patient experienced oliguric delayed graft function, and required haemodialysis. A kidney biopsy on postoperative Day 5 showed acute T-cell-mediated rejection with arteritis. The patient was treated with a 10-day course of anti-thymocyte globulin and responded well, with creatinine eventually settling at 200 µmol/L [corrected estimated glomerular filtration rate (eGFR) 38 mL/min], and remaining stable thereafter.

Recipient 2 had ESRD secondary to HIV nephropathy and hypertension. His preoperative antiretroviral regimen was darunavir, ritonavir, dolutegravir and lamivudine. His preoperative CD4 count was 398 cells/mm³ and his HIV viral load was 33 copies/mL. Postoperatively he achieved immediate allograft function, and was discharged on Day 8 post-transplant, with a creatinine of 248 µmol/L (corrected eGFR 31 mL/min). His function continued to improve and by 4 weeks post-transplantation, had settled to a baseline creatinine of 150 µmol/L (corrected eGFR 56 mL/min).

Both patients remain well after 2 years of follow-up. Neither patient has experienced loss of virological control, fall in CD4 count, opportunistic infection or any further rejection episodes. There has been no change in antiretroviral medication. Clinical and evolutionary data are summarized in Table 1.

Of note, Muller *et al.* described early changes related to HIV-associated nephropathy in three kidney transplant recipients who received organs from HIV-positive donors with no evidence of nephropathy on baseline biopsy [2]. In line with local policy, Recipient 1 did not undergo protocol biopsy because of well preserved and stable allograft function. Recipient 2 underwent a protocol biopsy at 6 months post-transplant for reduced allograft function. This showed no features suggestive of HIV-associated nephropathy, and both recipients have maintained stable allograft function without significant proteinuria after 2 years of follow-up. The role and optimal frequency of protocol biopsy in recipients of kidney transplants from HIV-positive donors remains to be determined.

Discussion

Kidney transplantation is now the standard of care for carefully selected patients living with HIV infection and ESRD in the

current era of highly active antiretroviral therapy. Prospective cohort studies report similar patient and graft survival compared to HIV-negative kidney transplant recipients. Drawing on favourable experience in South Africa we have undertaken the first UK kidney transplants between HIV-infected individuals with excellent outcomes after 2 years of follow-up. Our results and others' [5] demonstrate that kidney transplantation between carefully selected HIV-infected donors and recipients is a safe and effective treatment option with the potential to expand the organ donor pool for HIV-positive patients with end-stage kidney disease.

Authors' contributions

E.N. wrote the initial draft and checked the final version of the manuscript. N.K. and M.D. checked the final version of the manuscript. R.H. wrote the final version of the manuscript.

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Conflict of interest statement

None declared.

References

1. Stock PG, Barin B, Murphy B *et al.* Outcomes of kidney transplantation in HIV-infected recipients. *N Engl J Med* 2010; 363: 2004–2014
2. Muller E, Khan D, Mendelson M. Renal transplantation between HIV-positive donors and recipients. *N Engl J Med* 2010; 362: 2336–2337
3. Sawinski D, Forde KA, Eddinger K *et al.* Superior outcomes in HIV-positive kidney transplant patients compared with HCV-infected or HIV/HCV-coinfected recipients. *Kidney Int* 2015; 88: 341–349
4. Bhagani S, Sweny P, Brook G; British HIV Association. Guidelines for kidney transplantation in patients with HIV disease. *HIV Med* 2006; 7: 133–139
5. Ambaraghassi G, Cardinal H, Corsilli D *et al.* First Canadian case report of kidney transplantation from an HIV-positive donor to an HIV-positive recipient. *Can J Kidney Health Dis* 2017; 4: 1–6