Living donor renal transplantation in a patient with human immunodeficiency virus: a case report

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Case presentation

The patient was diagnosed in 1989, at age 27 years, with human immunodeficiency virus-1 (HIV-1) infection. He later presented with hypertension and left loin discomfort. Workup revealed proteinuria of 0.51 g over 24 hours and impaired renal function, with serum creatinine of 230 μmol/L (normal range, 59-104 μmol/L). An ultrasound scan showed bilateral shrunken kidneys with loss of corticomedullary differentiation. Renal biopsy was not performed in view of the bilateral shrunken kidneys. His renal function progressively deteriorated, and he commenced automated peritoneal dialysis in June 2017 at age 55 years. His elder brother volunteered to donate a kidney. The patient's HIV infection was well controlled with lamivudine, abacavir, lopinavir, and ritonavir. Lopinavir/ritonavir was switched to raltegravir in view of a potential drug-drug interaction between ritonavir and calcineurin inhibitors. Pre-transplantation CD4+ count was 717 cells/μL and HIV viral load was undetectable. Human leukocyte antigen matching revealed one mismatch between donor and recipient. Both donor and recipient tested cytomegalovirus antibody positive. The recipient was started on cyclosporine, mycophenolate mofetil, and prednisolone for immunosuppression according to our centre's protocol.

Living donor renal transplantation was successfully performed in September 2018 when the patient was 56 years old. Postoperative ultrasound of the graft kidney and radioisotope scan showed good graft perfusion and function. Valganciclovir and pentamidine inhalation were given as prophylaxis against cytomegalovirus and *Pneumocystis jirovecii*, respectively, in view of his underlying glucose-6-phosphatase deficiency. The lowest creatinine level since hospital discharge was 112 μmol/L. At 6 months post-transplantation, he was found to have a low level of donor-specific anti-DQ7 antibody (DSA), which persisted at repeat testing 9 months post-transplantation. Cyclosporine was therefore switched to tacrolimus to optimise immunosuppression. The tacrolimus trough level has been maintained at 5 to 8 μg/L since commencement (Fig a). Despite the presence of DSA, the patient has enjoyed stable renal function with no proteinuria; thus, renal biopsy was not performed (Fig b). In his latest follow-up, at 51 months post-transplantation, his renal function remained stable with a creatinine level of 141 μmol/L. He also has excellent HIV control with abacavir, dolutegravir, and lamivudine. CD4+ cell count has been maintained in the range of 600 to 800 cells/μL since transplantation (Fig c). He did not experience any infections after transplantation.

Discussion

To the best of our knowledge, this is the first reported case of living donor renal transplantation in a patient with HIV in Hong Kong. The global prevalence of HIV is increasing, and its association with chronic kidney disease is notable. In a local cohort, 16.8% of Chinese HIV-infected patients developed chronic kidney disease.[1] With the advancement of highly active antiretroviral therapy (HAART), life expectancy among people living with HIV (PLHIV) approaches that of the general population, leading to more cases of end-stage renal failure requiring management. The combination of intense immunosuppression and intrinsic immunodeficiency can expose HIV-infected transplant recipients to life-threatening opportunistic infections. It is crucial to achieve excellent HIV control before proceeding with transplantation. The American Society of Transplantation recommends that PLHIV achieve a CD4+ cell count of more than 200 cells/μL during the 3 months prior to transplantation and an undetectable HIV viral load while receiving HAART.[2] Our patient met these criteria prior to transplantation.

Kidney transplantation in PLHIV has been explored in many Western countries over the past

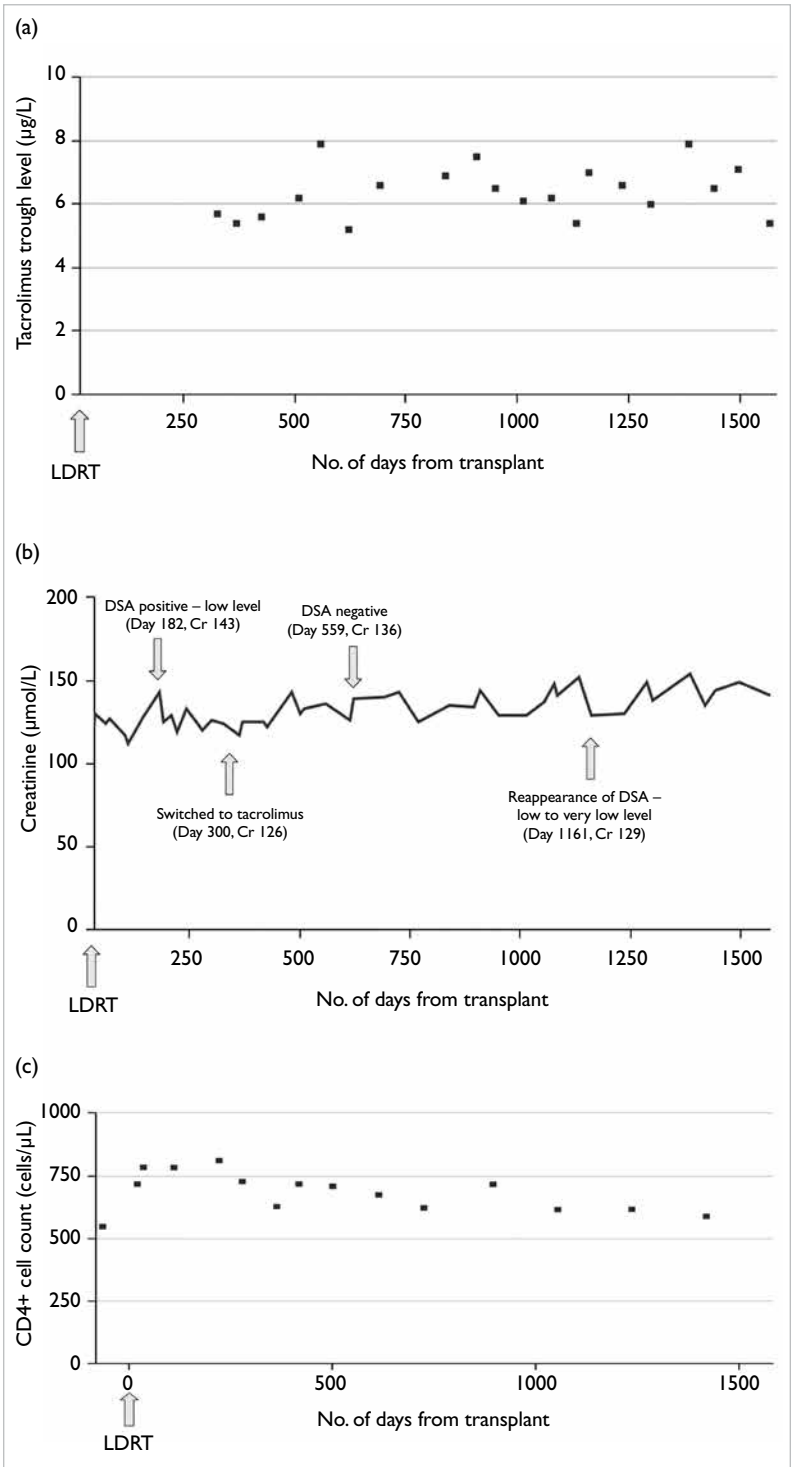

FIG. (a) Tacrolimus trough levels over time. (b) Creatinine levels over time, starting 1 month after renal transplantation. (c) CD4+ cell counts before and after renal transplantation

Abbreviations: Cr = creatinine (μmol/L); DSA = donor specific antibody; LDRT = living donor renal transplantation

decades. In a systematic review, the 1- and 3-year patient survival rates after transplantation were reported at 97% and 94%, respectively, with graft survival at 91% and 81%.[3] In another cohort study that compared 510 HIV-infected kidney transplant recipients with HIV-negative controls, comparable 5- and 10-year survival rates were reported; 5-year patient and graft survival were 88.7% and 75%, respectively. Co-infection of HIV and hepatitis C virus was an important prognostic marker for poor graft and patient survival.[4] These excellent survival data encouraged us to perform the first kidney transplant in an HIV-infected patient. Despite these promising results, the rejection rate in HIV-infected recipients is significantly higher, up to 2- to 3-fold, potentially due to drug-drug interactions between HAART and immunosuppressants or immune dysregulation.[5,6] The pathophysiology behind this increased rejection rate is unclear, but strategies such as induction therapy with anti-interleukin-2 receptor antibody or antithymocyte globulin and optimised immunosuppressive therapy are utilised to mitigate risks. Nonetheless, the use of antithymocyte globulin is controversial due to its association with marked CD4+ cell suppression (ie, <200 cells/μL), prolonged recovery, and subsequent infection risk.[7] Therefore, antithymocyte globulin induction should be reserved for HIV-infected recipients with very high immunological risk.

The optimal immunosuppression regimen for HIV-infected recipients is yet to be determined. Tacrolimus is favoured over cyclosporine for reducing acute rejection risks.[8] Observational studies and the landmark ELITE-Symphony trial suggest lower rejection rates with tacrolimus, up to 2-fold.[6,8] Our centre initially chose cyclosporine due to the patient's low immunological risk profile with only one human leukocyte antigen mismatch but switched to tacrolimus after the development of DSA 6 months post-transplantation. This case highlights the challenges of balancing overimmunosuppression and rejection risks in HIV-infected recipients. Ongoing evidence supports the use of tacrolimus as the first-line immunosuppressive agent, irrespective of immunological risk, with future randomised controlled trials needed to establish the best regimen.

Managing drug-drug interactions in HIV-infected transplant recipients is complex. Non-nucleoside reverse transcriptase inhibitors induce cytochrome P450 enzymes, while protease inhibitors significantly inhibit these enzymes, notably raising calcineurin inhibitor levels in the plasma. Ritonavir, a strong CYP3A4 inhibitor commonly used in HAART, requires a substantial increase in tacrolimus dosage up to 70-fold upon its discontinuation to maintain effective immunosuppression.[9] To avoid drug-drug interactions, our patient was switched to an integrase strand transfer inhibitor-based HAART regimen prior to transplantation. Nonetheless, there was a risk of serum creatinine elevation. Dolutegravir has been shown to inhibit organic cation transporter 2, which inhibits active creatinine secretion into

renal tubules, leading to a slight elevation in serum creatinine level without affecting the glomerular filtration rate. After administering dolutegravir, serum creatinine clearance in healthy subjects has been reported to decrease by 10% to 14%.[10]

In conclusion, renal transplantation in PLHIV can offer improved quality of life and survival compared with continued dialysis, provided there is excellent HIV control and careful management of immunosuppression and drug-drug interactions. Challenges remain in preventing and treating acute rejection to improve long-term graft survival. We observed an early appearance of DSA 6 months post-transplantation in our patient. Although the DSA was transiently suppressed after switching to tacrolimus, it reappeared later. The appearance of DSA and its potential long-term impact on graft survival require further investigation. Our experience, alongside data from Western cohorts, supports expanding renal transplantation among HIV-infected patients, with a focus on tailored immunosuppressive strategies and management of complications.

Author contributions

All authors contributed to the concept or design of the study, acquisition of the data, analysis or interpretation of the data, drafting of the manuscript, and critical revision of the manuscript for important intellectual content. All authors had full access to the data, contributed to the study, approved the final version for publication, and take responsibility for its accuracy and integrity.

Conflicts of interest

All authors have disclosed no conflicts of interest.

Declaration

This case has been presented during oral presentation at the 18th Congress of The Asian Society of Transplantation (CAST) in Hong Kong SAR, China, 25-28 July 2023.

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Ethics approval

The patient was treated in accordance with the Declaration of Helsinki and provided informed consent for all procedures.

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