Deceased Donor Kidney Transplantation in a Human Immunodeficiency Virus–Infected Recipient: A Case Report

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ABSTRACT

Human immunodeficiency virus (HIV) infection has traditionally been considered an absolute contraindication for transplantation because immunosuppression will accelerate the disease progression and increase mortality. New antiretroviral agents have given rise to new perspectives and transplantation practices. Now renal transplantation is the gold standard treatment for end-stage renal disease in HIV-infected patients, but increased rejection and toxicity rates and compliance with treatment are important issues. Therefore, patient selection and follow-up should be done carefully in this patient group. Here we present a 51-year-old, male, HIV-infected patient who was diagnosed with HIV at his routine serologic investigation at 2015. Highly active antiretroviral therapy was initiated. One haplotype-matched kidney transplantation from a deceased donor was performed on October 19, 2016. Induction therapy was not administered, and the immunosuppressive regimen included tacrolimus, mycophenolate mofetil, and prednisolone. After 26 months, serum creatinine was 1.1 mg/dL and proteinuria 0.1 g/day. There was no development of donor-specific antibodies. The patient's current HIV viral load remains undetectable (and had been the entire time post-transplantation) while his $CD4^+$ T-cell count currently is 543/mm^3.

KIDNEY transplantation is the best treatment modality in end-stage renal disease (ESRD) [1]. Human immunodeficiency virus (HIV) was first isolated in 1983. It has been identified in more than 200 countries, and it causes opportunistic infections, end-stage organ damage, and death [2]. ESRD is more common in HIV-infected patients than the general population. HIV infection has traditionally been considered an absolute contraindication for transplantation because immunosuppression will accelerate the disease progression and increase mortality [2]. New antiretroviral agents have given rise to new perspectives and transplantation practices. Successful renal transplantation and post-transplant follow-up trials in HIV-infected recipients were published in recent years [3]. Here we present a successful kidney transplantation in a patient with an HIV infection.

CASE REPORT

A 51-year-old man was diagnosed with hypertensive nephrosclerosis 20 years ago; his past medical history and family history were not significant. The disease progressed to ESRD within a 6-year period; hence, he was on hemodialysis treatment since 2008. Predialysis viral serology was negative for hepatitis B, hepatitis C, and HIV. HIV infection was diagnosed at his routine serologic investigation in 2015. HIV RNA viral load was 4,525,290 copy/mL, and the $CD4^+$ T-cell count was 159 copy/mm^3. Highly active antiretroviral therapy (HAART) was also initiated, consisting of tenofovir (300 mg orally once a week) and dolutegravir (50 mg orally twice a day). One year after treatment, HIV RNA viral load was undetectable and the $CD4^+$ T-cell count was 567 copy/mm^3. No opportunistic infection or malignancy was detected after HIV diagnosis. There was no history of any blood transfusion, drug use, or homosexual intercourse.

Pretransplant viral serology was negative for both donor and recipient for hepatitis B and hepatitis C, while seropositivity was noted for Epstein-Barr virus, cytomegalovirus, and varicella zoster

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0041-1345/19
https://doi.org/10.1016/j.transproceed.2019.01.102

virus in both. Donor HIV serology was negative. One haplotype-matched kidney transplantation from a deceased donor (49-year-old man, 19 hours of cold ischemia time) was performed on October 19, 2016. Flow cytometry crossmatch was negative, and the panel reactive antibody level was 0%. The transplantation operation was uneventful. Induction therapy was not administered, and the immunosuppressive regimen included tacrolimus, mycophenolate mofetil, and prednisolone. Post-transplant infection prophylaxis included valganciclovir and fluconazole for 3 months and trimethoprim-sulfamethoxazole lifelong. During postoperative hospitalization, the creatinine level decreased to 1.5 mg/dL from 7.3 mg/dL and urine output increased to 2350 mL/day from 450 mL/day. There was no need for dialysis after transplantation. He was discharged 10 days after transplantation. Tenofovir dosage increased to 300 mg once a day and dolutegravir continued at the same dose after transplantation.

The patient's HIV viral load and $CD4^+$ T-cell count was evaluated on a monthly basis. For the entire 6 months post-transplantation, the patient's HIV viral load remained at undetectable levels, while his $CD4^+$ T-cell count was 520 copy/mm^3. Tacrolimus levels were regularly monitored (every 2 weeks for the first 6 months). Twenty-six months post-transplantation, the patient was in good condition, serum creatinine was 1.1 mg/dL, and proteinuria 0.1 g/day. There was no development of donor-specific antibodies. The patient's current HIV viral load remains undetectable (and had been the entire time post-transplantation) while his $CD4^+$ T-cell count currently is 543/mm^3.

DISCUSSION

ESRD is a significant cause of morbidity and mortality in HIV-infected patients. The prevalence of ESRD in HIV infection without antiretroviral treatment is approximately 25% [4]. ESRD rates in HIV-infected patients are 4 times higher than HIV negative population [5]. Pathogenesis of renal damage in HIV is complex and multifactorial. HIV-associated nephropathy is the most common cause of ESRD, and other causes include hemolytic uremic syndrome, IgA nephropathy, membranous glomerulonephritis, and antiretroviral treatments, which could cause nephrotoxicity with different mechanisms [6]. Also, ESRD may occur secondary to pre-existing conditions, such as diabetes and hypertension. HIV infection was considered a contraindication for kidney transplantation because of increased morbidity and mortality, and dialysis was the only treatment modality available for ESRD patients with an HIV infection until 2001. After the initiation of HAART, mortality and morbidity decreased, and the increase in survival rates encouraged physicians to transplant. Prospective cohort studies showed that HIV-infected recipients achieve a significant survival benefit compared with remaining on dialysis [7]. Despite the increase in the number of HIV-infected ESRD patients in our country, the number of patients undergoing kidney transplantation is extremely low [8]. To the best of our knowledge, this is the first cadaveric kidney transplantation in a patient with an HIV infection in Turkey.

Despite advances in treatment, rejection rates are 3- to 5-fold higher in HIV-infected recipients compared with noninfected recipients. Drug interactions, immune abnormalities due to the HIV infection, and limited use of induction therapy are responsible for increased rejection rates. The best immunosuppressive regimen in HIV-infected renal transplant recipients has not been completely established. Anti-thymocyte globulin (ATG) treatment is generally not preferable because of the risks for lymphopenia and infections [9]. Some centers use anti-interleukin 2 treatments as induction therapy instead of ATG because of lesser rates of lymphopenia and a tendency to infections. New research was performed in kidney transplant recipients with HIV infections to evaluate induction therapy outcomes. It interestingly showed that basiliximab was more associated with infections than ATG. It was thought that this was a result of higher rejection rates in patients treated with basiliximab. More immunosuppressive treatments after rejections could be the main reason for this entity [10]. In our case, we did not use induction therapy because of guideline recommendations and the patient did not have the high immunologic risk.

Another important issue in HIV-infected patients is drug-drug interactions between maintenance immunosuppressive therapy and HAART [11]. Protease inhibitors and non-nucleoside reverse transcriptase inhibitors are eliminated by cytochrome P450 similar to tacrolimus and cyclosporine. Severe toxicity has been described because of combined treatment with such protease inhibitors and calcineurin inhibitors [11]. Raltegravir and dolutegravir are new integrase inhibitors that are not metabolized by cytochrome P450, so they could be preferable in HIV-infected renal transplant recipients for prevention of drug interactions [12]. In our patient, we did not change the antiviral regimen after transplantation because the disease was under control. We increased the tenofovir dose with the increase of creatinine clearance, and we monitored the level of tacrolimus daily for the first month because of the drug interaction. No toxicity or rejection was observed in our patient.

Guidelines for kidney transplantation in HIV-infected patients recommended that 1. patients must be compliant with HAART therapy, 2. $CD4^+$ T-cell counts must be above 200/mm^3 for the last 3 months, 3. HIV RNA must be undetectable for the last 3 months, 4. the patient has no opportunistic infection history for 6 months, 5. the patient must show no evidence compatible with lymphoma, progressive multifocal leukoencephalopathy, and chronic intestinal cryptosporidiosis, and 6. the patient must be evaluated for substance abuse, social support, mental illness, comorbidities, economic factors, and adherence to treatment [13]. Our patient met all of the conditions listed here.

In conclusion, renal transplantation is the gold standard treatment for ESRD in HIV-infected patients, but increased rejection and toxicity rates and compliance with treatment are important issues. Therefore, patient selection and follow-up should be done carefully in this patient group.

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