Plausible Role of Acute HIV Infection Mediated Immune Activation in Causing Renal Allograft Rejection: A Case Report

Vivek Jayaschandran, MD¹ Prejith P. Rajendran, MD¹ Mamata Khanal, MD¹ Prathik Krishnan, MD¹
 Poornima Ramadas, MD¹ Asha Alex, MD¹ Lakshmi Nambiar, MD¹ David A. Hirschwerk, MD²
 Joseph P. McGowan, MD² Nicole Ali, MD¹ Amit Basu, MD¹ Madhu Bhaskaran, MD¹
 Ernesto P. Molmenti, MD, PhD, MBA¹

¹ Department of Transplant Program, North Shore University Hospital, New York

² Department of Infectious Disease Medicine, North Shore University Hospital, New York

Address for correspondence Madhu Bhaskaran, MD, North Shore University Hospital, Transplant Center, 1554 Northern Boulevard, Manhasset, NY 11030 (e-mail: mbhaskar@nshs.edu).

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Abstract

Keywords

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Current research states that AIDS pathogenesis has its roots in a chronic activation of immune system secondary to human immunodeficiency virus (HIV)–induced proliferation of T cells, B cells, NK cells, and macrophages. Immune activation due to acute HIV infection can be highly detrimental to allograft survival in a renal transplant recipient. In this report, we describe a 32-year-old African-American male patient who underwent a second live donor renal transplant, following which he developed acute allograft rejection coincident with newly acquired HIV seropositivity.

Recent decades have witnessed significant leaps in the field of transplantation, with renal transplantation becoming the standard of care in end-stage renal disease (ESRD). Despite significant improvements, the posttransplantation course still remains treacherous. Complications that occur early posttransplant, including infections and rejection, tend to have a negative impact on the short-term and long-term survival of the allograft. Acute allograft rejection remains one of the most feared posttransplant complications though it can be controlled to a great degree through use of novel induction agents and immunosuppressants. In this case report, we describe a unique instance of acute allograft rejection coincident with newly acquired human immunodeficiency virus (HIV) seropositivity in a renal transplant recipient.

Case Report

The subject is a 32-year-old African-American male patient with ESRD who underwent his first live donor renal transplant in 2000, for kidney disease secondary to hypertension

and focal segmental glomerulosclerosis. He presented in August 2010 with elevated serum creatinine level (10.2 mg/dL) following allograft failure due to chronic rejection. During the posttransplant phase, he was on a maintenance protocol comprising tacrolimus, mycophenolate mofetil, and prednisone. He was started on hemodialysis and presented to the transplant center of a tertiary care hospital. Pretransplant evaluation of the recipient and the live donor was done in November 2011. It showed seropositivity for cytomegalovirus (CMV), negative donor-specific antibody screen, and negative HIV status. Virology screening tests were repeated 2 weeks before transplant, as per protocol, and these confirmed the negative HIV status of the donor and the recipient. The patient underwent a second live donor transplant, with ureteral stent placement, in December 2011. Postperfusion biopsy findings were suspicious of early antibody-mediated rejection. However, his pretransplant creatinine value of 11.5 mg/dL gradually decreased to 2.21 mg/dL over the next 1 month and repeated donor-specific antibody screens were negative. For transplant, the patient was induced with

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basiliximab and steroids, and later maintained on tacrolimus, mycophenolate mofetil and prednisone. Prophylactic regimen included trimethoprim/sulfamethoxazole, valganciclovir, and clotrimazole. Two months posttransplant, he developed an episode of urosepsis with elevation in creatinine levels, the highest value being 3.8 mg/dL. Biopsy during this admission showed acute tubular necrosis. He was successfully managed in-patient with piperacillin-tazobactam along with reduction in dosage of tacrolimus. Tacrolimus dosage was gradually increased following recovery and stabilization of creatinine levels. Stent removal was done 1 month later. During a routine follow-up in August 2012, 8 months posttransplant, he was found to have very high creatinine value of 10.43 mg/dL. A renal biopsy at this time confirmed acute allograft rejection. During the subsequent evaluation, patient gave history of unprotected sexual contact with his HIV-positive partner and follow-up investigations confirmed his newly acquired HIV-seropositive status. His laboratory tests at the time of diagnosis showed an HIV-1 RNA viral load of 336,408 copies/mL and an absolute CD4 count of 6/ μ L. He was initiated on antiretroviral therapy (ART) using renal dose adjusted abacavir, lamivudine, and raltegravir. Acute graft rejection was managed using antithymocyte globulin. Following this, his graft function improved with decrease in creatinine levels and has since remained in the range of 3 to 5 mg/dL. In February 2013, he was restarted on valganciclovir following an episode of CMV viremia. Most recent laboratory tests in August 2013 revealed an undetectable RNA viral load, a CD4 count of 462/ μ L, a serum creatinine value of 4.35 mg/dL, and negative polymerase chain reaction for CMV and BK virus.

Discussion

Several factors have been implicated in determining short-term and long-term allograft survival. Well-known risk factors for acute rejection in renal transplant recipients include: type of donor kidney, HLA antibodies, delayed allograft function and donor illnesses. Chronic rejection and consequent graft failure are more common in recipients who have experienced recurrent episodes of acute rejection, have higher degree of HLA mismatch, have received inadequate immunosuppressant therapy, or have been previously sensitized leading to antibody production. Other relevant factors include drug noncompliance, tissue injury, and opportunistic infections including BK virus nephropathy.

In this instance, we hypothesize the role of immune activation that happens with acute HIV infection in contributing to acute rejection of the renal allograft. Recent research points out that HIV infection leads to chronic immune system

activation which plays a central role in AIDS pathogenesis.¹⁻³ HIV induces proliferation of CD4 and CD8 T cells, B cells, NK cells, and macrophages. This has been proven through analysis of frequency of T-cell markers of activation, as well as direct labeling techniques. HIV is known to replicate most efficiently in "activated CD4 T cells" and hence T-cell proliferation helps the virus by making more targets available for it to divide.^{1,4} In our patient, presence of alloreactive T cells may have contributed to accelerated HIV infection.

Possible explanations for immune system activation during HIV infection include the following: innate and adaptive immune response against HIV and its antigen; direct effect of HIV antigens binding to cell surface receptors; translocation of microbial products from the intestinal lumen to the circulation due to depletion of CD4 T cells in intestinal lamina propria; increased levels of pro-inflammatory cytokines that promote activation of non-HIV-specific T cells; concomitant infections; and depletion of regulatory T cells.¹

ART in HIV-infected patients will cause suppression of viral replication which is followed by a rapid decline in the turnover of CD4 T cells, thereby slowing disease progression.⁴

We feel that acute HIV infection mediated activation of immune system and T-cell proliferation may have contributed to the episode of acute rejection in our patient. This was further supported by the observation that use of ART, along with dose adjusted immunosuppressants in this patient, promoted significant improvement in allograft function and decline in creatinine values, along with improvement in renal histology.

Acknowledgment

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