Transmission of human immunodeficiency virus infection by renal transplantation

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ABSTRACT

The rare occurrence of human immunodeficiency virus (HIV) transmission through organ transplantation cannot override the huge impact that it has on the patient. We report a case of HIV transmission by renal transplantation in a 33-year-old housewife, who received a living related transplantation from her sister. Both the patient and her donor were negative by HIV antibody testing prior to transplantation, but were found to be infected in the ninth month after transplant. Further testing suggested that the donor was in the window period at the time of organ donation after having acquired the infection from her husband.

Key words: Human immunodeficiency virus, transmission, kidney transplantation

Introduction

Organ transplantation as a means of transmission of human immunodeficiency virus (HIV) infection is a true reflection of both the advances and current limitations in the practice of medicine. We report a case of HIV transmission through renal transplantation. This case highlights the shortcomings of the current HIV screening practices.

Case Report

A 33-year-old housewife, who had been diagnosed to have end-stage renal disease (ESRD) in August 2007, and had subsequently received live renal donation from her sister in October 2007, was evaluated nine months after transplant for complaints of dysmenorrhea and irregular periods. Surprisingly, her investigations revealed that she was reactive for antibodies against HIV. Her CD4 cell count was 81 cells/mL.

The patient had received hemodialysis two months prior to renal transplantation and denied a history of any high-risk behavior or blood transfusions. She was non-reactive for HIV antibodies, which was confirmed twice, two months before surgery. Her donor was her younger sister, a 30-year-old housewife, who also denied any high risk behavior. The donor had been tested once for HIV antibodies prior to donation and was found to be negative. The patient had an uneventful perioperative and postoperative course and was on triple immunosuppression, consisting of tacrolimus, mycophenolate mofetil, and prednisolone, with a stable serum creatinine of 1.3 mg/dL, at discharge.

Since then, the patient had been regularly coming for follow-up at our transplant clinic; and her course was marked by two episodes of biopsy-proven acute cellular rejection in the fourth and seventh months, which were managed successfully with steroid boluses. The diagnosis of HIV infection at nine months after transplant was purely incidental, as she was being evaluated for dysmenorrhea at that time.

Retrospectively, the strongest risk factor for acquiring HIV infection seemed to be the renal transplantation surgery that the patient had undergone nine months back. Her donor was again tested for antibodies to HIV, and this time came out to be reactive. The donor's husband, who was a truck driver, was then tested and also found to be reactive

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Access this article online	
Quick Response Code:	Website: www.indianjnephrol.org
	DOI: 10.4103/0971-4065.97135

for HIV antibodies. Both the donor and her husband were clinically asymptomatic with CD4 cell counts of 568 and 786 cells/μL, respectively.

The patient was started on antiretroviral therapy with stavudine, lamivudine, and nevirapine; and the pre-existing immunosuppressive drug regimen was continued. Three weeks later, the patient developed graft dysfunction, and underwent an allograft biopsy for the same. The biopsy showed evidence of acute cellular rejection and thrombotic microangiopathy; for which she received steroid boluses and her tacrolimus was changed to sirolimus. Since then, she has remained stable with the last serum creatinine of 1.8 mg/dL and CD4 cell count of 335 cells/μL.

Discussion

Renal transplantation offers the best chance of survival to ESRD patients across the globe. The hope of having a good and productive life after renal transplantation, is however associated with the risk of immunosuppression and occasionally, transmission of infections like HIV, hepatitis B and C through the transplanted organ.

Since 1999, the risk of transfusion-transmitted HIV infection has markedly decreased, after the introduction of mandatory nucleic acid amplification testing (NAT), in the blood banks in the USA.[1] This is due to the shortening of the infectious window period with NAT. However, cases of transfusion-transmitted HIV infection still continue to be reported.[2-4]

In contrast to the mandatory screening of blood for HIV infection by both antibodies and NAT, the screening policies for solid organ transplantation have included only mandatory HIV antibody testing. It has been suggested that in the potential living donor with risk factors for HIV exposure, who is negative by the HIV antibody test, a nucleic-acid testing should be conducted.[5] In this context, the high-risk donor has been defined in the guidelines issued by Centers for Disease Control and Prevention (CDC), in 1994.[6] The reliability of these criteria rests mainly on the history given by the donor or close relatives, and together with the circumstantial difficulties faced during cadaveric donation; there is always some room for error.

Since the recognition of HIV infection, several reports have been published regarding its transmission through organ donation. In 1992, a detailed 'look back' investigation, to ascertain the route of HIV infection in a female, who had received a bone allograft in 1985, revealed that six other recipients of solid organs or unprocessed fresh frozen bone, from the concerned HIV seronegative deceased donor were also HIV-infected.[7] The presence of HIV infection in the seronegative donor was confirmed by a culture of the donor's frozen splenic tissue and detection of HIV by polymerase chain reaction and p24 antigen. In 1993, Simonds reviewed the published reports in the English literature of HIV transmission through organ and tissue transplantation, and identified 50 cases of HIV transmission associated with kidney transplantation.[8] A majority of these transplantations had occurred before the routine donor screening for HIV antibody was introduced, in 1985. In the era of mandatory HIV antibody screening before organ donation, the factors attributed to HIV transmission were the window period or pre-seroconversion donation, hemodilution due to transfusions or fluid resuscitation, or the unavailability of blood test reports prior to transplantation.

Since then, there have been only three reported cases of HIV transmission related to organ donation. In 2004, Maitra *et al.* had reported a case of possible HIV transmission through an unrelated, commercial live renal donation from India.[9] In 2008, Ahn and Cohen reported the first ever case of HIV and hepatitis C virus (HCV) co-transmission from a seronegative, but high-risk deceased donor.[10] The donor's stored serum later tested positive for both HIV and HCV infections by NAT. The most recent report has been of a 27-year-old ESRD female acquiring HIV infection through a cadaveric renal donation.[11]

In our case, although pre-transplant serum samples of the patient or her donor were not available for NAT, the simultaneous detection of HIV infection during the post transplant period, in the patient, her donor and the donor's husband indicate transmission through renal transplantation from the donor to the patient, and through the sexual route from the donor's husband to the donor. It is likely that the transmission to the patient occurred in the window period before donor's seroconversion. Phylogenetic linkage of HIV sequences from the patient and her donor could have confirmed the transmission, but that was not done in this case.

One of the previously cited recent cases of HIV transmission through solid organ transplantation[10] has prompted a consensus conference report on NAT of organ donors for HIV, HCV, and hepatitis B virus (HBV).[12] This report cites insufficient evidence to recommend routine NAT in donors with no identified high-risk factors, as the benefit may not outweigh the risk in the form of loss of donor organs. With respect to living donors, the report recommends no mandatory routine NAT for average risk living donors; and consider delaying transplantation

in high-risk donors, to buy time for repeat serological testing with the hope that the window period is over, or consider NAT near the time of organ transplantation; and if this delay is not possible, NAT should be considered in high-risk donors.

The psychosocial impact of acquiring infections like HIV after the burden of organ failure and subsequent organ transplantation cannot be overlooked. The patient should be explained the definite, although very small risk of acquiring such infections through transplantation. Therefore, strict adherence to informed consent procedures and evaluation of high-risk factors, preferably through questionnaires, should be done.

As non-nucleoside reverse transcriptase inhibitors are inducers and protease inhibitors are inhibitors of the CYP3A4 metabolizing enzyme isoform, changes in the drug levels of calcineurin inhibitors and mammalian target-of-rapamycin inhibitors, which are metabolized by the same enzyme, occur when these drugs are co-administered.[13] These important drug interactions between antiretroviral and immunosuppressive drugs need consideration when HIV-infected organ transplant recipients are treated.

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How to cite this article: Mukhopadhyay P, Kumar v, Rathi M, Kohli HS, Jha V, Sakhuja V. Transmission of human immunodeficiency virus infection by renal transplantation. Indian J Nephrol 2012;22:133-5.

Source of Support: Nil, **Conflict of Interest:** None declared.