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Transplant of a Kidney from a Hepatitis C Viremic Donor to a Naïve Recipient without Viral Transmission: A Case Report

Authors' Contribution:
Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
Literature Search F
Funds Collection G

ADF Badi Rawashdeh
AD John Hulse
AEF Avinash Agarwal

Division of Transplant Surgery, University of Virginia, Charlottesville, VA, U.S.A.

Corresponding Author: Badi Rawashdeh: br6ff@hscmail.mcc.virginia.edu
Conflict of interest: None declared

Patient: Male, 49-year-old
Final Diagnosis: HCV infection
Symptoms: Haematuria
Medication: —
Clinical Procedure: —
Specialty: Transplantology

Objective: Unusual clinical course

Background: Kidneys from deceased donors who were positive for hepatitis C virus (HCV) on a nucleic acid amplification test (NAT) are not given to anti-HCV antibody-negative recipients. This is because of the high risk of HCV transmission, combined with the lack of effective antiviral treatment.
Several studies have demonstrated rates of transmission of HCV from anti-HCV-positive/HCV NAT-positive donors to anti-HCV-negative recipients of 100%.
Ours is the first report of transplantation of a kidney from an anti-HCV antibody-positive/HCV NAT-positive donor into an anti-HCV antibody-negative recipient who remains anti-HCV antibody-negative at 3 months after transplant with no treatment.

Case Report: A 49-year-old man had a history of end-stage renal disease that was presumed to be secondary to type ll diabetes. He received a kidney from a deceased donor who was HCV antibody-positive/NAT-negative.
The patient's HCV antibody status was checked prior to transplant and he was found to be negative and nonreactive. Since the transplant, his HCV viral load has been checked 5 times, on postoperative days 15, 23, 44, 62, and 64; each time, it has been undetectable. Furthermore, the patient's HCV antibody status was rechecked 1 month after transplant and it remained negative and nonreactive.

Conclusions: Further research is required on the accuracy of polymerase chain reaction as an indicator of donor HCV infection when the quantity of the viral load is not reported.

Keywords: Hepacivirus • Hepatitis C Antibodies • Kidney Transplantation

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Background

Historically, because of the high risk of hepatitis C virus (HCV) transmission combined with the lack of effective antiviral therapy for the disease, kidneys from deceased donors that were HCV nucleic acid amplification test (NAT)-positive have not been given to HCV antibody-negative recipients. Instead, they were turned down or the organs were given only to HCV-infected recipients. However, with the increasing gap between organ availability and demand and the advent of safe and highly effective direct-acting antiviral agent (DAA) therapy in 2011, kidneys from HCV NAT-positive donors have been transplanted into uninfected recipients; the outcomes have been good, particularly when compared to continuing on the wait list for transplant [1,2].

Recently, screening for HCV infection has become more rigorous. Donor HCV infection status is routinely checked with serologic tests for antibodies and with NAT. NAT directly measures viral RNA using polymerase chain reaction (PCR). Serologic studies can take from 2 to 6 months following exposure to become positive, while HCV NAT can detect the virus within 5 to 7 days of exposure. Using NAT results in a decreased risk of undetected infection and minimizes the risk of disease transmission [3].

Trials of transplantation of kidneys from HCV antibody-positive/NAT-negative to HCV-naïve (HCV antibody-negative/NAT-negative) recipients have shown low rates of HCV transmission. In addition, several recent studies have shown the feasibility and safety of transplanting kidneys from HCV NAT-positive donors to naïve recipients with a 100% incidence of transmission and universal complete remission using DAA [4,5].

Herein we report a case in which a kidney from an HCV antibody-positive/NAT-positive donor was transplanted into an HCV-naïve patient who remains seronegative 3 months postoperatively and has required no treatment.

Case Report

The patient, a 49-year-old man, was on hemodialysis for end-stage renal disease presumed to be secondary to type ll diabetes. His medical history also included hypertension and hyperlipidemia. He was willing to receive organs from donors who were HCV antibody-positive and/or HCV NAT-positive.

He received a donor kidney transplant from a deceased 23-year-old woman with a Kidney Donor Profile Index score of 38%. She had a known history of narcotic abuse and her cause of death was brain anoxia due to drug intoxication. She was HCV antibody-positive/NAT-positive. In addition, the donor was cytomegalovirus (CMV)- and Epstein-Barr virus (EBV)-positive.

The recipient's HCV antibody status was checked prior to transplant and was negative. He had no preexisting donor-specific antibodies, with a negative Luminex crossmatch test and calculated panel-reactive antibodies of 3%. Cold ischemia time was 23 h 57 min. The transplant was performed without complications and the patient's hospital course was unremarkable. Graft function was immediate and the patient was discharged on postoperative day (POD) 3.

Induction immunosuppression was achieved intraoperatively with methylprednisolone and anti-thymocyte globulin. The patient was placed on tacrolimus, mycophenolate, and prednisone for maintenance immunosuppression. Initially, he was prescribed valganciclovir, trimethoprim/sulfamethoxazole, and fluconazole for prophylaxis. The trimethoprim/sulfamethoxazole was later switched to dapsone for hyperkalemia, and that was later changed to atovaquone after the patient experienced leukopenia. His postoperative course to date has been unremarkable. His HCV viral load has been checked 5 times since transplant (PODs 15, 23, 44, 62, and 64) and each time it has been undetectable. Furthermore, the patient's HCV antibody status was rechecked 1 month after transplant and he remained HCV antibody-negative. His liver function is normal and he has not experienced EBV, BK, or CMV viremia.

Discussion

The present case is unique because it is the first to be reported in the literature in which a kidney from a PCR-proven, HCV antibody-positive/NAT-positive donor was transplanted into an HCV-naïve patient who remains seronegative 3 months postoperatively without any treatment.

In August 2015, the Organ Procurement and Transplantation Network/United Network for Organ Sharing implemented a policy of performing HCV NAT on all HCV-seropositive donors [3]. The combination of a donor's antibody and NAT status provides an understanding of the chronicity and transmissibility of their infection. In particular, NAT provides an accurate assessment of the risk of HCV transmission from transplantation [1].

A donor who is HCV antibody-positive/NAT-negative has an infection that spontaneously cleared or was successfully treated or a false-positive antibody result. Such patients have a very low risk of HCV transmission [1]. Dao et al prospectively reported the rate of transmission of HCV disease for kidneys from 40 HCV antibody-positive/NAT-negative donors transplanted to 52 HCV-naïve recipients. All of the recipients received HCV PCR testing within 3 months of transplantation to monitor for HCV disease transmission. De novo HCV infection was detected in a single recipient (1.9%) and later determined to be a case of transmission from an HCV antibody-positive/

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NAT-positive donor with an initial false-negative NAT that was completed using a sample collected on donor hospital admission [5]. Although these patients do not develop viremia, transplantation of HCV antibody-positive/NAT-negative kidneys to HCV-naïve recipients often causes HCV seroconversion (antibody positivity). De vera et al reported their experience with 32 HCV-naïve patients who received kidney allografts from 25 donors who were HCV antibody-positive/NAT-negative. All of the patients were HCV NAT-negative at 1 and 3 months after transplant, suggesting the absence of HCV transmission, but 14 patients (44%) became HCV antibody-positive after transplant [6]. Transplantation of kidneys from HCV antibody-positive/NAT-negative donors into HCV-naïve recipients has been reported previously in smaller patient populations, with a 0% transmission rate. HCV transmission was determined based on periodic after transplant HCV antibody and NAT testing [7,8].

In contrast, donors who are HCV antibody-positive/NAT-positive (active infection) or HCV antibody-negative/NAT-positive (acute infection) pose a high risk for disease transmission [1]. In the largest retrospective, single-center cohort study to date, Molnar et al investigated the feasibility and safety of transplantation of kidneys from HCV antibody-positive/NAT-positive donors to 53 HCV-naïve recipients. All of the recipients became viremic after transplantation and successfully completed antiviral treatment. By the end of treatment, all of them had undetectable HCV RNA levels and they remained virus-free 12 weeks later. The authors reported good graft function with no graft losses or patient deaths [9].

Similarly, Kardash et al studied 7 HCV-naïve patients who received kidneys from 5 deceased HCV antibody-positive/NAT-positive donors. Viremia was detectable in all 7 renal transplant recipients within 3 days after transplantation. After determination of HCV genotype, antiviral treatment was initiated within a median of 7 days after transplantation and was continued for 8 to 12 weeks. For all recipients, the viral load was undetectable at the end of treatment and they exhibited a sustained virologic response 12 weeks later. All recipients exhibited normal liver enzyme activity at the end of treatment [4]. More recently, Goldberg et al, in an open-label pilot clinical trial, showed that all HCV-naïve patients who received kidneys from HCV antibody-positive/NAT-positive donors had detectable HCV RNA viral loads on day 3 after transplantation. Once HCV RNA was detected, elbasvir-grazoprevir (EBR-GZR) was initiated, successfully achieving a cure in all recipients (cure was defined as a sustained virologic response 12 weeks after the end of treatment) [2].

Furthermore, in an open-label pilot clinical trial, Durand et al explored the safety and efficacy of DAA prophylaxis in the case of organ transplant from HCV-infected donors to 10 HCV-negative patients. In their non-randomized, single-center trial, all 10 recipients received a single oral dose of EBR-GZR on the way to the operating room. The median time between the first dose of EBR-GZR and reperfusion of the transplanted kidney was 5.1 hours (interquartile range 3.5 hours to 7.7 hours). Among the 10 HCV donor-positive/recipient-negative transplantations, there were no treatment-related adverse events and HCV RNA was not detected in any recipient 12 weeks after treatment [10].

As mentioned previously and demonstrated in these studies, an HCV antibody-positive/NAT-positive donor has an active infection and poses a 100% risk for disease transmission after transplantation, while an HCV antibody-positive/NAT-negative patient poses a low risk for transmission [1,2,4-6,9]. A false-positive NAT could account for the case we have described. The false-positive rate for NAT in deceased organ donors has not been well studied. Levitsky et al reported an estimated false-positive rate <0.2% that was based on unpublished data [1]. Estimates from tissue and blood donor NAT screening studies have found false-positive rates of 0.1% to 0.85% [11]. Another possible explanation is that the donor's viral load was very low. Only qualitative HCV NAT results were reported, so the viral load is unknown. The present case could parallel the relatively low HCV transmission rates among healthcare providers who have been exposed to HCV-contaminated fluids. A recent report estimated these rates to be as low as 0.1% [12]. While this has not been studied to our knowledge, donors with HCV viral loads near the threshold of detection could have transmission rates as low as those for NAT-negative donors.

Conclusions

The present case represents the first reported incident of a kidney from an HCV antibody-positive/NAT-positive donor transplanted into an HCV-naïve recipient who remains seronegative 3 months postoperatively with no treatment. Given the above-mentioned studies, which have demonstrated 100% transmission rates from HCV antibody-positive/NAT-positive donors, our case was most likely due to either a false-positive donor NAT or a very low HCV viral load. Further research is required on the accuracy of PCR as an indicator of donor HCV infection when the quantity of the viral load is not reported.

Conflict of Interest

None.

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