Reversal of Donor Hepatitis C Virus–Related Mesangial Proliferative GN in a Kidney Transplant Recipient

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Traditionally, hepatitis C virus (HCV)–positive kidneys were exclusively transplanted into recipients with preexisting HCV infection. With the introduction of direct-acting antivirals (DAAs) in 2015 and evidence of their safety and efficacy in the immediate post-transplant period, transplantation of kidneys from donors with HCV viremia into recipients without HCV infection dramatically increased.1 The acceptance of HCV-positive kidneys not only reduces waiting time but also potentially improves the quality of the organ received because HCV-positive donors tend to be younger and have fewer comorbidities.2,3 Nevertheless, despite mounting evidence supporting the safe use of kidneys from donors with HCV infection,4,5 with 32% of transplant centers currently choosing to opt out of receiving regional and national offers of kidneys determined to be positive by HCV nucleic acid testing,5 there is still a high discard rate of such kidneys.

Recent trials of transplanting HCV-positive kidneys into HCV-negative recipients have been encouraging, with 100% HCV cure rates and good allograft outcomes in the relative short term.1,3 However, these studies did not report biopsy data, making it difficult to assess the clinical consequences of preexisting HCV-related kidney injury or the effects that DAA use has on kidney histology after transplantation. In this research letter, we describe successful kidney transplantation from an HCV-positive donor with mesangial proliferative GN into an HCV-negative recipient.

A 53-year-old Black man with ESKD presumed to be secondary to hypertension underwent a deceased donor kidney transplantation after being on hemodialysis for 21 months. He had a negative HCV antibody test and normal liver function tests. The donor was a 49-year-old White woman with history of asthma and intravenous drug and alcohol abuse, who died following a respiratory arrest secondary to either an infection or vaping injury. The donor was HCV antibody positive and HCV nucleic acid testing positive at the time of death and had a kidney donor profile index of 75%. The donor’s urine at the time of procurement was negative for glucose, red blood cells, or white blood cells. Proteinuria and albuminuria were not quantified. Supplemental Table 1 shows detailed characteristics of the donor, recipient, and transplant.

METHODS
The procurement biopsy (frozen sections) showed 61 glomeruli with no evidence of glomerulosclerosis and minimal arteriolar sclerosis and tubular atrophy. The postreperfusion biopsy was notable for diffuse acute tubular injury and mesangial proliferative GN with IgM-dominant deposits (Figure 1). HCV RNA was undetectable on the day of transplant and 2 days after. On postoperative day 4, the recipient was noted to have an HCV viral load of 30 IU/ml and normal liver function tests, prompting initiation of glecaprevir combined with pibrentasvir, in accordance with our center’s policy to initiate DAAs when HCV viral load becomes detectable in the recipient. On postoperative day 7, the patient became aviremic, and his HCV RNA remained undetectable. The patient’s post-transplant course was complicated by delayed graft function, requiring hemodialysis for 2 weeks after transplant (Figure 2). Biopsy of the engrafted kidney on days 12 and 28 after transplantation demonstrated unchanged mesangial proliferative GN with...
IgM-dominant deposits (Figure 1). A rise in serum creatinine level on day 100 post-transplantation prompted another biopsy, which showed markedly diminished granular mesangial staining for IgM, along with borderline cellular rejection. He also developed BK viremia and received a course of high-dose intravenous Ig at 2 g/kg, along with overall reduction in maintenance immunosuppression. His renal function remained stable throughout. Initial proteinuria and hematuria resolved, as shown in Figure 2.

Of note, the donor’s other kidney was transplanted at a different institution. To our knowledge, no postreperfusion biopsy or for-cause biopsies were performed for the mate kidney to date.

**DISCUSSION**

The introduction of DAAs for HCV, resulting in cure rates reaching 100%, has provided a new supply of organs for patients with ESKD. When HCV is not accounted for, the median donor kidney donor profile index was found to be 47%. This suggests that transplant centers are likely more stringent with their criteria when accepting HCV-positive donor kidneys, and many HCV-positive kidneys are still being discarded. HCV-positive kidneys offer recipients a survival advantage, decreasing their mortality by 48% compared with staying on the transplant wait list awaiting an HCV-negative kidney. Additionally, these organs are cost saving, at an average of $190,000 per patient.

During deceased donor kidney evaluation, the presence of HCV-related kidney disease is excluded solely by evaluation of kidney function and urinalysis. Although proteinuria in the donor with HCV may be informative, this is often confounded by the presence of AKI and the associated tubular proteinuria at the time of procurement. Because procurement biopsies are performed in only approximately one-half of all deceased donor kidney transplants and because postreperfusion biopsies are not routinely performed across most transplant centers in the United States, data on initial kidney biopsies from HCV-positive donors are lacking. In this patient, although procurement biopsy did not document any glomerular pathology, postreperfusion biopsy demonstrated segmental mesangial proliferative GN with IgM-dominant deposits, suggesting that these pathologic changes were donor derived. Other than with chronic HCV infection, mesangial proliferative GN with IgM-dominant deposits is most frequently seen in rheumatologic disorders, in shunt nephritis, and in hematologic malignancies. Careful review of the clinical information available on DonorNet pointed to chronic HCV infection as the most likely cause for the biopsy findings. Serologic workup in the recipient was negative for an autoimmune disease or a malignancy. Although the recipient had very brief and mild HCV viremia, the development of mesangial proliferative GN typically requires considerable duration of viremia. Notably, the findings also were present on the two subsequent for-cause biopsies at 12 days and at 28 days post-transplant, despite the absence of viremia in the patient. The mesangial IgM deposits by immunofluorescence decreased significantly by day 100 post-transplant, suggesting reversal of the HCV-associated kidney changes after antiviral therapy. A parallel can be drawn to the well-described reversal of diabetic kidney changes following a period of euglycemia in pancreas transplant recipients.

Data on HCV-positive kidney biopsies post-transplantation are sparse. In the Transplanting Hepatitis C Kidneys into Negative Kidney Recipients trial, one recipient developed proteinuria that was attributed to HCV, which improved after the patient received antiviral medications, although whether a biopsy was performed was not reported. Chacsca et al. compared the effect of...
HCV treatment before versus after kidney transplant. Postreperfusion biopsies were performed on 14 of the 36 transplanted organs, revealing no pathologic abnormalities in 11 kidneys and very mild changes in three kidneys that were not specifically described by the authors. In kidney biopsies obtained per follow-up protocol in 19 patients at 4 and 12 months post-transplant, the only described findings were interstitial fibrosis and tubular atrophy. To the best of our knowledge, this is the first report describing successful transplantation of an HCV-positive kidney with donor-derived HCV-associated GN. The Organ Procurement and Transplantation Network mandates transplant programs to report any post-transplant discovery of donor disease or malignancy to the host organ procurement organization and the network, which in turn, must notify other transplant programs that had received organs from the same donor. No similar regulatory requirements currently exist that specifically mandate programs performing HCV-positive kidney transplants to share information about the outcomes of mate kidney recipients. The data surrounding HCV-positive donors are evolving, and better sharing of information between transplant programs is pivotal.

In conclusion, our data suggest that when selected carefully, kidneys from HCV-positive donors with HCV-associated GN can be safely transplanted into HCV-negative patients with good short-term allograft outcome and that antiviral treatment can reverse HCV-associated histologic changes. Long-term studies are needed to confirm these findings, which could further expand the pool of deceased donor kidneys for kidney transplant recipients.

**DISCLOSURES**

S. Mohan is a scientific advisory board member for Angion Pharmaceuticals and a deputy editor of Kidney International Reports, outside the submitted work. S. Mohan reports grants from the National Institutes of Health and personal fees from Angion Biomedica and Kidney International Reports, outside the submitted work. L. Ratner reports personal fees from CareDx, CSL Behring, Hansa BioPharma, and Natera and other from Gilead and Hansa BioPharm, outside the submitted work. All remaining authors have nothing to disclose.
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SUPPLEMENTAL MATERIAL

This article contains the following supplemental material online at http://jasn.asnjournals.org/lookup/suppl/doi:10.1681/ASN.2020060820/-/DCSupplemental.

Supplemental Table 1. Recipient, donor, and transplant characteristics.

REFERENCES