Successful lung transplantation from a hepatitis C RNA–positive donor to a hepatitis C treatment–experienced recipient with cystic fibrosis

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Timeline chart of HCV load kinetics before and after transplantation.

Central Message

HCV viral load became detectable again after transplantation with an HCV+ donor allograft. HCV was successfully treated with sofosbuvir/velpatasvir throughout the course.

See Commentary on page e159.

The advent of direct-acting antivirals (DAAs) in 2014 has transformed the landscape of hepatitis C virus (HCV) treatment, allowing patients to achieve cure after 8 to 12 weeks of safe and well-tolerated therapy.¹ Because of the already limited organ donor pool and the availability of high numbers of HCV-viremic donors resulting from the opioid epidemic, this development has led to immense interest in transplanting organs from HCV-viremic donors into non-viremic recipients.² In 2017, the first pilot of 10 noninfected patients who received kidney transplants from HCV-viremic donors demonstrated excellent allograft and patient outcomes, with cure of HCV infection using DAAs after transplant.³ This was followed by successful reports of HCV “viremic donor to nonviremic recipient” lung,⁴ heart,⁵ and even liver transplants.⁶ Because of this paradigm shift, the 2017 American Society of Transplantation Consensus Conference endorsed the transplantation of organs from HCV-viremic donors into HCV-negative recipients, but only under monitored Institutional Review Board (IRB)-approved protocols and studies.⁷

To remain eligible for the expanded HCV-infected donor pool, transplant candidates with chronic HCV infection have generally not been offered treatment for their HCV before transplantation because of concerns about the ethics of receiving an HCV-infected organ after sustained virologic response (SVR) has been achieved. However, in a recent study of 13 non-HCV-infected patients who received heart transplants from HCV-infected donors, 1 patient did have a history of previously treated HCV.⁵ Even though this patient received a heart from an HCV viremic donor, she did not develop post-transplant HCV viremia (and was thus not re-treated), which was thought to be a result of low-grade viremia in the donor.

We report the first case of a critically ill patient with cystic fibrosis and chronic HCV infection who received treatment for HCV and who successfully underwent bilateral lung transplantation from an HCV-viremic donor, with reinfection and subsequent cure of her HCV.

A 30-year-old woman with cystic fibrosis was admitted for acute on chronic respiratory failure requiring intubation and mechanical ventilation. Because of clinical deterioration, she underwent an accelerated evaluation. During her pretransplant evaluation, she was found to be HCV antibody positive with an initial HCV viral load of 357,681 IU/mL (genotype 2). A liver biopsy demonstrated cystic fibrosis–related liver disease and focal portal-to-portal bridging fibrosis. Because of concerns that her liver function would rapidly deteriorate after transplantation because of the combination of an HCV flare and potentially hepatotoxic medications, she was started on a pangenotypic DAA, sofosbuvir (400 mg)/velpatasvir (100 mg), chosen in part because it does not interact with calcineurin inhibitors and other post-transplant medications (Figure 1). Insurance approval was obtained for a 12-week course of therapy, in accordance with national guidelines for HCV-genotype 2.⁸

Given her critical condition, the University of Pittsburgh Medical Center IRB granted us permission to offer her

FIGURE 1. Timeline chart of HCV load. Date of transplant used as reference. Viral load became detectable again immediately after transplantation and was successfully treated with sofosbuvir/velpatasvir. Asterisk designates the presence of viremia, but below the limit of detection. HCV, Hepatitis C virus.

lungs from HCV-infected donors to reduce her waitlist time. Six weeks after being listed, she received an organ offer. The donor was a 23-year-old woman with a history of HCV and intravenous drug abuse who was pronounced brain dead after an anoxic brain injury. The donor was HCV positive by nucleic acid testing and had no history of treatment for HCV. No information on the donor's HCV genotype was available at the time of organ offer. Our patient's HCV viral load was undetectable 5 days before lung transplant and detectable, but below the limit of quantitation both the day before and the day of transplant (Figure 1).

The patient underwent a bilateral sequential lung transplantation from this donor. She received basiliximab and methylprednisolone induction, with standard immunosuppressive regimen and dosing (tacrolimus, mycophenolate mofetil, and prednisone). Alemtuzumab was not used because of the HCV infection. Both donor and recipient were seropositive for cytomegalovirus and Epstein-Barr virus. Her postoperative course was complicated by acute renal insufficiency requiring temporary renal replacement therapy, with complete recovery of kidney function before discharge. The sofosbuvir/velpatasvir dosing was not adjusted while she was on renal replacement therapy. She was discharged home on postoperative day 31 in excellent condition.

Blood obtained from the donor demonstrated that she had HCV genotype 3 with a viral load of 53,433 IU/mL. Post-transplant HCV viral load kinetics are shown in Figure 1.

HCV genotyping of post-transplant viremia was not performed because of insufficient target. At the time of transplant, our patient had already received treatment with sofosbuvir/velpatasvir (which would treat both the patient's genotype 2 HCV and her donor's genotype 3 HCV) for 42 days, with a negative viral load while on therapy. Given that she was reinfected with HCV genotype 3, we recommended that she receive 12 additional weeks from the time of transplant, because the HCV guidelines recommend 12 weeks of therapy for genotype 3.⁸ However, this was denied by her insurance company. Ultimately, she received 8 weeks of sofosbuvir/velpatasvir after transplant, for a total of 12 weeks of treatment. HCV testing 12 weeks after discontinuation of therapy was negative (SVR 12). At the time of submission, she is doing well approximately 2 years after transplant, with SVR documented at 1 year. Her liver function is normal, and no repeat biopsies have been clinically indicated.

To our knowledge, this is the first case of an HCV treatment-experienced patient who cleared HCV viremia on therapy and underwent successful double-lung transplant from a donor with HCV viremia. Post-transplant SVR was achievable with the use of the pangenotypic DAA sofosbuvir/velpatasvir. Emerging data have shown the safety and efficacy of transplanting HCV-viremic organs into nonviremic patients, which will allow patients to receive transplants sooner and thus prevent waitlist-associated deaths.³⁻⁶ Our case and a case of an HCV treatment-experienced heart transplant recipient who

received an organ from an HCV viremic donor demonstrate that these observations hold true for treatment-experienced patients.⁵ We are in agreement with the American Society of Transplantation Consensus Guidelines, in that centers considering these transplants should have an IRB-approved protocol, a thorough informed consent process, and logistic and financial considerations, particularly regarding insurance approval of HCV medications.⁷ Our patient was counseled about the fact that she would be reinfected with HCV, the possibility of infection with a different genotype than her own, and the possibility that her insurance company may not approve coverage beyond her initial planned treatment course. Indeed, her insurance company ultimately denied the 12 weeks of post-transplant therapy that we had recommended. However, she received 8 weeks of therapy after transplant (12 weeks in total) and achieved SVR at 12 weeks and at 1 year.

We report the first case of an HCV treatment-experienced patient who underwent successful double-lung transplant from an HCV-infected donor while being treated with a pangenotypic DAA. We believe that critically ill patients with prior HCV should be considered for lung transplantation from otherwise medically acceptable HCV-infected organs under an IRB-approved protocol, with a multistep consent process to prevent waitlist mortal-

ity and with logistic and financial considerations for DAA coverage after transplant.

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