Commentary: Direct-acting antiviral regimens usher in the era of hepatitis C virus–positive donors in lung transplant

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Central Message

Direct-acting antiviral regimens open up the use of HCV-positive donor organs. Potential recipients need to be clearly counseled regarding the risks of complications and possible treatment failure.

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Therapy for hepatitis C virus (HCV) has been revolutionized with the introduction of all-oral pangenotypic direct-acting antiviral (DAA) regimens. Extremely high sustained virologic response (SVR) rates, equivalent to cure, can now be achieved with short-duration therapy with minimal side effects. DAAs have expanded the donor pool not only to include HCV-infected donors but also to include HCV-negative patients as recipients of HCV-positive organs.¹

In this issue of the *Journal*, Harano and colleagues² describe an HCV-infected patient with cystic fibrosis and respiratory failure who successfully underwent lung transplantation from an HCV-positive donor. The patient was started on a regimen of sofosbuvir and velpatasvir before the transplant because of concerns regarding posttransplant liver deterioration. Whether she was cleared of HCV before transplant is unknown, because confirmation of this status requires HCV RNA undetectability for a period off therapy.

This case highlights several important points. First, transplanting HCV-positive solid organs into HCV-negative recipients can be associated with excellent outcome in the era of DAAs.

Second, the timing of DAAs is important. The decision to start DAAs was based on concerns of rapidly deteriorating liver function after lung transplant. Although liver biopsy showed bridging fibrosis, the pre-DAA treatment hepatitic activity is unclear, because there is no information on alanine aminotransferase or disease activity on histology. Furthermore, acute flares are not usually seen in chronic carriers, even with immunosuppression. What is more worrisome is the risk of fibrosing cholestatic hepatitis, which occurs 3 to 18 months after transplant leading ultimately to liver failure, and which can be prevented with DAAs.³ It may be argued that DAAs could have been delayed until after the transplant, when the donor HCV genotype would be available. Treatment may also be disrupted in the early posttransplant period for various

reasons, leading to viral rebound or lower rates of SVR. Although this patient received a timely graft, had the donor not become available until completion of DAA, then she might have been left with reinfection with HCV after achievement of SVR and potentially been left with posttransplant HCV and limited access to further DAA therapy.

Third, DAAs must be readily available, so that therapy can be given in a timely manner. Delays in DAA treatment not only may affect the liver but may result in irreversible extrahepatic sequelae.⁴ Fortunately, this patient had SVR achieved despite low-level viremia at 3 weeks posttransplant with a difficult-to-treat genotype, after only 8 weeks of additional postoperative therapy. If the patient had not had SVR achieved, she would have required further DAA therapy, possibly with longer treatment duration, with an alternative regimen, including ribavirin. Patients must therefore be fully informed before consent of the potential consequences of receiving a HCV-positive organ, not only regarding new infection or reinfection but also the consequence of potential treatment failure.

The availability of HCV-positive organs can be life-saving, but there are dilemmas and potential pitfalls. Early patient education regarding the use of HCV-positive grafts, as opposed to only when a HCV-positive graft becomes

available, is key for acceptance. Further clinical trials on the use of HCV-positive organs in HCV-negative recipients will be required before such practices become mainstream.

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