

Successful Treatment of a Reinfected Liver Graft Because of Receipt of a HCV-Positive Kidney

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ABSTRACT

Transplantation of hepatitis C virus (HCV)-positive organs has undergone a paradigm shift because of the advent of direct-acting antivirals. We present the case of a 57-year-old man successfully treated initially with pegylated interferon and ribavirin after HCV recurrence postliver transplantation. He subsequently developed end-stage renal disease and received a genotype 1a HCV-positive kidney transplant. A 12-week course of ledipasvir/sofosbuvir and low-dose ribavirin was initiated and sustained virologic response was achieved. This constitutes the first reported case of a patient successfully treated for HCV a second time after receiving an HCV-positive organ.

INTRODUCTION

The approach to transplanting hepatitis C virus (HCV)-positive organs has undergone a recent paradigm shift because of increasing availability and access to highly effective antiviral treatment. For decades, HCV-positive organs were declined for transplantation because of the high probability of disease transmission and aggressive recurrence.¹ This was mainly influenced by the cost, toxicity, and relative inefficacy of HCV treatment options available before the introduction of highly effective direct-acting antiviral (DAA) agents. With DAA agents achieving sustained virological response (SVR) rates >96% post-transplant, experts have questioned whether donor HCV infection should remain a cause for declining organs.² With the understanding that HCV-positive donors are a viable source for transplantable organs, transplant programs have aimed to keep up with increasing demand for transplant and to decrease the length of time patients spend on waiting lists by transplanting those organs. Multiple studies have demonstrated that HCV transmitted during transplantation can be safely eliminated in the recipient post-transplantation with DAA agents.²⁻⁴ We present a case of a liver transplant recipient successfully treated post-transplant for HCV who was reinfected after kidney transplantation from an HCV-positive donor and successfully treated once again with successful achievement of SVR.

CASE REPORT

A 57-year-old man with genotype 3a HCV infection complicated by end-stage liver disease received orthotopic liver transplantation from a HCV-negative donor in 2007. Postoperatively, he was treated with a 6-month course of pegylated interferon and low-dose ribavirin, which successfully led to the cure of HCV. His medical history was also significant for type II diabetes mellitus and hypertension. Over the next few years, he developed end-stage kidney disease due to diabetic nephropathy requiring intermittent hemodialysis as of 2015. He underwent evaluation for kidney transplantation, and in 2017, a suitable hepatitis C nucleic acid amplification test (NAAT)-positive kidney became available for transplantation. The risks and benefits of this strategy were reviewed with the patient and both the liver and kidney transplant teams, and he accepted the offer.

He underwent successful kidney transplantation from a HCV NAAT-positive deceased donor with genotype 1a. The patient subsequently developed detectable HCV RNA 1 month after transplantation, indicating reinfection of his liver graft, although his liver enzymes and function tests remained normal. Three months postkidney transplant, he was treated with a 12-week course of 1 tablet daily of ledipasvir/sofosbuvir and low-dose ribavirin of between 200 and 400 mg per day. Low-dose ribavirin was used because of anemia and suboptimal renal function at the time of treatment initiation. After treatment, SVR was achieved and cure was

Table 1. Key laboratory values

Date	Hemoglobin (g/dL)	ALT (U/L)	Total bilirubin (mg/dL)	INR	Albumin (g/L)	Creatinine (mg/dL)	HCV RNA (IU/mL)
December 2009 (start of 1st treatment course)	10.3	119	0.7	1.0	35	1.63	0 ^a
June 2010 (end of 1st treatment course)	10.0	51	0.41	1.0	34	1.41	0
September/October 2017 (start of 2nd treatment course)	11.8	27	0.53	1.0	40	0.85	37,224,355
January 2018 (end of 2nd treatment course)	11.2	40	0.76	1.0	38	0.88	0

ALT, alanine aminotransferase; HCV, hepatitis C virus; INR, international normalized ratio; PCR, polymerase chain reaction.

^aHCV RNA level measured 1 month after initiation of antiviral therapy. A baseline HCV RNA level immediately before treatment initiation is not available; however, a positive qualitative HCV PCR result was recorded.

documented. He is maintained on tacrolimus and prednisone for immunosuppression and has recovered well from his surgeries and maintains good liver and kidney function. Key laboratory values are presented in Table 1.

DISCUSSION

This case is the first reported case in the literature of a patient cured postliver transplantation for HCV who was subsequently successfully treated for reinfection with HCV after receiving a solid organ transplantation from an HCV-positive donor. This example further demonstrates the safety of using organs from HCV-positive donors in view of the availability of highly effective HCV treatment in the form of DAA agents, which allows for expansion of the donor pool. Furthermore, it shows that cure is achievable for recurrent HCV infection with DAA agents even in the context of solid organ transplantation and chronic immunosuppression.

Historically, a large proportion of kidney grafts from HCV-positive donors were not procured. This proportion lies at approximately 40% of HCV-positive kidney grafts today compared with less than 10% of liver grafts with increasing numbers of HCV-positive donors because of the opioid epidemic.⁵⁻⁷ Meanwhile, the demand for transplantation has reached unprecedented levels because of the increasing prevalence of end-stage organ dysfunction and increasing indications. With approximately 2.5% of the population having positive HCV antibodies, the goal of using HCV seropositive and/or viremic donor organs to safely reduce waitlist mortality via the expansion of the available organ pool has become a reality.⁸ The rate of liver transplantation of organs from HCV-positive donors into HCV-negative recipients has tripled between 2015 and 2016 and doubled for kidney transplantation proper.⁹

To date, the experience using HCV-positive organs in HCV-negative recipients has been positive with widespread success eradicating HCV post-transplant and preventing chronic infection.¹⁰⁻¹² This strategy in kidney transplantation has been

modeled to save money and improve outcomes as compared to remaining on dialysis waiting for a HCV-negative organ with savings approaching \$200,000 US.^{13,14} Given the improvement of quality of life post-transplantation, the use of HCV-positive donors to increase organ availability shows promise. Although the risk is reduced using a HCV antibody-positive, NAAT-negative organ, careful monitoring is required post-transmission because of the risk of possible transmission despite negative RNA levels.¹⁵

The case we have presented provides a proof of concept on re-transplant as a possible area of investigation for expanding the donor pool with HCV-positive organs. Our patient effectively gained 4 years of not being on the waitlist with end-stage kidney disease and the possible complications related to long-term dialysis by accepting an organ from an HCV-positive donor. Access to DAA agents is necessary for the short-term and long-term survival of patients treated with this strategy, and obtaining detailed informed consent by the patient for this type of procedure involving a “diseased” organ and acceptance of DAA agent therapy post-transplant is also required.¹ The limitations of DAA therapies must be explored, and their drug interactions with post-transplant immunosuppressive regimens and other common medications are not well established. It is also not well known if patient selection plays a role when finding recipients for HCV-positive organs.¹⁶ As data accumulates regarding safety of using HCV-positive organs for HCV-negative recipients, further education will be required; a significant minority of recipients do not accept to receive a HCV-positive organ currently.¹⁷ Because the transplantation community continues to implement the acceptance of HCV-positive organ transplantation to HCV-negative patients, prospective studies on outcomes and timing of treatment are necessary to offer insight into any unknown complications.

DISCLOSURES

Authors contributions: H. Azhari wrote the manuscript. LA Tibbles and KW Burak edited the manuscript and revised it for

intellectual content. SE Congly revised the manuscript for intellectual content, approved the final manuscript, and is the article guarantor.

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