Kidney transplantation from an anti-hepatitis C virus antibody-positive donor into an anti-hepatitis C virus antibody-negative recipient: A case report

Sapana Verma, Kentaro Ide*, Seiichi Shimizu, Lalit Kumar Das, Hiroyuki Tahara, Masahiro Ohira, Kohei Ishiyama, Yuka Tanaka, Hirotaka Tashiro, Hideki Ohdan

Department of Gastroenterological and Transplant Surgery, Applied Life Sciences, Institute of Biomedical and Health Sciences, Hiroshima University, Japan

A R T I C L E   I N F O

Article history:
Received 7 January 2016
Received in revised form 8 May 2016
Accepted 26 May 2016
Available online 3 June 2016

Keywords:
Renal transplantation
HCV
Door pool

A B S T R A C T

Patients who test positive for hepatitis C virus (HCV) antibody are not considered suitable living kidney donor candidates for HCV negative recipients. Here, we report a case of an HCV positive patient treated successfully with antiviral therapy, achieving sustained virologic response (SVR), who subsequently donated a kidney to an HCV negative recipient without viral transmission. This suggests that HCV positive patients who achieve SVR may safely donate kidneys.

A 66-year-old male with end-stage renal disease had been on hemodialysis for 7 years. His 63-year-old wife was a candidate for living donation, but had a history of HCV infection. She had received interferon-beta treatment 12 years previously. After the treatment, SVR was achieved and her liver enzymes were normalized. The recipient received a preconditioning regimen comprising a single dose of rituximab combined with cyclosporine microemulsion and mycophenolate mofetil 2 weeks before the transplantation for the desensitization of anti-blood type antibody. The operation was performed with no adverse events. Protocol kidney biopsies at 3 and 12 months showed no signs of rejection. The recipient's liver function tests remained within the normal range, HCV antibody testing was negative, and HCV RNA was undetectable at the 1-year follow-up. At the time of this writing, the recipient is healthy with a serum creatinine level of 1.2 mg/dL. Likewise, the donor is healthy with follow up indicating SVR, normal liver enzymes, and normal renal function.

In conclusion, only in selected cases, HCV antibody positive donors may be taken into consideration as a kidney donor.

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1. Introduction

Renal transplantation is an optimal choice of treatment and a lifesaving procedure for end stage renal disease and is practiced worldwide. However, the shortage of well-matched living donors remains a significant problem. It is now considered acceptable medical practice to transplant a kidney from an HCV seropositive donor into a patient with known HCV infection [1]. Renal transplantation from HCV positive donors to HCV negative recipients, however, is not considered safe due to the chance of HCV transmission, which may further lead to liver disease and liver dysfunction. However, it should be considered that the potential risk of death in these patients without transplantation likely outweighs the risk of viral transmission. HCV can now be completely treated with the use of antiviral therapy that consists of interferon and directly-acting antiviral agents (DAA) [2]. It is conceivable that a successfully treated HCV patient, who has achieved SVR, may serve as a kidney donor for a hepatitis C negative recipient without viral transmission. Here, we report a case of an HCV positive patient treated successfully with antiviral therapy who subsequently donated a kidney to an HCV negative recipient without viral transmission.

Abbreviations: HCV, hepatitis C virus; SVR, sustained virologic response; DAA's, Directly-Acting Antiviral agents

* correspondence to: Department of Gastroenterological and Transplant Surgery, Applied Life Sciences, Institute of Biomedical and Health Sciences, Hiroshima University, 1-2-3 Kasumi Minami-ku Hiroshima 734-8551, Japan.

E-mail addresses: sapana_21@hotmail.com (S. Verma), ideken@hiroshima-u.ac.jp (K. Ide), s.kiyomizu@hotmail.com (S. Shimizu), drlalit_das@hotmail.com (L.K. Das), itahara@hiroshima-u.ac.jp (H. Tahara), mohira@hiroshima-u.ac.jp (M. Ohira), ishiyama@hiroshima-u.ac.jp (K. Ishiyama), yukasan@hiroshima-u.ac.jp (Y. Tanaka), htashiro@hiroshima-u.ac.jp (H. Tashiro), hohdan@hiroshima-u.ac.jp (H. Ohdan).
2. Case report

A 66-year-old man, blood type B, with end-stage renal disease due to autosomal dominant polycystic kidney disease had been on hemodialysis for 7 years. His 63-year-old wife, blood type A, was a candidate for living donation. She had a history of genotype 2a HCV infection with moderate chronic hepatitis and severe fibrosis (A2/F3; New Inuyama classification) and had received interferon-beta treatment 12 years previously. After the treatment, SVR and normalization of liver enzymes were achieved. Approval was obtained from the institutional review board of the Hiroshima University Hospital and informed consent was obtained from both the donor and the recipient. The recipient was given a preconditioning regimen consisting of a single dose of rituximab (375 mg/m²) combined with cyclosporine microemulsion (target trough level: 50–100 ng/ml) and mycophenolate mofetil (500 twice daily) 2 weeks before the transplant for the desensitization of anti-blood type antibody. As anti-blood type isoagglutinin titers were below 1:16, double-filtration plasmapheresis was not required.

After extensive discussion during multidisciplinary rounds, everyone involved with the patient-care team agreed that it was safe to proceed. The operation was performed with no adverse events. Induction quadruple immunosuppression protocol consisted of cyclosporine microemulsion, mycophenolate mofetil, basiliximab and methylprednisolone. After transplantation, the patient’s immune status was evaluated regularly by a mixed lymphocyte reaction using intracellular carboxyfluorescein diacetate succinimidyl ester (CFSE-MLR assay) and immunosuppressant therapy was optimized accordingly [3,4]. Protocol kidney biopsies performed at 3 and 12 months showed no signs of rejection. The recipient’s liver function tests remained within the normal range, HCV antibody testing was negative, and HCV RNA was undetectable at the 1-year follow-up. At the time of this writing, the recipient is healthy with a serum creatinine level of 1.2 mg/dL. The donor is also doing well; follow up showed SVR, normal liver enzymes, and normal renal function without hypertension, proteinuria, or microhematuria.

3. Discussion

The disparity between organ demand and supply in renal transplantation remains a significant problem. Reports indicate that in order to address this problem, grafts from donors with active infections were used, after giving proper antibiotic prophylaxis, and that outcomes were similar to those with organs from non-infected donors [5]. Similarly, there have been additional reports which suggest that in addition to the normal expanded criteria, donors with advanced age, obesity, hypertension, decreased GFR, proteinuria and microscopic hematuria or with further anatomical specifications such as obstruction at the ureterovesical junction, kidney stones, renal cysts, and complex vascular anatomy should also be evaluated as donor candidates in order to increase the number of potential donors [6].

Regarding expansion of the donor pool, ABO incompatible living kidney transplantation has been performed for decades to address the serious shortage of organ donors, especially in eastern countries. Some reports suggest that because of newer preconditioning therapy, almost 30% total living donor kidney transplants done in Japan are ABO incompatible cases, and outcomes are excellent [7]. With the help of desensitization modalities and modern immunosuppression, there is not much difference between graft and patient survival between ABO incompatible and ABO compatible renal transplantation. Indeed, with the effectiveness of modern day immunosuppression, living donor ABO incompatible renal transplantation is a viable alternative to deceased donor transplantation [8,9].

Due to the global organ shortage, the KDIGO guidelines recommend using kidneys from HCV positive donors in HCV-positive recipients. However, it is also accepted that HCV positive grafts should not be used in HCV negative recipients, since the risk of HCV transmission approaches 100%. Following renal transplantation, patients with HCV infection have an elevated risk of developing proteinuria, chronic allograft nephropathy, secondary infection, new-onset diabetes, transplant glomerulopathy, and neoplasia. The increased mortality observed among patients with HCV infection is largely the result of a high incidence of cardiovascular disease, other infections, and liver disease.

However, over the last 25 years, therapy for HCV has become highly successful, with SVR increasing steadily since the introduction of IFNα monotherapy, then by the addition of ribavirin, and later by pegylated IFN pegylated interferon-α (PEG-IFN-α) [10,11]. Recently, anti-HCV therapy was further improved by the approval of direct-acting antivirals (DAAs). Reports suggest that with the highly effective treatment of HCV by new DAAs, the management of HCV has significantly improved and that undetectable HCV RNA 12 weeks after treatment withdrawal have been identified to be cure for HCV now [2]. Almost 99% patients who have achieved SVR after antiHCV treatment remain virus-free for a longer period of time [10]. Another study conducted in the Japanese population found that patients who achieved SVR after antiviral treatment in liver transplant patient with recurrent HCV had prolonged and better survival compared to those who did not achieve SVR [11].

Under these circumstances, it is not known if the patients have achieved SVR, they probably deserve consideration for living kidney donors, but there have been very few reports of successful transplants in this situation. Bouatou et al. recently reported the first successful case of ABO incompatible kidney transplantation from an HCV antibody positive, HCV RNA negative donor to an HCV antibody negative recipient [12]. The recipient had no liver disease or acute HCV infection at 1 year of follow up. In this case, the donor seemed to have achieved SVR spontaneously. We report our case with detailed history of donor’s HCV treatment and that achievement of SVR with HCV RNA undetectable 12 years after the first treatment. This allowed us to consider this candidate as potential donor for our recipient.

Similar reports from Cruzado et al. suggest that successfully treated chronic HCV infection should not preclude an individual from donating a kidney to an HCV negative recipient [13]. The donor is this case had a long history of chronic hepatitis C and was treated for 1 year with antiviral therapy before transplantation was done. HCV viral load in the recipient was negative even 2 years after transplantation. Another small cohort study done by Rozental et al. showed that HCV negative recipients who received kidneys from HCV positive deceased donors had better survival with less rejection compared to HCV positive recipients who received kidneys from HCV positive donors early in the transplant period [14].

Here, we report a case of an HCV positive patient treated successfully with antiviral therapy who subsequently donated a kidney to an HCV negative recipient without viral transmission. However, there is an ethical concern in using a kidney from a living donor who, in spite of SVR, theoretically might have a risk of relapse. Furthermore, the donor kidney may harbor HCV virus even after the patient has achieved SVR, so the theoretical possibility of HCV transmission cannot be ruled out. Although our observation suggests a possible way to increase the living donor pool for kidney transplantation, longitudinal studies with close clinical and virologic monitoring of donors and recipients will be required to investigate the safety of widespread kidney donation from HCV antibody positive donors who have achieved SVR (Fig. 1).
4. Conclusion

In conclusion, only in selected cases, HCV antibody positive donors may be taken into consideration as a kidney donor.

Disclosure

The authors have no conflicts of interest to disclose.

Acknowledgments

This work was supported by a Grant-in-Aid for Sciences Research (C) from the Japan Society for the Promotion of Science and a Grant-in-Aid from the Japanese Ministry of Health, Welfare and Labour.

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