Case Report

Successful Antiviral Treatment with Direct-Acting Antivirals for Hepatitis C Virus Infection during Peritransplant Period in a Kidney Transplant Recipient

Giovanni Varotti,1 Ferdinando Dodi,2 Ernesto Paoletti,3 Andrea Bruno,1 and Iris Fontana1

1Kidney Transplant Unit, San Martino University Hospital, Genoa, Italy
2Department of Infectious Diseases, San Martino University Hospital, Genoa, Italy
3Department of Nephrology, San Martino University Hospital, Genoa, Italy

Correspondence should be addressed to Giovanni Varotti; gvarotti@hotmail.com

Received 28 October 2021; Revised 23 November 2021; Accepted 30 November 2021; Published 11 December 2021

Academic Editor: Mariano Ferraresso

Copyright © 2021 Giovanni Varotti et al. This is an open access article distributed under the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

Introduction. Hepatitis C virus (HCV) infection continues to represent a poor prognostic factor in kidney transplant (KTx) patients. New direct-acting antiviral agents (DAA) have dramatically changed the therapy management for HCV, showing optimal safety and efficacy. Different types of DAA have been proposed for HCV eradication in ESRD and KTx patients with evidence of a high-sustained virologic response (>95%) [2].

1. Introduction

Hepatitis C virus (HCV) infection is associated with an increased risk of morbidity and mortality in end-stage kidney disease (ESRD) and in kidney transplant (KTx) patients [1].

The new antiviral direct-acting agents (DAA) have dramatically changed the management of HCV therapy by showing optimal safety and efficacy.
Timing for DAA therapy in HCV-positive kidney wait-list patients continues to be controversial. Although no specific limitation or contraindication is described in international guidelines [3, 4] and many studies have indicated that DAAs can be safely administered after renal transplantation, some caution is recommended due to the potential difficult dose adjustment with immunosuppressants, especially in the early posttransplant period [5].

We report a case of a KTx performed during the antiviral DAA therapy.

2. Case Report

The patient was a 44-year-old man suffering from chronic HCV Hepatitis (genotype 1b) associated with ESRD secondary to malignant hypertension. The patient first had a KTx in 2005 and had been on hemodialysis since 2016. Liver function was normal, and the ultrasound elastography showed light liver fibrosis (METAVIR score F1). In March 2019, the patient was listed for a second KTx as a sensitized patient (panel-reactive antibody peak 85%). Four months later, antiviral DAA therapy was started (glecaprevir/pibrentasvir 300 mg/120 mg daily, for 8 weeks) [4]. HCV-RNA viral load at the initiation of DAA therapy was $3 \times 10^6$ IU/L. After 30 days, a left kidney from a 63-year-old deceased donor was offered. Given the good compatibility (no mismatches), we decided to proceed with the KTx without discontinuing the DAA therapy. A standard straightforward kidney transplant was performed.

Immunosuppression included thymoglobulin and prednisone for induction and tacrolimus and mycophenolate for maintenance.

After a transient delay graft function, creatinine levels progressively decreased, and from postoperative day 3, tacrolimus reached target levels and remained stable in the following period (Figure 1). No episodes of acute rejection occurred, and the 8-week DAA therapy was carried out without interruption. All HCV-RNA viral load controls after KTx resulted undetectable. On postoperative day 15, the patient was discharged and remains in healthy condition with normal renal function and was HCV-negative after 24 months of follow-up.

3. Discussion

To the best of our knowledge, there are no other cases reporting KTx being performed during DAA therapy.

In accordance with the international HCV guidelines [3, 4], the duration of the DAA therapy was 8 weeks. In fact, recent evidences have shown that an 8-week treatment of glecaprevir/pibrentasvir in naive patients without cirrhosis (any genotype) can achieve optimal sustained virologic response rates, not inferior to those achieved with a 12-week treatment, as reported by previous studies [6–8].

Moreover, the best timing for DAA therapy continues to be debated because while DAA therapy performed before transplant avoids risk of HCV progression, the idea of eradicating the HCV after the Tx has the advantage of expanding the pool of donors to those HCV-positive.

As a consequence, there is a trend to use DAA post-Tx in centers with a high volume of HCV-positive donors and vice versa [9].

In the specific case of HCV-positive wait-listed patients, there are two options: to start DAA therapy prior to transplant, requiring the patient to be temporarily suspended from the waiting list, and consequently losing the chance of a possible transplant. Alternatively, DAA therapy can be postponed for at least six months post-KTx, increasing, however, the risk of HCV-related complications [4–6]. Although there are no specific contraindications to start DAA early post-KTx, some limitations can occur with respect to the potential interaction with immunosuppressant drugs (Table 1). In particular, coadministration of glecaprevir/pibrentasvir with systemic tacrolimus is associated with an increased tacrolimus Cmax and AUC. As a consequence, its use is recommended with caution and with strict therapeutic blood monitoring.
In our case, as a result of optimal donor/recipient immunological matching, we decided to proceed with the KTx, and following a strict monitoring of the tacrolimus plasmatic concentration, we experienced no particular difficulties in the management of immunosuppression dosages (Figure 1). If our findings are confirmed, patients should not necessarily be suspended from waiting lists during DAA therapy as it should not be considered a contraindication for KTx.

Abbreviations

HCV: Hepatitis C virus
ESRD: End-stage renal disease
KTx: Kidney transplantation
DAA: Direct-acting antiviral agent.

Data Availability

The data used to support the findings of this study are included within the article.

Disclosure

All authors participating in the intellectual content, conception, and design of the paper have taken public responsibility for its contents and have agreed to have their names listed as contributors. Neither this manuscript nor parts of it have been previously submitted for publication.

Conflicts of Interest

The authors declare that they have no conflicts of interest.

Authors’ Contributions

Giovanni Varotti and Ferdinando Dodi designed and wrote the manuscript; Andrea Bruno collected the data; and Ernesto Paoletti and Iris Fontana critically revised the manuscript.

References

[1] N. L. Latt, "Update on the management of hepatitis C virus infection in the setting of chronic kidney disease and kidney transplantation," Gastroenterología y Hepatología, vol. 14, pp. 687–705, 2018.
[2] M. Fernández-Ruiz, N. Polanco, A. García-Santiago et al., "Impact of anti-HCV direct antiviral agents on graft function and immunosuppressive drug levels in kidney transplant recipients: a call to attention in the mid-term follow-up in a single-center cohort study," Transplant International, vol. 31, no. 8, pp. 887–899, 2018.
[3] M. G. Ghany, T. R. Morgan, and AASLD-IDSA Hepatitis C Guidance Panel,"Hepatitis C guidance 2019 update: American Association for the Study of Liver Diseases–Infectious Diseases Society of America recommendations for testing, managing, and treating hepatitis C virus infection," Hepatology, vol. 71, no. 2, pp. 686–721, 2020.
[4] J. M. Pawlotsky, F. Negro, A. Aghemo et al., "EASL recommendations on treatment of hepatitis C: final update of the series," Journal of Hepatology, vol. 73, no. 5, pp. 1170–1218, 2020.
[5] A. Cohen-Bucay, J. M. Francis, and C. E. Gordon, “Timing of hepatitis C virus infection treatment in kidney transplant candidates,” Hemodialysis International, vol. 22, pp. S61–S70, 2018.
[6] N. Reau, P. Y. Kwo, S. Rhee et al., “Glecaprevir/pibrentasvir treatment in liver or kidney transplant patients with hepatitis C virus infection,” Hepatology, vol. 68, no. 4, pp. 1298–1307, 2018.
[7] E. Gane, E. Lawitz, D. Pugatch et al., “Glecaprevir and pibrentasvir in patients with HCV and severe renal impairment,” The New England Journal of Medicine, vol. 377, no. 15, pp. 1448–1455, 2017.
[8] E. Lawitz, R. Flisiak, M. Abunimeh et al., “Efficacy and safety of glecaprevir/pibrentasvir in renal impaired patients with chronic HCV infection,” Liver International, vol. 40, no. 5, pp. 1032–1041, 2020.
[9] B. A. Kiberd, K. Doucette, A. J. Vinson, and K. K. Tennankore, “Hepatitis C virus–infected kidney waitlist patients: treat now or treat later?,” American Journal of Transplantation, vol. 18, no. 10, pp. 2443–2450, 2018.
[10] http://www.hepdruginteractions.org.