One Viral Reactivation After the Next: Case Study in HCV-positive Renal Allograft Transplantation

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Background

Rationale:

- Direct-acting antiviral therapy (DAA) has enabled kidney transplantation (KT) with hepatitis-C virus (HCV)-positive allografts[1-6]
- Multiple studies have shown that kidney function tests remain stable ≥ 3 months post-KT with HCV+ allografts.[7] Adults awaiting KT have shown increasing receptivity to HCV+ allografts since mid-2000s[1-6]
- However, factors associated with HCV reactivation in transplant recipients require further understanding

Objective:

- This patient's case was followed and analyzed due to unique features of HCV reactivation many months after KT with an HCV+ allograft, in the context of other new viral infections despite maintaining therapeutic levels of immunosuppression

Case Presentation

- A 48-year-old male with a history of ESRD secondary to FSGS was found to have hepatitis-C virus (HCV) reactivation after KT with an HCV-positive allograft. He was negative for HCV, HBV, HIV1/2, and BK polyoma before KT
- Induction therapy included thymoglobulin, and his maintenance immunosuppressive regimen included mycophenolate mofetil, tacrolimus, and prednisone
- A week after KT, the patient tested positive for HCV genotype 1a and was started on sofosbuvir/velpatasvir. HCV viral load (VL) was undetectable 2 months later
- As of January 2022, urinalysis and hepatic function tests remained unremarkable. However, the patient was positive for BK polyoma and COVID-19 at that time
- By February, HCV VL was positive with the same genotype as prior. This raised the possibility of HCV reactivation from the allograft
- Given HVC VL recurrence, the patient underwent therapy with sofosbuvir/velpatasvir/voxilaprevir, achieving sustained viral response (SVR) as of October 2022

Following Key Data Points

Figure 1. Creatinine and tacrolimus trough levels measured over

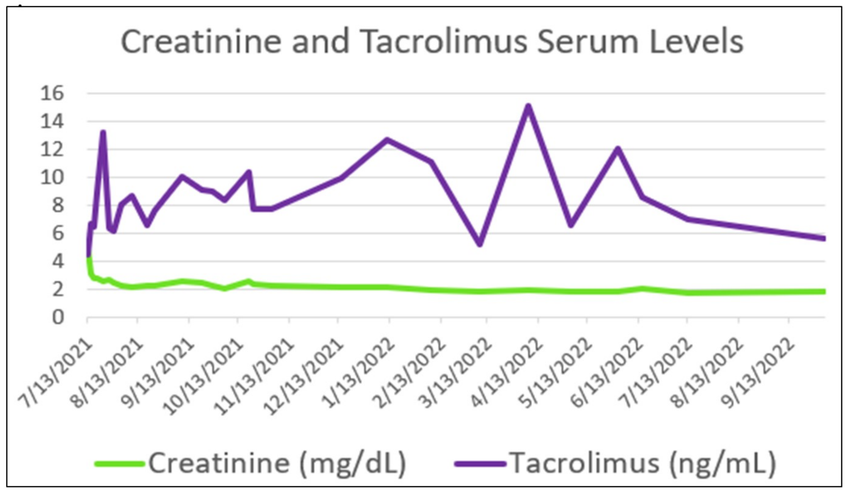
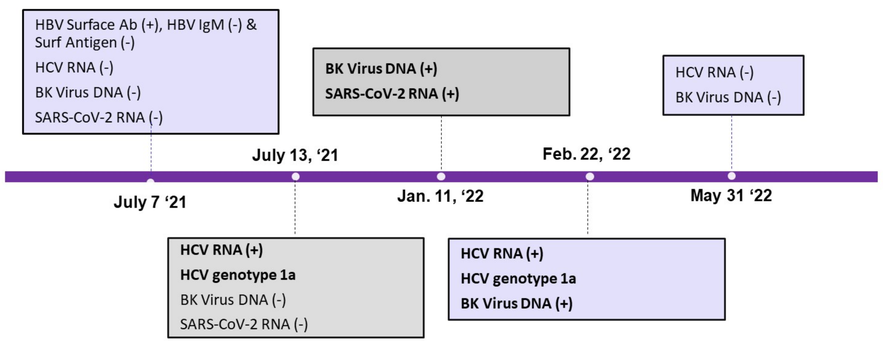


Table 1. Liver function tests followed over time before and after KT.

Date	Bilirubin (Total) [0.1 to 1.2 mg/dL]	AST [8 to 33 U/L]	ALT [4 to 36 U/L]	ALP [44 to 147 IU/L]
7/7/2021	0.6	19	16	75
7/19/2021	0.3	20	21	71
8/2/2021	0.2	15	16	91
1/11/2022	0.3	25	25	113
2/7/2022	0.4	**41**	**61**	119
4/7/2022	0.3	**47**	**70**	112
5/31/2022	0.3	15	8	115

Figure 2. Timeline of viral reactivations.



Discussion

- Recent guidelines for preventing HCV reactivation in allograft-positive KT recipients state that individuals should achieve SVR after 8-12 weeks of DAA[1]
- Achievement of SVR can be affected by several variables, including viral factors (viral load and genotype), host characteristics (age, gender) and treatment regimen (duration, dosage, immunosuppression)
- This patient may not have fully achieved SVR (depending on guideline parameters used) because his VL was positive 3 months after completion of therapy
- Tacrolimus levels can temporarily ↑ in HCV-infected patients and then decline after clearance of viremia, possibly due to altered hepatic metabolism.[1,7] This patient's tacrolimus levels consistently remained within therapeutic range prior to HCV infection
- Reactivation of BKV, a DNA virus that establishes lifelong infection in renal tubular and uroepithelial cells, is common among KT recipients, but there is insufficient evidence to establish a causal association between BKV activation and HCV reactivation[2,5,7]
- This case highlights the importance of close follow-up monitoring for HCV and BKV among KT recipients and the need to explore the relationship between BKV infection, HCV reactivation, and immunosuppression regimen

References & Acknowledgments

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