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CLINICAL CORRESPONDENCE

Rapid reinfection of severe acute respiratory syndrome coronavirus 2 confirmed with sequencing in a solid organ transplant recipient

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Dear Editors,

Since December 2019, the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) pandemic has afflicted millions throughout the world. Until now, we have experienced several surges from different variants of concern including delta and omicron[1]; however, the impact of these variants on different susceptible groups remains unclear, especially with the latest variant, Omicron. The immune suppression that solid organ transplant (SOT) recipients receive places them at greater risk for morbidity and mortality in addition to limiting their ability to mount protection after being vaccinated.[2,3] Although reports exist that SOT recipients can still develop higher T-cell mediated immunity after natural infection compared to vaccination,[4] this may not be enough to prevent re-infection. While re-infection has been reported in the general population,[5] we still have very limited data on re-infection in the immunocompromised population.[6] The Centers for Disease Control and prevention (CDC) defined re-infection as infections requiring 90 days duration between the first and second infections and ideally divergence in whole-genome sequencing (WGS) data.[7] In a clinical setting where WGS is not always feasible, it may be difficult to differentiate between re-infection and prolonged shedding as SOT recipients are known to have polymerase chain reaction or even culture positivity longer than the immunocompetent host. SOT recipients who at higher risk for progression should benefit from early initiation of treatment with agents such as Remdesivir[8] and monoclonal antibody[9] if the positive SARS-CoV-2 testing is recognized as a new infection. Thus, prompt diagnosis of both initial and re-infection, especially with a different variant, is key in this population. We report a case of re-infection diagnosed at 43 days after initial infection in a kidney transplant recipient.

1 | CASE REPORT

A 56-year-old female, with end-stage renal disease due to polycystic kidney disease, had a preemptive living unrelated kidney transplant in 2011. She had received three doses of the BNT162b2 vaccine and reported no international or domestic travel since early 2021. Three months after the third dose of the BNT162b2 vaccine, she developed 2 days of mild cough and fever. Nasopharyngeal swab for SARS-CoV-2 performed with the Roche Cobas 6800 at that time became positive in mid-November 2021 with a cycle threshold (Ct) value of 21.6, which was approximately 2 and 4 weeks prior to the first Omicron variant identified in the United States of America and Miami-Dade County, respectively. At the time of initial infection, she remained on mycophenolic acid 360 mg and tacrolimus 2 mg oral twice daily with no dose reduction. For treatment, she received casirivimab/imdevimab with symptom resolution within 3 days of infusion.

Six weeks after the initial infection, she developed 3 days of cough and weakness and reported exposure to a person who was recently diagnosed with coronavirus disease (COVID-19). She was tested again with polymerase chain reaction (PCR) and was positive for

Abbreviations: CDC, Centers for Disease Control and Prevention; COVID-19, coronavirus disease; Ct, cycle threshold; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; SOT, solid organ transplant; WGS, whole-genome sequencing.

SARS-CoV-2 with the BioFire respiratory viral panel, for which a Ct value is not reported. At this time, we sent the sample for additional analysis with the TaqPath SARS-CoV-2 assay (Thermo Fisher, Waltham, MA) to identify the 69-70del mutation in the Spike gene, which is a feature of both Alpha and Omicron (BA.1) variants. The Alpha variant was not circulating widely in the USA or South Florida at the time of the patient's clinical presentation. Thus, we presumed this represented a re-infection with Omicron as the initial diagnosis was prior to community circulation of Omicron and treated her with remdesivir for three days. Subsequently, the sample was analyzed by WGS and determined to be the Omicron variant (BA.1). Mycophenolic acid was withheld, and she was started on oral dexamethasone. Her symptoms resolved 3 days after completion of remdesivir. Ten days after diagnosis, we placed her back on her original immunosuppressive medication regimen. At the last follow-up, 25 days after re-infection, she remains stable without any sequelae with a negative nasopharyngeal swab PCR.

2 | DISCUSSION

This is the first report of re-infection within 3 months of initial infection in a SOT recipient, with the second infection due to the Omicron (BA.1) variant, 6 weeks after a diagnosis of initial infection. The completion of three-dose mRNA vaccination and receipt of casirivimab/imdevimab could not prevent symptomatic SARS-CoV-2 re-infection.

Vaccination is one of the most important strategies to prevent infection with SARS-CoV-2, but immunogenicity after vaccination is diminished in SOT recipients.[3] Thus, several strategies including four doses of mRNA vaccinee have been attempted however, breakthrough infection in SOT recipients has been widely reported.[10] Also, previous studies showed casirivimab/imdevimab may continue to have some benefit to prevent certain variants for several months; yet, this may not be the case for Omicron.[11] Due to the limited effect against Omicron by casirivimab/imdevimab along with waning immunogenicity with vaccination and natural infection, this recipient developed symptomatic COVID-19 from re-infection with Omicron (BA.1).

Very little is known about re-infection due to the Omicron variant in immunocompromised individuals. Given the high transmissibility and immune evasion properties of this variant, the incidence of reinfection will likely exponentially rise. As seen in this patient, we report a case developing re-infection around 6 weeks from the initial infection. Per CDC's definition of at least 90 days, which may be reasonable for the general population, our case would not be classified as re-infection. However, the first infection occurred before the first Omicron variant in the United States was reported and re-infection occurred with new onset of symptoms with confirmed Omicron (BA.1) variant by WGS, even though we do not have PCR negative result between the first and second infections. For COVID-19, this new variant could likely cause breakthrough infection and reinfection. Consequently, it might be reasonable to adjust the reinfection criteria specifically for immunocompromised population so that the physician can provide the proper treatment in timely manner.

Genome sequencing did not take place with the first infection, thus not allowing us to define with certainty the COVID-19 variant. However, the first identified Omicron case in our region took place several weeks after the patient's first infection.

In conclusion, we report SARS-CoV-2 re-infection due to the Omicron variant 43 days post initial breakthrough infection after three doses of the BNT162b2 vaccine and treatment with a monoclonal antibody in a kidney transplant recipient. Casirivimab/imdevimab may not be able to prevent infection from the omicron variant. We should be aware of this phenomenon in order to initiate and optimize the management of our immunocompromised patients during a pandemic with numerous circulating variants.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

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REFERENCES

1. Prevention TCfDCa. Omicron variant: what you need to know.
2. Raja MA, Mendoza MA, Villavicencio A, et al. COVID-19 in solid organ transplant recipients: a systematic review and meta-analysis of current literature. *Transplant Rev (Orlando)*. 2021;35(1):100588. https://doi.org/10.1016/j.trre.2020.100588. 01.
3. Boyarsky BJ, Werbel WA, Avery RK, et al. Antibody response to 2-Dose SARS-CoV-2 mRNA vaccine series in solid organ transplant recipients. *JAMA*. 2021;325(21):2204–2206. https://doi.org/10.1001/jama.2021.7489. 06 01.
4. Ferreira VH, Marinelli T, Ierullo M, et al. Severe acute respiratory syndrome coronavirus 2 infection induces greater T-Cell responses compared to vaccination in solid organ transplant recipients. *J Infect Dis*. 2021;224(11):1849–1860. https://doi.org/10.1093/infdis/jiab542.
5. Helfand M, Fiordalisi C, Wiedrick J, et al. Risk for reinfection after SARS-CoV-2: a living, rapid review for American College of Physicians practice points on the role of the antibody response in conferring immunity following SARS-CoV-2 infection. *Ann Intern Med*. 2022;175(4):547–555. https://doi.org/10.7326/M21-4245.
6. Tomkins-Tinch CH, Daly JS, Gladden-Young A, et al. SARS-CoV-2 reinfection in a liver transplant recipient. *Ann Intern Med*. 2021;174(8):1178–1180. https://doi.org/10.7326/L21-0108.
7. Prevention TCfDCa. Coronavirus disease 2019 (COVID-19) 2021 case definition. Accessed Jan 28, 2022.
8. Gottlieb RL, Vaca CE, Paredes R, et al. Early remdesivir to prevent progression to severe COVID-19 in outpatients. *N Engl J Med*. 2022;386(4):305–315. https://doi.org/10.1056/NEJMoa2116846.

9. Yetmar ZA, Beam E, O'Horo JC, et al. Monoclonal antibody therapy for COVID-19 in solid organ transplant recipients. *Open Forum Infect Dis*. 2021;8(6):ofab255. https://doi.org/10.1093/ofid/ofab255.
10. Heftdal LD, Schultz M, Lange T, et al. Incidence of positive SARS-CoV-2 PCR after COVID-19 vaccination with up to eight months of follow-up: real life data from the Capital Region of Denmark. *Clin Infect Dis*. 2022;ciac012. https://doi.org/10.1093/cid/ciac012.
11. Takashita E, Kinoshita N, Yamayoshi S, et al. Efficacy of antibodies and antiviral drugs against COVID-19 omicron variant. *N Engl J Med*. 2022;386(10):995–998. https://doi.org/10.1056/NEJMc2119407.

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