Seroconversions After Withdrawal From Mycophenolate Mofetil in Solid Organ Transplant Recipients Without a Third Dose of BNT162b2 mRNA Coronavirus Disease 2019 Vaccine: A Case Series

Tetsuji Morishita, MD, PhD,[1,2] Akiyoshi Sakai, BA,[3] and Hidetoshi Matsunami, MD, PhD[4]

To control the burden of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection, vaccines have emerged for preventing severe coronavirus disease 2019.[1] Poor antibody response to 2 doses of vaccine against SARS-CoV-2 has been reported in solid organ transplants recipients.[2-7] Mycophenolate mofetil is one of the key immunomodulators used by solid organ transplant recipients and it also provokes weak antibody responses to anti–SARS-CoV-2 vaccines.[2] A third dose of BNT162b2 vaccine to solid organ transplant recipients has been considered as one alternative to achieve adequate antibody responses.[3] In transplant patients, withdrawal of immunosuppressive drugs is impractical because of the risk of rejection of the transplanted organ, but other options include switching to other drugs, calcineurin inhibitor or steroid, reducing the dose of antimetabolites, or withdrawal from mycophenolate mofetil.

We report the cases of 3 solid organ transplant recipients treated with mycophenolate mofetil at the Matsunami General Hospital (Gifu, Japan) who had each received a second dose of BNT162b2 mRNA (Pfizer/BioNTech) vaccine between March 2021 and October 2021 (Table 1). The SARS-CoV-2 S-immunoglobulin (Ig)G assay reagent kit (Fujirebio Co., Tokyo, Japan) was used to measure S receptor-binding domain IgG antibody titers. Titers >1.0 AU/mL were considered to represent seropositivity. None of the recipients received the third dose of vaccination or had developed prior clinically relevant and polymerase chain reaction–confirmed SARS-CoV-2 infection. All recipients completed their second dose of BNT162b2 mRNA vaccine at 21-d intervals. The institutional review board approval was obtained.

In these 3 recipients, antibody titers 1 mo after the second vaccine administration showed seronegative antibody responses with a receptor-binding domain IgG antibody titer of 0.2, 0.8, and <0.1 AU/mL, respectively. The baseline characteristics and immunosuppression regimens are summarized in Table 1. All 3 recipients had received immunosuppression regimens including mycophenolate mofetil (1000 mg/d). After detailed discussions with attending physicians and solid organ transplant recipients regarding the potential risks and benefits, mycophenolate mofetil was tapered and terminated. The conversion to calcineurin inhibitor monotherapy was successful, with adequate control of rejection maintained. One month after withdrawal from mycophenolate mofetil, antibody titer had elevated to 2.4, 36.7, and 6.0 AU/mL, respectively, and seroconversion was confirmed in all 3 recipients.

In solid organ transplant recipients requiring continuous immunosuppression, no specific alternatives to the standard immunization strategy have been proposed for these blunted antibody responses. Mycophenolate mofetil suppresses T-lymphocytic responses to allogeneic cells and also suppresses primary, but not secondary, antibody responses.[8] In contrast, calcineurin inhibitors attenuated humoral immunity, cellular responses were preserved. We therefore assume that withdrawal from mycophenolic acid favors antibody production in solid organ transplant recipients. There may be cases where patients who have discontinued mycophenolate mofetil need to resume the drug afterward. In such cases, the possibility of a decline in antibody titers after restarting mycophenolate mofetil should be considered.

The efficacy and safety of a third dose of mRNA coronavirus disease 2019 vaccine in solid organ transplant

Received 16 November 2021. Revision received 23 November 2021.

Accepted 25 November 2021.

[1] Department of Internal Medicine, Matsunami General Hospital, Gifu, Japan.

[2] Matsunami Research Park, Gifu, Japan.

[3] Department of Clinical Laboratory, Matsunami General Hospital, Gifu, Japan.

[4] Matsunami General Hospital, Gifu, Japan.

The authors declare no conflicts of interest.

This study was supported by Sosaikouseikai Clinical Foundation.

T.M., A.S., and H.M. participated in study idea, design, and article. All authors participated in data ascertainment, article discussion, and article revisions.

The data sets generated or analyzed during the present study are not publicly available because of ethical/privacy reasons but are available from the corresponding author on reasonable request.

Correspondence: Tetsuji Morishita, MD, PhD, Department of Internal Medicine, Matsunami General Hospital, 185-1 Dendai, Kasamatsu-cho, Hashima-gun, Gifu 501-6062, Japan. (tmori@u-fukui.ac.jp).

ISSN: 0041-1337/20/1064-e238

DOI: 10.1097/TP.0000000000004043

TABLE 1.

Characteristics of solid organ transplant recipients who developed seroconversion after withdrawal from mycophenolic acid

No.	Age[a] /sex	Organ/donor	Years since transplant	Days from second vaccination	Immunosuppressive therapy Pre/post	Antibody titer[b] (AU/mL) Pre/post
1	68/M	Liver/deceased	16	103	Calcineurin inhibitor + mycophenolate mofetil/calcineurin inhibitor	0.2/2.4
2	67/F	Kidney/deceased	15	110	Calcineurin inhibitor + mycophenolate mofetil/calcineurin inhibitor	0.8/36.7
3	63/M	Liver/deceased	15	101	Calcineurin inhibitor + mycophenolate mofetil/calcineurin inhibitor	<0.1/6.0

[a]Age at measurement.
[b]RBD IgG antibody titer.
F, female; M, male; RBD IgG, receptor-binding domain immunoglobulin G.

recipients have been studied.[2,3] However, a large proportion of recipients failed to obtain sufficient antibody titers. Our therapeutic approach was well tolerated and led to serological recovery of antibody responses after withdrawal from mycophenolate mofetil without a third dose of vaccine. A point of notice for withdrawal of mycophenolate mofetil, we need to monitor the health of transplanted organs, particularly with respect to rejection by the host immune system. This case series could represent a useful alternative strategy for improving the immunogenicity of vaccines in solid organ transplant recipients.

ACKNOWLEDGMENTS

The authors are greatly indebted to the staff of Matsunami General Hospital and Matsunami Health Promotion Clinic for their generous cooperation in establishing the case report. They also gratefully acknowledge the special efforts of Matsunami Research Park.

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