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CASE REPORT

Adequate immune response after SARS-CoV-2 infection and single dose vaccination despite rapid heart transplantation

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Abstract

Adequate immune response to vaccination remains a challenge in patients after solid organ transplantation. We report a case of a 61-year-old male patient who received a left ventricular assist device as a bridge to transplant therapy. Three months before transplantation, he suffered mild SARS-CoV-2 infection and was successfully discharged thereafter. Eight days before his successful heart transplantation, he received mRNA BNT 162b2 vaccination. Immediately after transplantation, we detected sufficient rise of nucleocapsid and spike antibodies despite immune suppression therapy. We suspect potential booster effects of the previous SARS-CoV-2 infection giving rise to adequate immune response following single vaccination.

Keywords Orthotopic heart transplantation; SARS-CoV-2; COVID-19; Vaccination; Immune response; Immune suppression

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Introduction

The current severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) pandemic represents an increased risk for patients awaiting heart transplantation (HTx) to suffer from severe coronavirus disease 2019 (COVID-19). Although these patients were excluded from previous vaccine trials,[1] recent reports recommend mRNA vaccination in transplant recipients, because safety and reactogenicity following two doses of SARS-CoV-2 vaccination were similar in solid organ transplant recipients in the range of previous vaccine trials.[2] In the case of vaccination, the problem could, however, be enhanced, as the immune response for T- and B-cell populations seem to be reduced, as recent case reports demonstrated.[3]

This report reveals for the first time adequate immune response to single dose early mRNA-based vaccination following an oligosymptomatic SARS-CoV-2 infection in solid organ transplantation.

Case report

Ethical approval

The study followed the principles of the Declaration of Helsinki and was approved by the local university ethics committee. The patient gave his written informed consent to the report.

Case report

A 61-year-old Caucasian man suffered cardiogenic shock due to ST-segment elevation myocardial infarction and received a primary percutaneous revascularization of the left anterior descending coronary artery and the diagonal branch with implementation of mechanical circulatory support (Impella CP®, Abiomed, Inc., Danvers, MA, USA) prior to revascularization

immediately after hospital admission. Following repetitive cardiac arrest due to asystole mechanical circulatory support was escalated to additional venous–arterial extracorporeal membrane oxygenation. Echocardiography revealed severe impairment of the left ventricular function (ejection fraction < 20%) but preserved right ventricular function and no relevant valve pathologies. After initial stabilization on combined mechanical circulatory support but without recovery of left ventricular function and without any reasonable expectations for future left ventricular improvement, we implanted a permanent left ventricular assist device (HeartMate 3™, Abbott Laboratories, Chicago, IL, USA) as bridge to transplantation therapy 38 days after the initial event.

On 117 days after left ventricular assist device implantation, the patient developed fever without any additional coronavirus disease 2019 (COVID-19)-related symptoms. Polymerase chain reaction (PCR) of a nasopharyngeal swab for SARS-CoV-2 was positive. The mean virus cycle-threshold (Ct) value of the PCR was 20.1. The patient was quarantined but did not required oxygen supplementation or specialized COVID-19 therapy as his chest x-ray was free of pulmonary infiltrates. Ten days later, he was released from isolation at a Ct-value of >30.0 for detection of SARS-CoV-2 in accordance with current recommendations of the German Centre for Disease Control (Robert Koch Institute, Berlin). Since then, no SARS-CoV-2 has been detected in any further testing. Thus, he was finally discharged to a rehabilitation clinic in stable haemodynamic conditions 174 days after the initial event.

Three months later, on the waiting list for HTx, the patient inadvertently received a mRNA BNT 162b2 (Pfizer-BioNTech) COVID-19 mRNA vaccination, 3 months after SARS-CoV-2 infection, despite a recommended period of 6 months for vaccination after SARS-CoV-2 recovery by mistake.

Eight days after vaccination (231 of left ventricular assist device support), he was successfully transplanted. The graft was transplanted in orthotopic bicaval technique with uneventful post-operative period. Primary therapy for immune suppression regimen included tacrolimus, corticosteroids, and mycophenolate. In order to assess the SARS-CoV-2-specific immune response during immunosuppression, patient was sequentially tested for anti-SARS-CoV-2 antibodies as well as for SARS-CoV-2 neutralization efficacy (NT). Quantitative determination of antibodies against SARS-CoV-2 spike and nucleocapsid proteins was performed using commercially available test systems by Roche Diagnostics and Euroimmun (specific SARS-CoV-2 IgG-antibody, Elecsys® Anti-SARS-CoV-2, Roche Diagnostics; Anti-SARS-CoV-2-QuantiVac-ELISA, Euroimmun). SARS-CoV-2 neutralization test was performed as described previously.[4] Since the first post-operative day, detected neutralizing anti-SARS-CoV-2 spike antibodies were always above the detection limit (>384.0 BAU/mL, reference < 25.6 BAU/mL) with a neutralizing titre of 1:2560 (*Table 1*, *Figure 1*). In addition, anti-SARS-CoV-2 antibodies were also always above the detection limit (>2500 U/mL). Furthermore, SARS-CoV-2-IgG/A/M antibodies (reference < 1.0 U/mL) continuously increased during the post-operative period from 17.4 U/mL (16 days after HTx) to 38.2 U/mL (29 days after HTx).

Therefore, we could demonstrate an increase of SARS-CoV-2 antibodies, suggesting optimal protection against COVID-19 infection in the future. Further observation will continue. Meanwhile, the patient was successfully discharged.

Discussion

This case report reveals for the first time the adequate SARS-CoV-2-specific immune response pattern in a recovered patient who received single mRNA COVID-19 vaccination and HTx 3 months after infection.

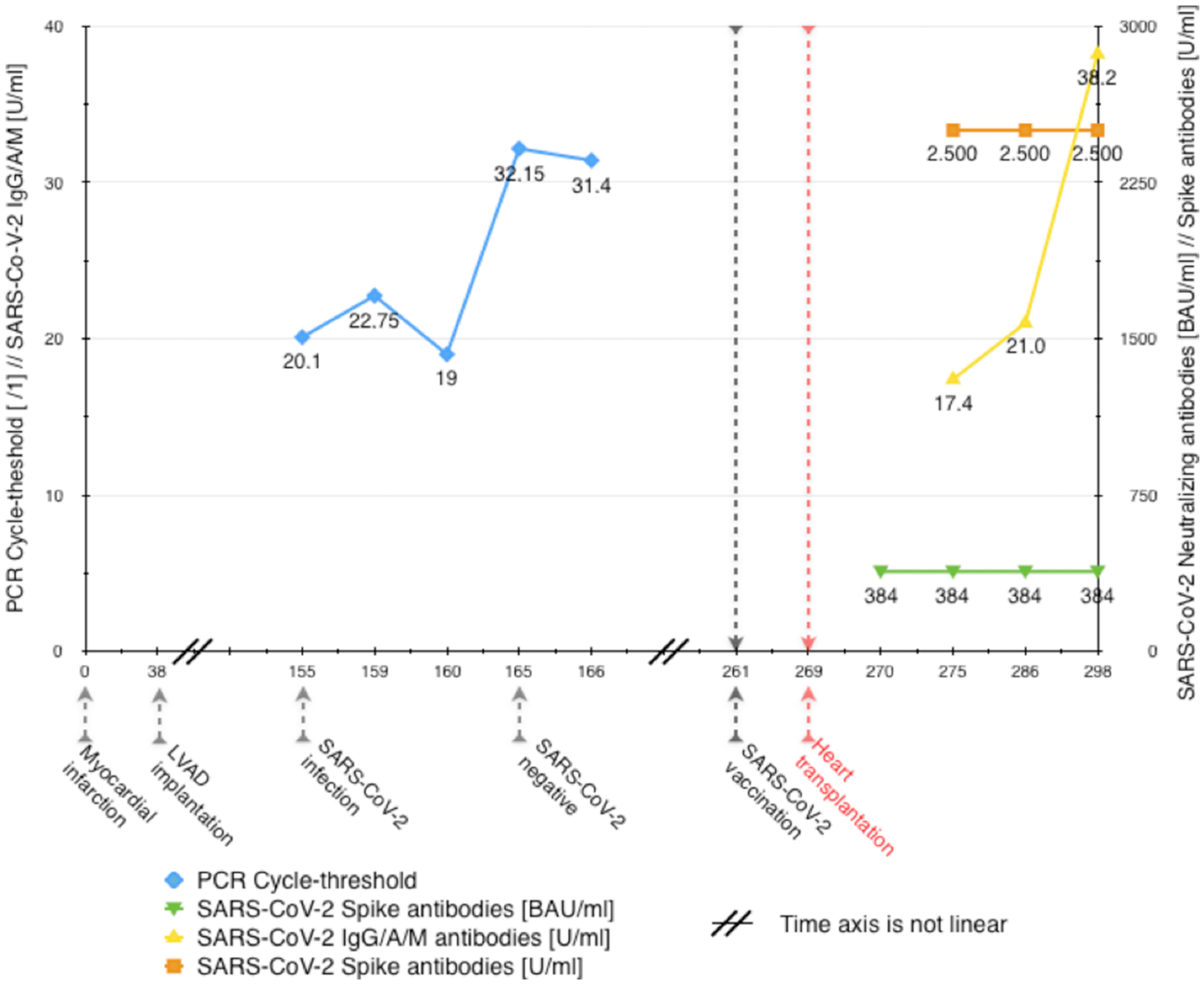
The vaccine mRNA-1273 encodes the stabilized perfusion SARS-CoV-2 spike protein and has demonstrated high efficiency to protect against SARS-CoV-2 infection.[5,6] Based on these results, one observational trail recruited US transplant recipients in order to study the reactogenicity to mRNA vaccination with two doses and compare the immune response to the report of the original trials.[2] The results suggested the vaccination to be safe and effective in organ transplant patients.[2] However, other studies of more than 400 transplant recipients undergoing mRNA vaccination deciphered poor anti-SARS-CoV-2 spike protein antibody response, only after the first and second dose vaccination.[7,8] The authors

Table 1 Serological results of SARS-CoV-2 antibodies

	Reference	Day 270	Day 285	Day 286	Day 298
Anti-SARS-CoV-2 spike antibodies, BAU/mL	<25.6	>384.0	>384.0	>384.0	>384.0
Anti-CoV-2 spike antibodies, U/mL	<0.8	n/a	>2500	>2500	>2500
CoV-2-IgG/A/M antibodies, U/mL	<1.0	n/a	17.4	21.0	38.2
Neutralizing titre	0	1:2560	1:2560	1:2560	1:2560

BAU, binding antibody units.
SARS-CoV-2 serology after heart transplantation following acute myocardial infarction and consecutive left ventricular assist device implantation as well as mild COVID-19. Times are displayed in relation to the initial myocardial infarction (Day 0). Serology was first assessed at the first post-operative day after the heart transplantation (Day 270 after the initial event). Laboratory references are displayed for healthy individuals as control.

Figure 1 Graphical presentation of performed procedures SARS-CoV-2 laboratory values during the whole observation period. Times are displayed in relation to the initial myocardial infarction (Day 0). SARS-CoV-2-specific serology was first assessed at the first post-operative day after the heart transplantation (Day 270 after the initial event). Technical cut-off of SARS-CoV-2 neutralizing antibody ELISA was 384 BAU/mL. For better visibility, time axis is not displayed linear. BAU, binding antibody units; PCR, polymerase chain reaction.



suggested a higher early risk for the vaccination in transplant patients.[7,8] Also, the fatal outcome of two reported cases of SARS-CoV-2 infection after HTx seemed to be related to a poor immune response, an observation that was also confirmed in a prospective study from Israel.[9] In lung and heart transplant patients, similar data were published showing no detectable humoral or T-cell response even after the boosting of the vaccine dose.[10]

In our patient, the mRNA vaccination was very well tolerated and the immune response sufficient, which may be due to a booster effect after 3 months after SARS-CoV-2 infection and before transplantation, similar as reported for non-transplant patients.[11] It must be taken into account that this patient has had a previous uncomplicated SARS-CoV-2 infection and a first dose vaccination prior to HTx. However, in our patient, the vaccination occurred 8 days before the HTx and accompanying immune suppressive therapy, so that the vaccination could already induce the production of immune competent T- and B-cells, similar to a booster effect. Therefore, we cannot compare this case to the cited studies, because they were done in patients already receiving immunosuppressive treatment at the time of the vaccination, while our patient was immunocompetent.[2,3,7–9] We do not know which proportion of the immune response was elicited by the infection and by the vaccination. But it is likely that the vaccination

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(still without immunosuppression) caused a strong booster effect, especially after the short period of 3 months after the infection.

Conclusion

In the present case, we present for the first time adequate SARS-CoV-2-specific immune response following single dose COVID-19 mRNA vaccination 3 months after SARS-CoV-2 infection, just prior to HTx. It seems worthwhile investigating the efficacy of early COVID-19 vaccination following SARS-CoV-2 infection in patients that are scheduled for immunosuppressive therapy.

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Conflict of interest

The authors have nothing to declare.

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Data availability statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

References

1. Mulligan MJ, Lyke KE, Kitchin N, Absalon J, Gurtman A, Lockhart S, Neuzil K, Raabe V, Bailey R, Swanson KA, Li P, Koury K, Kalina W, Cooper D, Fontes-Garfias C, Shi PY, Türeci Ö, Tompkins KR, Walsh EE, Frenck R, Falsey AR, Dormitzer PR, Gruber WC, Şahin U, Jansen KU. Phase I/II study of COVID-19 RNA vaccine BNT162b1 in adults. *Nature* 2020; **586**: 589–593.
2. Ou MT, Boyarsky BJ, Motter JD, Greenberg RS, Teles AT, Ruddy JA, Krach MR, Jain VS, Werbel WA, Avery RK, Massie AB, Segev DL, Garonzik-Wang JM. Safety and reactogenicity of 2 doses of SARS-CoV-2 vaccination in solid organ transplant recipients. *Transplantation* 2021. https://doi.org/10.1097/TP.0000000000003780
3. Tchana-Sato V, Ancion A, Tridetti J, Sakalihasan N, Hayette MP, Detry O, Delvenne P, Amabili P, Senard M, Hougrand O, Szecel D, Lavigne JP, Minga Lowampa E, Ponte C, Maquoi I, Morimont P, Van Den Bulck M, Delbouille MH, Defraigne JO, Lancellotti P. Clinical course and challenging management of early COVID-19 infection after heart transplantation: case report of two patients. *BMC Infect Dis* 2021; **21**: 89.
4. Müller L, Ostermann PN, Walker A, Wienemann T, Mertens A, Adams O, Andree M, Hauka S, Lübke N, Keitel V, Drexler I, Di Cristanziano V, Hermsen DF, Kaiser R, Boege F, Klein F, Schaal H, Timm J, Senff T. Sensitivity of anti-SARS-CoV-2 serological assays in a high-prevalence setting. *Eur J Clin Microbiol Infect Dis* 2021; **40**: 1063–1071.
5. Jackson LA, Anderson EJ, Rouphael NG, Roberts PC, Makhene M, Coler RN, McCullough MP, Chappell JD, Denison MR, Stevens LJ, Pruijssers AJ, McDermott A, Flach B, Doria-Rose NA, Corbett KS, Morabito KM, O'Dell S, Schmidt SD, Swanson PA 2nd, Padilla M, Mascola JR, Neuzil KM, Bennett H, Sun W, Peters E, Makowski M, Albert J, Cross K, Buchanan W, Pikaart-Tautges R, Ledgerwood JE, Graham BS, Beigel JH. An mRNA vaccine against SARS-CoV-2 - preliminary report. *N Engl J Med* 2020; **383**: 1920–1931.
6. Baden LR, El Sahly HM, Essink B, Kotloff K, Frey S, Novak R, Diemert D, Spector SA, Rouphael N, Creech CB, McGettigan J, Khetan S, Segall N, Solis J, Brosz A, Fierro C, Schwartz H, Neuzil K, Corey L, Gilbert P, Janes H, Follmann D, Marovich M, Mascola J, Polakowski L, Ledgerwood J, Graham BS, Bennett H, Pajon R, Knightly C, Leav B, Deng W, Zhou H, Han S, Ivarsson M, Miller J, Zaks T. Efficacy and safety of the mRNA-1273 SARS-CoV-2 vaccine. *N Engl J Med* 2021; **384**: 403–416.
7. Boyarsky BJ, Werbel WA, Avery RK, Tobian AAR, Massie AB, Segev DL, Garonzik-Wang JM. Immunogenicity of a single dose of SARS-CoV-2 messenger RNA vaccine in solid organ transplant recipients. *JAMA* 2021; **325**: 1784–1786.
8. Boyarsky BJ, Werbel WA, Avery RK, Tobian AAR, Massie AB, Segev DL, Garonzik-Wang JM. Antibody response to 2-Dose SARS-CoV-2 mRNA Vaccine Series in Solid Organ Transplant Recipients. *JAMA*. 2021; **325**: 2204–2206.
9. Itzhaki Ben Zadok O, Shaul AA, Ben-Avraham B, Yaari V, Ben Zvi H, Shostak Y, Pertzov B, Eliakim-Raz N, Abed G, Abuhazira M, Barac YD, Mats I, Kramer M, Aravot D, Kornowski R, Ben-Gal T. Immunogenicity of the BNT162b2 mRNA vaccine in heart transplanted patients-a prospective cohort study. *Eur J Heart Fail* 2021; **23**: 1555–1559.
10. Peled Y, Ram E, Lavee J, Sternik L, Segev A, Wieder-Finesod A, Mandelboim M, Indenbaum V, Levy I, Raanani E, Lustig Y, Rahav G. BNT162b2 vaccination in heart transplant recipients: clinical experience and antibody response. *J Heart Lung Transplant* 2021; **40**: 759–762.
11. Prendecki M, Clarke C, Brown J, Cox A, Gleeson S, Guckian M, Randell P, Pria AD, Lightstone L, Xu XN, Barclay W, McAdoo SP, Kelleher P, Willicombe M. Effect of previous SARS-CoV-2 infection on humoral and T-cell responses to single-dose BNT162b2 vaccine. *Lancet* 2021; **397**: 1178–1181.