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

Sophiko Erbel-Khursidze, Moritz Benjamin Immohr, Payam Akhyari, Igor Tudorache, Hug Aubin, Raphael Romano Bruno, Ralf Westenfeld, Torsten Feldt, Nadine Lübke, Artur Lichtenberg and Udo Boeken

Department of Cardiac Surgery, Medical Faculty and University Hospital Düsseldorf, Heinrich-Heine-University Düsseldorf, Moorstrasse 5, Düsseldorf, Germany; Division of Cardiology, Pulmonology and Vascular Medicine, Medical Faculty and University Hospital Düsseldorf, Heinrich-Heine-University Düsseldorf, Duesseldorf, Germany; Department of Gastroenterology, Hepatology and Infectious Diseases, Medical Faculty and University Hospital Düsseldorf, Heinrich-Heine-University Düsseldorf, Duesseldorf, Germany; and Institute of Virology, Medical Faculty and University Hospital Düsseldorf, Heinrich-Heine-University Düsseldorf, Duesseldorf, Germany

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

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, 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. 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. 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 require oxygen supplementation or specialized 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. 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 trial 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.7,8 The results suggested the vaccination to be safe and effective in organ transplant patients.5 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.
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

**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.
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.

**Conclusion**

The authors have nothing to declare.

**Funding**

The authors did not receive any funding for this study. Open Access funding enabled and organized by Projekt DEAL.

**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 K, 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, Frenc 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, Krak MR, Jain VS, Werbel WA, Avery RK, Massie AB, Segev DL, Garonzik-Wang JM. Safety and reactogenicity of 2 doses of SARS-CoV-2 vaccine in solid organ transplant recipients. *Transplantation* 2021. https://doi.org/10.1097/TP.0000000000037780

3. Tchana-Sato V, Ancion A, Tridetti J, Sakalihanes N, Hayette MP, Detry O, Delvenne P, Amabili P, Senard M, Hugrand O, Szczel D, Lavigne JP, Minga Lowampa E, Ponte C, Maquoi I, 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.

4. Jackson LA, Anderson EJ, Rouphael NG, Roberts PC, Makhene M, Coler RN, McCullough MP, Chappell JD, Denison MR, Stevens LJ, Prijssers 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.

5. Baden LR, El Sahly HM, Essink B, Kolfow K, Frey S, Novak R, Diemert D, Spector SA, Rouphael N, Cheadle 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.

6. 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.

7. 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.

8. Izhaki Ben Zadok O, Shaul AA, Ben-Avraham B, Yaari V, Ben Zvi H, Shostak Y, Pertsov B, Eliakim-Raz N, Abed G, Abuhalima 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.

9. 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.

10. Prendergast M, Clarke C, Brown J, Cox A, Glesson 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.

**Conflict of interest**

The authors have nothing to declare.

**Acknowledgements**

The authors thank the whole medical stuff of the Departments of Cardiac Surgery, and Cardiology, Pulmonology and Vascular Medicine of the Medical Faculty and University Hospital of the Heinrich-Heine-University Düsseldorf for their continuous effort and contribution in the treatment of heart failure patients.