Received: 20 April 2021 | Revised: 8 September 2021 | Accepted: 6 October 2021

DOI: 10.1111/petr.14175

LETTER TO THE EDITOR

WILEY

Allogeneic hematopoietic stem cell transplant after COVID-19 infection and its effect on the antibody titers to SARS-CoV-2

To the editor,

The pediatric guidelines for managing a prospective hematopoietic stem cell transplant (HSCT) patient or a post-transplant patient diagnosed with COVID-19 are still evolving. The latest EBMT guidelines still recommend deferral of HSCT if a patient is diagnosed with COVID-19.[1]

Here, we report a 12-year-old male child, with relapsed acute lymphoblastic leukemia, who was found to be positive on routine mandatory screening before HSCT, for the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection by the TrueNat test (Molbio Diagnostics). Subsequently, after clearance of the infection, he underwent the allogeneic HSCT procedure, with his 6/6 HLA-matched sister as the donor using peripheral blood stem cells as the product.

On the detection of the infection, he had been admitted to a dedicated COVID-19 isolation facility. He did not have any symptoms or signs of COVID infection and was discharged after 14 days. His total serum anti-SARS-CoV-2 antibody titers (IgG and IgM), estimated using chemiluminescent immunoassay (ADVIA Centaur COV2G assay by Siemens), were reactive, with an index of >10 (>1 taken as reactive). (The assay detects antibodies to spike protein receptor binding domain.) He was subsequently admitted for HSCT, after taking an informed consent. The donor tested negative before her harvest, and her antibody titers were non-reactive. The patient received a TBI + Etoposide-based conditioning with a CD34+ stem cell dose of 2.86 million/kg. The child received methotrexate and cyclosporine for graft-versus-host disease prophylaxis. Post-HSCT, he had mucositis and febrile neutropenia, which were managed appropriately.

The engraftment of neutrophils (on day +16) and platelets (on day +19) occurred successfully. The child was discharged on day +31. The chimerism analysis done on day +29 revealed 100% donor cells (XX). We tested the anti-SARS-CoV-2 antibody levels in the patient during the transplant and post-transplant period, and these were maintained above levels considered to be reactive (index range: 4.7 to >10; index >1 was considered as reactive; Table 1). The patient is presently 120 days post-transplant and is off all immunosuppression medications with no complaints. The child did not receive any intravenous immunoglobulin (IVIG) during this time, which could have altered the antibody levels. The child did not have any additional known exposure to SARS-CoV-2 during the admission for the HSCT. The antibody titers repeated on day +73 were still present at detectable levels.

Our group has previously reported good antibody response to SARS-CoV-2 post-autologous HSCT.[2] The immune response to COVID-19 is yet not studied post-allogeneic HSCT where the cells taking part in the immune process change to the donor's type. After allogeneic HSCT, neutrophils are the first cell lines to reconstitute, followed by the T cells and B cells. However, the recipient plasma cells can survive the conditioning. Plasma cells are non-dividing but can survive for months and secrete antibodies.[3] Sethi et al[4] have shown the persistence of individual recipient B-cell clones in post-HSCT patients, for at least 2 years by the use of next-generation sequencing–based B-cell repertoire analysis.

In our patient, it is likely that the persisting recipient B cells and plasma cells were the source of the anti-SARS-CoV-2 antibodies being sustained at a good level post-HSCT. Post-conditioning chemotherapy, the T- and B-cell immunity is depleted earlier in comparison with the antibodies may persist for longer durations. The efficacy of these antibodies in imparting a protection to SARS-CoV-2 is yet unestablished. Antibodies however are important in defense against viruses and provide lifelong surveillance and protection from future infections.[5]

We found evidence of sustained antibody production post-allogeneic HSCT in our patient even after myeloablative conditioning and post-replacement by the donor-derived hematopoietic system. The antibody response was sustained and detectable pre- and post-HSCT.

CONFLICT OF INTEREST

All the authors declare no conflict of interest.

AUTHOR CONTRIBUTIONS

AKG, MR, and AG contributed to the conception of the manuscript. All the authors contributed to the drafting of the manuscript and provided critical inputs, and approved the version of the manuscript to be published.

DATA AVAILABILITY STATEMENT

Data sharing is not applicable to this article as no new data were created or analyzed in this study.

© 2021 Wiley Periodicals LLC

TABLE 1 Timeline of the SARS-CoV-2 detection and antibody tests for the HSCT recipient and donor in relation to the HSCT

Date	SARS-CoV-2 PCR-based test of the patient	SARS-CoV-2 total antibodies index of the patient (index >1: reactive)	Timeline in relation to stem cell infusion (days from initial positive result)	SARS-CoV-2 PCR-based test of the sibling donor	SARS-CoV-2 total antibodies index of the sibling donor
25.10.2020	**Positive**	Not done	day −51 (0)	Not done	Not done
12.12.2020	Negative	**>10**	day −3 (48)	**Negative**	Not done
15.12.2020	Not done	Not done	day 0 (51)	Not done	Not done
24.12.2020	Not done	**>10**	day +9 (60)	Not done	**Not reactive**
01.01.2021	Not done	**9.6**	day +17 (67)	Not done	Not done
14.01.2021	Not done	**7.8**	day +30 (80)	Not done	Not done
26.02.2021	Not done	**4.7**	Day +73 (123)	Not done	Not done

Aditya Kumar Gupta[1]
Mohanaraj Ramachandran[1]
Aditya Gupta[2]
Jagdish Prasad Meena[1]
Tanima Dwivedi[3]
Kiran Bala[4]
Uma Kanga[5]
Urvashi Singh[4]
Ritu Gupta[3]
Rachna Seth[1]

[1]*Division of Pediatric Oncology, Department of Pediatrics, All India Institute of Medical Sciences, New Delhi, India*
[2]*Department of Pediatrics, All India Institute of Medical Sciences, New Delhi, India*
[3]*Department of Laboratory Oncology, National Cancer Institute, All India Institute of Medical Sciences, New Delhi, India*
[4]*Department of Microbiology, All India Institute of Medical Sciences, New Delhi, India*
[5]*Department of Transplant Immunology and Immunogenetics, All India Institute of Medical Sciences, New Delhi, India*

Correspondence
Aditya Kumar Gupta, Division of Pediatric Oncology, Department of Pediatrics, All India Institute of Medical Sciences, New Delhi, India.
Email: adivick@gmail.com

ORCID

Aditya Kumar Gupta https://orcid.org/0000-0002-3730-8944

REFERENCES

1. Ljungman P, Mikulska M, Styczynski J, et al. Coronavirus disease covid-19: EBMT recommendations. Version 14. https://www.ebmt.org/ebmt/documents/coronavirus-disease-covid-19-ebmt-recommendations-update-january-12-2021
2. Gupta AK, Ramachandran M, Meena JP, et al. Robust and sustained antibody response to SARS-CoV-2 in a child pre and post autologous hematopoietic stem cell transplant. *Pediatr Blood Cancer*. 2021;68(5):e28848. 10.1002/pbc.28848
3. van der Maas NG, Berghuis D, van der Burg M, Lankester AC. B cell reconstitution and influencing factors after hematopoietic stem cell transplantation in children. *Front Immunol*. 2019;10:782.
4. Sethi MK, Thol F, Stadler M, et al. VH1 family immunoglobulin repertoire sequencing after allogeneic hematopoietic stem cell transplantation. *PLoS One*. 2017;12(1):e0168096.
5. Murin CD, Wilson IA, Ward AB. Antibody responses to viral infections: a structural perspective across three different enveloped viruses. *Nat Microbiol*. 2019;4(5):734-747.

How to cite this article: Gupta AK, Ramachandran M, Gupta A, et al. Allogeneic hematopoietic stem cell transplant after COVID-19 infection and its effect on the antibody titers to SARS-CoV-2. *Pediatr Transplant*. 2022;26:e14175. https://doi.org/10.1111/petr.14175