Successful Hematopoietic Stem Cell Transplantation from a Donor Sibling Infected with SARS-CoV-2 Using Molnupiravir Prophylaxis

SARS-CoV-2 ile Enfekte Kardeş Donörden Molnupiravir Profilaksisi ile Başarılı Hematopoetik Kök Hücre Nakli

Neslihan Mandacı Şanlı[1], Gülşah Akyol[1], Zeynep Türe Yüce[2], Muzaffer Keklik[1], Ali Ünal[1]

[1]*Erciyes University Faculty of Medicine, Department of Hematology and Bone Marrow Transplant Center, Kayseri, Türkiye*
[2]*Erciyes University Faculty of Medicine, Department of Infectious Diseases and Clinical Microbiology, Kayseri, Türkiye*

To the Editor,

The coronavirus disease 2019 (COVID-19) pandemic, caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), is a global health threat with high fatality rates, especially among hematopoietic stem cell transplantation (HSCT) recipients [1]. In such an environment, there is a risk that stem cell donors may be found positive for SARS-CoV-2 by reverse-transcription polymerase chain reaction (RT-PCR). SARS-CoV-2 RNAemia may occur in approximately 15% of symptomatic patients and also in a minority of those who are asymptomatic, creating the possibility, which remains unconfirmed to date, of viral transmission through blood products, particularly in the setting of allogeneic HSCT [2].

Molnupiravir is an oral antiviral drug effective in reducing mortality and hospitalization rates in patients with COVID-19 [3]. In the literature, cases of HSCT performed with SARS-CoV-2-positive donors due to necessity have been reported for a small number of patients and none of those patients received molnupiravir prophylaxis [4,5,6,7]. To our best knowledge, our patient is the first to receive molnupiravir prophylaxis during the conditioning regimen. It may have acted by inhibiting SARS-CoV-2 replication and rapidly eliminating the virus [3].

A 42-year-old female patient with a diagnosis of acute myeloid leukemia received induction therapy (idarubicin and cytarabine) but did not respond. The patient then underwent two cycles of chemotherapy consisting of fludarabine and cytarabine. Before transplantation, her bone marrow was in complete remission morphologically. Minimal residual disease was below 1%. She was admitted for HSCT from an HLA-1-antigen-mismatched related sibling. The conditioning regimen consisted of intravenous busulfan (3.2 mg/kg/day, days -6 to -5) and fludarabine (30 mg/m^2/day, days -9 to -5). A nasopharyngeal swab from the donor before conditioning began was negative for SARS-CoV-2 by RT-PCR. Peripheral blood stem cells were mobilized with granulocyte colony-stimulating factor (G-CSF). G-CSF was administered to the donor for 4 days at home. On the 4th day of G-CSF administration, the donor's RT-PCR test was positive for SARS-CoV-2. Therefore, G-CSF administration was discontinued. CD34+ peripheral blood stem cells were collected from the donor by apheresis without continuing G-CSF administration in a negative pressure isolation room with contact isolation measures. The donor was asymptomatic and did not receive any medication for COVID-19. No side effects related to G-CSF medication were observed in the donor. There was no chance of finding another donor for the patient at this stage. It was decided to proceed with the transplant. If there was no transplant and the bone marrow remained aplastic, the patient would have been vulnerable to life-threatening infections due to immunosuppression. One day after mobilization, CD34+ peripheral blood stem cells were transfused to the patient. The HSCT procedure was carried out in a negative pressure isolation room with contact isolation measures. As prescribed by an infectious disease consultant, the patient received molnupiravir prophylaxis (800 mg every 12 h on days -1 to +3). In immunosuppressive patients, the antibody response may be insufficient after vaccination or infection due to the insufficiency of the cellular immune system. In addition, the presence of different variants can be a risk factor for re-infection [8]. Despite all these factors, measuring the antibody response of the recipient serologically could be useful in terms of contributing to the literature. However, antibody response could not be measured in our case, since it is not in routine practice in our hospital yet. Cyclosporine A, methotrexate, and anti-thymocyte globulin were used for graft-versus-host disease prophylaxis. The infection prophylaxis medicines were ciprofloxacin, voriconazole, and acyclovir. Neutrophil engraftment occurred on day 16 and platelet engraftment on day 19. The patient underwent weekly SARS-CoV-2 testing by RT-PCR after transplantation and all results were negative. Sufficient data on the transmission of SARS-CoV-2 to patients by blood products are not yet available. However, during the transplantation process, hepatitis B virus or cytomegalovirus prophylaxis is routinely applied and successful results are obtained [9,10]. It was thought that molnupiravir could prevent the development of infection in the recipient by suppressing viral replication. In our case, bone marrow examination showed

100% donor chimerism at the end of the fourth week. The patient is currently alive and healthy in the third month after transplantation.

This report illustrates that HSCT from donors with asymptomatic COVID-19 may be feasible with the administration of molnupiravir prophylaxis. This is thought to be related to the effect of molnupiravir to inhibit SARS-COV-2 replication and rapidly eliminate SARS-CoV-2 in the event of possible COVID-19 transmission. In addition, our case is important in helping clinicians prepare for such occurrences and put plans and strategies into place for possible COVID-19 in this highly vulnerable patient population.

Keywords: SARS-CoV-2, COVID-19, Hematopoietic stem cell transplantation, Molnupiravir

Anahtar Sözcükler: SARS-CoV-2, COVID-19, Hematopoetik kök hücre nakli, Molnupiravir

Ethics

Informed Consent: Obtained.

Authorship Contributions

Surgical and Medical Practices: N.M.Ş., Z.T.Y., A.Ü.; Concept: N.M.Ş., Z.T.Y., M.K., A.Ü.; Design: N.M.Ş., G.A., Z.T.Y., M.K., A.Ü.; Data Collection or Processing: N.M.Ş., Z.T.Y.; Analysis or Interpretation: N.M.Ş.; Literature Search: N.M.Ş., G.A., Z.T.Y.; Writing: N.M.Ş.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study received no financial support.

References

1. Shahzad M, Chaudhary SG, Zafar MU, Hassan MA, Hussain A, Ali F, Anwar I, Ahmed M, Ahmed N, Khurana S, Rauf MA, Anwar F, Hematti P, Callander NS, Abhyankar SH, McGuirk JP, Mushtaq MU. Impact of COVID-19 in hematopoietic stem cell transplant recipients: a systematic review and meta-analysis. Transpl Infect Dis 2022;24:e13792.
2. Chang L, Yan Y, Wang L. Coronavirus disease 2019: coronaviruses and blood safety. Transfus Med Rev 2020;34:75-80.
3. Wen W, Chen C, Tang J, Wang C, Zhou M, Cheng Y, Zhou X, Wu Q, Zhang X, Feng Z, Wang M, Mao Q. Efficacy and safety of three new oral antiviral treatment (molnupiravir, fluvoxamine and Paxlovid) for COVID-19: a meta-analysis. Ann Med 2022;54:516-523.
4. Koç A, Doğru Ö, Eker N, Tufan Taş B, Şenay RE. Hematopoietic stem cell transplantation to a patient with acute myeloid leukemia from a sibling donor positive for SARS-CoV-2 by RT-PCR test. Turk J Hematol 2022;39:144-151.
5. Anurathapan U, Apiwattanakul N, Pakakasama S, Pongphitcha P, Thitithanyanont A, Pasomsub E, Hongeng S. Hematopoietic stem cell transplantation from an infected SARS-CoV2 donor sibling. Bone Marrow Transplant 2020;55:2359-2360.
6. Lázaro Del Campo P, de Paz Arias R, Ramírez López A, de la Cruz Benito B, Humala Barbier K, Sánchez Vadillo I, López de la Guía A, de Soto Álvarez T, Jiménez Yuste V, Canales Albendea M. No transmission of SARS-CoV-2 in a patient undergoing allogeneic hematopoietic cell transplantation from a matched-related donor with unknown COVID-19. Transfus Apher Sci 2020;59:102921.
7. Leclerc M, Fourati S, Menouche D, Challine D, Maury S. Allogeneic hematopoietic stem cell transplantation from SARS-CoV-2 positive donors. Lancet Haematol 2021;8:e167-169.
8. Ong DSY, Fragkou PC, Schweitzer VA, Chemaly RF, Moschopoulos CD, Skevaki C; European Society of Clinical Microbiology and Infectious Diseases (ESCMID) Study Group for Respiratory Viruses (ESGREV). How to interpret and use COVID-19 serology and immunology tests. Clin Microbiol Infect 2021;27:981-986.
9. Türe Z, Kalın Ünüvar G, Kahveci HN, Keklik M, Ulu Kılıç A. Overlooked prophylaxis of hepatitis B in patients undergoing hematopoietic stem cell transplantation. Erciyes Med J 2021;43:31-36.
10. Li PH, Lin CH, Lin YH, Chen TC, Hsu CY, Teng CJ. Cytomegalovirus prophylaxis using low-dose valganciclovir in patients with acute leukemia undergoing allogeneic hematopoietic stem-cell transplantation. Ther Adv Hematol 2021;12:2040620721998124.

Address for Correspondence/Yazışma Adresi: Neslihan Mandacı Şanlı, M.D., Erciyes University Faculty of Medicine, Department of Hematology and Bone Marrow Transplant Center, Kayseri, Türkiye
E-mail : ortoforia@hotmail.com ORCID: orcid.org/0000-0002-6298-9884

Received/Geliş tarihi: December 16, 2022
Accepted/Kabul tarihi: May 10, 2023

DOI: 10.4274/tjh.galenos.2023.2022.0526