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Case Report

Successful Hematopoietic Stem Cell Transplant from a Two-Year-Old COVID Patient: A Case Report and Review of Literature

**Khadija Ashraf,
Fatima Sharif,
Ayesha Junaid,
Tariq Mahmood Satti**

Abstract

Hematopoietic stem-cell transplantation involves transplanting multipotent hematopoietic stem cells, typically sourced from bone marrow, peripheral blood, or umbilical cord blood in order to treat variety of medical conditions. Here, we report a case of a four-year-old boy diagnosed with Beta Thalassemia Major, who received successful allogeneic HSCT from a fully HLA-matched sibling aged two. The donor in this case tested positive for SARS-CoV-2 through PCR of a nasopharyngeal swab. Our objective is to contribute our firsthand experience to the scarce literature on HSCT from donors who have tested positive for COVID-19.

Keywords: Hematopoietic stem cell transplant, Covid-19, successful

Department of Hematology, Shifa International Hospital, Pakistan

Address for Correspondence

*Dr Khadija Ashraf
Khadijashraf@live.com*

Introduction

Hematopoietic stem cell transplant (HSCT) is the treatment of choice for a variety of hematological disorders including malignancies, hemoglobinopathies, immunodeficiency and aplastic anemia.¹ Over the last few years, the workflow of transplant centers has been significantly impacted by disease burden of Coronavirus disease - 2019 (COVID-19).² Knowledge about the effect of COVID-19 infection on stem cells is limited, however a recent study demonstrated that severe SARS-CoV-2 infection can cause dysregulation of hematopoiesis in the bone marrow, with stem cells being more prone to apoptosis.³ This raises concern about the suitability of COVID-19 positive individuals for stem cell donation.

The National Institute for Health and Care Excellence (NICE) has issued guidelines which recommend that all HSCT donors should be tested for COVID-19 by Polymerase Chain Reaction (PCR) of throat and nasal swabs at least once prior to donation, ideally on the day of donation.⁴ NICE guidelines also advised a three-month deferral period in case a stem cell donor tested SARS-CoV-2 positive. However, in conditions where HSCT was urgently required, this deferral period could be adjusted based on clinical risk assessment.⁴ Therefore, since 2020, few cases are being reported of HSCT from COVID-19 positive donors where the risk-benefit analysis did not allow deferral of transplant.⁵

We present the case of a four year old boy, diagnosed case of Beta Thalassemia Major, who underwent allogeneic HSCT from a fully HLA-matched two year old sibling. The donor of HSCT in this case tested positive for SARS-CoV-2 by PCR of nasopharyngeal swab. We aim to add our experience to the limited reports available in the literature regarding HSCT from COVID positive donors. Amalgamation of such data could contribute to development of revised guidelines for evidence based management of similar cases in the future.

Case Report

The donor for bone marrow harvest was a two year old boy, the youngest brother of our transplant recipient diagnosed with Beta Thalassemia Major. Donor and recipient were fully HLA matched and their blood groups were compatible (both B+). The donor was a known case of Beta Thalassemia Minor. Baseline laboratory investigations were unremarkable and he was in good health. However, he tested positive for SARS-CoV-2 by PCR of nasopharyngeal specimen, 72 hours prior to the harvest procedure.

An infectious disease specialist was consulted. As the donor had no signs and symptoms of COVID-19 such as fever, cough, shortness of breath or evidence of pulmonary disease on chest Xray, he was labelled a low risk case of asymptomatic COVID. Bone marrow harvest was performed in the operating room with appropriate precautions to prevent transmission of COVID-19. The procedure lasted 30 minutes, during which 160 ml of

bone marrow harvest was extracted. Post procedure he remained well and was discharged the next day in stable condition.

The recipient was 4 year old boy diagnosed with Thalassemia Major at the age of 4 months. PCR for thalassemia gene tested positive for Fr8-9/Cd5 mutation. He had been kept on hypertransfusion protocol with hemoglobin levels to be maintained at around 10g/dl. He had received continuous iron chelation (deferasirox 400mg) along with folic acid supplementation. Pre-transplant he received conditioning regimen with Busulfan-Cyclophosphamide and Antithymocyte Globulin was started. Bone marrow transplant was done with infusion of 15 million stem cells on the same day of harvest collection. Post-transplant he received Cyclosporin, antibiotic cover with cefixime and was given methotrexate on days 3 and 4 after transplant. Neutrophil and platelet engraftment occurred on Day 13 and Day 18 post-transplant, respectively.

Figure 1 shows the platelet count and absolute neutrophil counts in this patient. He has been followed up till six months post-transplant and remains well.

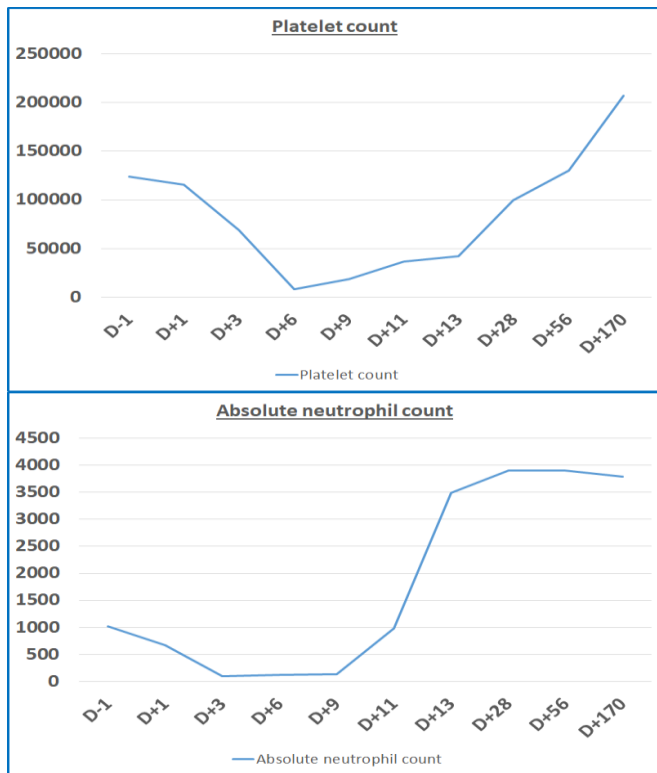


Figure 1. Platelet count and absolute neutrophil count of transplant recipient starting from pre-transplant (Day -1) to post transplant up till Day 170.

Discussion

As per NICE guidelines on HSCT, in order to reduce the risk of COVID-19 transmission and resulting complications, strict precautionary measures should be followed by donors of stem cell transplant for at least 4 weeks prior to harvest procedure.⁴ Our patient is among the very few reported cases of HSCT from a SARS-CoV-2 positive donor.

00A similar case reported by Anurapathan et al was published in 2020. Successful bone marrow transplant was done in a 7 year old female, known case of Beta Thalassemia Hemoglobin E, from a COVID positive donor sibling. Recipient was placed in isolation unit post-transplant. Recipient tested negative for COVID-19 infection and achieved engraftment on day 12 and 100% chimerism at day 20 post-transplant.⁶ Our patient had also achieved neutrophil engraftment by Day 13 post transplant. However, the authors of this study concluded that the risks of COVID-19 transmission by bone marrow harvest are still unknown so the best strategy would be to optimize donor care and prevent SARS-CoV-2 infection in donors prior to harvest procedure.

According to another report, successful stem cell transplant was carried out in a diagnosed case of mantle cell lymphoma by HLA matched sibling with history of travel. The donor tested positive for SARS-CoV-2 on day 3 post-harvest. PCR was carried out every 48 hours in the recipient to check for SARS-CoV-2 transmission, however it remained negative. Engraftment took place on day 18 and full chimerism was achieved.⁷

Ahmet koc et al similarly reported a successful case of HSCT from COVID positive donor in a patient diagnosed with Acute Myeloid Leukemia. Transplant was delayed for one day after donor tested positive for SARS-CoV-2 but considering the circumstances, harvest and infusion of stem cells was carried out a day later. Recipient was tested for SARS-CoV-2 weekly with no development of any signs or symptoms. Later engraftment took place at day 14 followed by chimerism of 100% by 4th week.⁸

The most recent case of HSCT from COVID positive donor was reported in July 2022 and this is the first case in which the recipient was also already COVID positive prior to harvest infusion.⁹ The recipient was a 63 year old female with high risk Myelodysplastic Syndrome. Both donor and recipient had the Omicron variant of SARS-

CoV-2. Neutrophil engraftment was achieved on Day +21 and full chimerism on Day +30 post-transplant. In this case the authors also assessed T-cell response to SARS-CoV-2 by interferon- γ release fluorescence immunoassay and they suggested that potential role of humoral and cell-mediated immunity transferred from the donor to the recipient should not be underestimated.

Conclusion

In conclusion, HSCT was successfully carried out from an asymptomatic SARS-CoV-2 positive donor in a young patient with Beta Thalassemia Major. We did not find any evidence of SARS-CoV-2 transmission via bone marrow harvest, similar to previous reports. However, current EBMT and NICE guidelines still do not recommend HSCT from COVID positive donors. Due to limited data available and unpredictable nature of COVID-19 and its variants, we recommend that donors should be counselled to take full precautions to prevent COVID-19 infection at least two weeks prior to stem cell harvest. More evidence in the form of large, multicenter studies is needed before any change can be made to the existing guidelines.

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