




Hematopoietic stem cell transplantation from an infected SARS-CoV2 donor sibling

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Received: 10 May 2020 / Revised: 20 May 2020 / Accepted: 3 June 2020 / Published online: 11 June 2020
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To the Editor:

COVID-19 pandemic is a global health threat with high fatality rate especially in the elderly and the immunocompromised. Current knowledge about its prevalence, spreading capability, and clinical patterns is still limited, resulting in difficulty in surveillance and management strategy [1, 2]. Patients undergoing hematopoietic stem cell transplantation (HSCT) are a group of patients with special immunocompromised situation and could have potentially devastating outcome if get sick with COVID-19. Since there are 90,000 HSCT carried out annually worldwide, it is possible that this might be the case [3].

We report a case of 7-year-old female diagnosed with beta-thalassemia hemoglobin E who receives regular transfusion with filtered packed red blood cell since 1 year of age. She was admitted for HLA-matched sibling HSCT on April 7, 2020. Conditioning regimen consisted of iv. busulfan 130 mg/m²/day × 4 days (day −9 to day −6) and iv. cyclophosphamide 50 mg/kg/day (day −5 to day −2) [4] was given and transplantation day (D0) was planned to be on April 17, 2020. The patient and her mother who stayed with her wore appropriate personal protective equipment during their stay in pre-transplantation period. They did not experience any fever or respiratory symptoms.

The donor, her younger brother, was admitted one day before planned D0 and had nasopharyngeal swabbed for

SARS-CoV2. This pre-operative swab is done routinely in every patient planned for anesthesia according to the hospital policy. Swab result was positive for SARS-CoV2 and was confirmed by another test done 7 h later. Despite the swab result he was doing well without fever or any other symptoms. We decided to go on with transplantation since the patient would have a slim chance of survival if she does not receive donor stem cells. Surveillance swab for the family were done and positive results were also found in the patient's aunt and mother who closely took care of the patient.

Bone marrow harvest was carried out under general anesthesia in the operating room using airborne infection isolation routine. Pre-operative medication consisted of one dose of favipiravir, hydroxychloroquine, and darunavir/ritonavir. All involved medical staffs wore enhanced personal protection equipment. Bone marrow with stem cells at a dose of 4.94×10^6 CD34+ cells/kg was harvested, processed and given to the patient on the same day. This harvested marrow was tested negative for SARS-CoV2 by RT-PCR.

The patient stayed in airborne infection isolation unit after transplantation. Her GVHD prophylaxis consisted of iv cyclosporine at a dose of 3 mg/kg/day starting on day-3 together with short course methotrexate 5 mg/m² on day +1, +3, +6, and +11 [4]. The infection prophylaxis medicines were penicillin, ciprofloxacin, and micafungin. Her transplantation was uneventful. Neutrophil engraftment occurred on day +13. The peripheral blood nucleated cell chimerism showed 100% of donor cells on day +20. We subsequently tested RT-PCR SARS-CoV2 in nasopharyngeal swab and blood together with serology tests in the blood from patient, donor, mother, and aunt as shown in Table 1. She was transferred back to the BMT unit after 14 days of negative results from all tests. Since all of three COVID-19 patients did not have seroconversion, it is possible that all patients were asymptomatic and might have low viral load, which would not elicit antibody response. Infected patients without seroconversion have been reported [5].

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Table 1 The results of RT-PCR of nasopharyngeal swabs and antibody to SARS-CoV2 from patient, donor, mother and aunt.

Day of transplant	4/16 -1	4/17 ^a 0	4/18 1	4/19 2	4/20 3	4/21 4	4/22 5	4/24 7	4/27 10	5/1 14
Donor RT-PCR IgM IgG	pos	0.00 0.05			neg					0.00 0.02
Recipient RT-PCR IgM IgG	neg		neg 0.47 0.07	neg	neg	neg	neg	neg	neg	neg 0.26 0.04
Mother RT-PCR IgM IgG	pos		neg		neg					0.53 0.06
Aunt RT-PCR IgM IgG	pos		neg		neg					0.05 0.06

IgM and IgG were performed by MAGLUMI™ 2019-nCoV IgM (CLIA) and MAGLUMI™ 2019-nCoV IgG (CLIA), respectively. Cut-off value of positivity is 0.69 AU/mL for both IgG and IgM.

neg negative, *pos* positive.

^aDay of stem cell infusion (day 0).

Current EBMT recommendations do not recommend stem cell donation when donor is COVID-19 positive [6]. This report illustrates that transplantation from COVID-19 donors is feasible and viral transmission through stem cell transplantation did not happen since the stem cells product is RT-PCR negative for SARS-CoV2. However, donor care in the COVID-19 era should be revisited. Necessary measures are needed to ensure that the donor is healthy and free of any disease, including COVID-19, at the time of transplantation. This would ensure the safety of medical personnel who closely take care of donors. In addition, whether harvested marrow could transmit SARS-CoV2 is still unknown. A report from Singapore demonstrated that the virus could be found in blood about 8% of infected patients [7]. This possibly poses risk of transmission of the virus via the graft from a donor to a recipient.

Acknowledgements We would like to thank the Ramathibodi Foundation.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

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