Bone Marrow Transplantation (2020) 55:2193–2195
https://doi.org/10.1038/s41409-020-0913-6

CORRESPONDENCE

COVID-19 pandemic and impact on hematopoietic stem cell transplantation

Kamal Kant Sahu[1] · Ahmad Daniyal Siddiqui[1] · Jan Cerny[2]

Received: 27 March 2020 / Revised: 8 April 2020 / Accepted: 15 April 2020 / Published online: 4 May 2020

To the Editor:

Currently, the world is witnessing a health crisis in the form of COVID-19 pandemic [1]. For oncologists, especially for stem cell transplant specialists, the stress is high to perform to their best of capability for their cancer patients. In general, the hematopoietic stem cell transplantation (HSCT) is a high-risk procedure. The novelty of the COVID-19 disease, lack of literature, absence of antiviral agent, and vaccine has added more uncertainty while preparing for and recovering from HSCT.

Accomplishing an HSCT is the result of a collaborative effort including the transplant team working closely with the referring physicians, and for the case of unrelated allogeneic transplants, there needs to be a good communication and co-ordination between the transplant center and donor center teams. In addition to this, the well-being of transplant recipients and donors is mandatory for the procedure. In the current situation, with the COVID-19 pandemic unraveling around the globe, the transplant specialists ought to anticipate a complex path ahead with unexpected challenges. Accomplishing HSCT becomes more complex in cases of matched unrelated donor transplantation due to the additional logistic issues of transportation of the harvested stem cells.

In transplant programs across the globe, physicians are trying to prevent COVID-19 infection in transplant recipients and their respective donors so that HSCT could be conducted smoothly and risk-free. Both EBMT and ASTCT's special subgroups, transplant infectious disease-special interest group, have issued interim guidelines for recipients, and donors of HSCT (https://mdedge.com/hematology-oncology/article/219068/transplant/covid-19-astct-issues-interim-guidelines?channel=63993, https://ebmt.org/sites/default/files/2020-03/EBMT%20COVID19%20guidelines%20v.4.3%20%282020-03-23%29.pdf). EBMT has recently updated their recommendations (version 4.3 dated 23 March, 2020) and we have summarized the same as below.

(A) Recommendations for Transplant candidate patient (HSCT and cellular therapy recipients)

(Adapted from EBMT, version 4.3 dated 23 March, 2020)

- All recipients should have COVID-19 RT-PCR tested negative before starting conditioning regimen irrespective of respiratory symptoms.
- All recipients who are supposed to be admitted for HSCT/cellular therapy are advised for home isolation for 14 days before starting the transplant conditioning. Also, to avoid the non-necessary clinic visits to reduce the risk to a minimum. This is now very well helped by the sudden emergence and ability to use telemedicine visits in place of in-person visits, especially in the United States.
- If a recipient has a close contact with COVID-19 confirmed case:

  All transplant-related procedures (PBSC mobilization, BM harvesting, and conditioning) should not be performed within at least 14 days and preferably 21 days from the last date of contact

  AND

  The recipient should be closely monitored for COVID-19 symptoms

  AND

  COVID-19 RT-PCR negativity is confirmed before any transplant procedure is undertaken.
- If a recipient gets a COVID-19 disease, European Centre for Disease Prevention and Control recommends

✉ Kamal Kant Sahu
drkksahu85@gmail.com

[1] Division of Hematology and Oncology, Department of Medicine, Saint Vincent Hospital, Worcester, Massachusetts, United States

[2] Division of Hematology and Oncology, Department of Medicine, UMass Memorial Health Care, University of Massachusetts Medical School, Worcester, Massachusetts, United States

deferral based on the risk of dying due to cancer in the absence of HSCT/cellular therapy.

High-risk cancer disease: Deferral until the recipient COVID-19 patient is asymptomatic and has two repeated virus PCR negativity at least 1 week apart (deferral of 14 days minimum).

Low-risk cancer disease: Deferral for 3 months.

(B) Recommendations for donor

(World Marrow Donor Association (WMDA) issued the recommendations and the EBMT has endorsed these guidelines version 4.3 dated 23 March, 2020)

- If a donor gets a COVID-19 disease, he/she must be excluded from from stem cell donation. As of now, there are no recommendations as when COVID-19 positive donor can be cleared for donation but at least 3 months deferral can be considered unless the need for donation is urgent when individual consideration should be made.
- If a donor gets a close contact with a COVID-19 confirmed case, the decision depends on the urgency of transplant: [A] In the case of nonurgent transplant: Stem cell harvest shall be deferred for at least 28 days AND donor should be watched closely for any symptoms. [B] Urgent need of transplant: If the donor is completely well, AND a COVID-19 test is negative AND there are no suitable alternative donors, an earlier collection may be considered subject to careful risk assessment if local quarantine requirements permit.
- If a donor has traveled to high-risk areas for COVID-19 (as defined by health authorities) or came to close contact with an individual traveling from such an area, the donor should be excluded from donation for at least 28 days.
- A donor is expected to follow all the health hygiene and precautions such as avoiding crowded places and large group gatherings (as per WHO recommendations) within 28 days before the donation date.

(C) Recommendations for post HSCT and post CAR-T cell recipients

(Adapted from EBMT, Version 4.3 dated 23 March, 2020)

- To follow all the necessary precautions such as hand washing and social distancing in order to restrict the exposure to infected individuals.
- To refrain from unnecessary travel and in case required, to travel by private car rather than using public transportation.
- To test for COVID-19 with diagnostic procedures as per national guidelines. Recipients belonging to high-risk transmission area of SARS-CoV-2 virus infection or having a close contact to a person to such areas should be tested. COVID-19 testing can be repeated if there is strong clinical suspicion for COVID-19 due to the chance of false-negative results. Multiplex PCR is recommended that allows testing for non-SARS-CoV-2 viral infections as well.
- If detected positive for COVID-19, the recipient should be evaluated with imaging study preferably CT chest and for the need of oxygen requirement.
- Bronchoalveolar lavage (BAL) is not routinely recommended due to the risk of airborne transmission to health care workers. Only if other coinfections are suspected and in cases with mechanical ventilation, bronchoscopy should be performed and BAL samples should be tested for COVID-19 and other co-pathogens.

Guidelines are generated based on evidences, but unfortunately till now there is a lack of enough clinical experience on COVID-19 in HSCT setting to pave formal guidelines. The currently available recommendations issued from the transplant societies of the United States (ASTCT) and Europe (EBMT) are interim and additional guidance is expected to be following in the next few weeks.

Recognizing the paramount importance of data gathering, international donor registries like WMDA, and Center for International Blood and Marrow Transplant Research (CIBMTR) have made necessary changes in their data collection forms in order to capture all the details of the impact of the COVID-19 pandemic on the transplant and cellular therapy recipients (https://share.wmda.info/display/DMSR/Coronavirus+-+COVID-19#/, https://cibmtr.org/ReferenceCenter/Covid19/Pages/default.aspx#comm). CIBMTR has modified Transplant Essential Data track and Comprehensive Report Form track reporting to include a new organism option COVID-19 (SARS-CoV-2) that will entail more detailed data collection (https://cibmtr.org/DataManagement/Communications/TrainingNewsletters/Documents/Collecting_Data_on_the_Impact_of_the_COVID_19_on_our_Recipients_015.pdf).

Dr Ljungman (EBMT) recently shared their data from Europe on post HSCT COVID-19 cases. As of March 20, 2020, 15 cases of COVID-19 cases in post-HSCT setting (15 allogenic and 3 autologous) have been reported from Europe. Most cases were reported from Spain (five patients) followed by Italy (three patients). The median age of the patients was 59 years, ten patients presented with upper respiratory symptoms and remaining with lower respiratory tract systems. Out of these, one patient has already succumbed to COVID-19 illness (https://ebmt.org/covid-19-and-bmt).

Despite practicing all the correct steps and following recommendations, last-minute hurdles can overturn all the strategies for which a transplant team should be ready to

tackle the unpredicted situations. Few of them could be (1) donor getting infected between clearance for donation and the actual date of the cell apheresis, or (2) harvest center staff falling sick to COVID-19 disease on the day of harvest, or (3) difficulties to transport harvested stem cells across the border due to travel restrictions. Similarly, the ASTCT has endorsed the "Practical Guidance for the BMT Centers" suggested by the Adult BMT Service team at Memorial Sloan Kettering Cancer Center [MSKCC, v1.0 March 25, 2020] (https://astct.org/viewdocument/guidance-for-bmt-centerfunctioning?CommunityKey=d3949d84-3440-45f4-814290ea05adb0e5&tab=librarydocuments). The MSKCC BMT guide also recommends cryopreservation of all related and unrelated donor products just like WMDA and EBMT. They also recommended considering peripheral stem cell collection over marrow collection, to prefer domestic donors/cord blood banks over international ones, and to have a backup donor preferably for allogeneic HSCT in case required. Therefore, the use of alternative donors such as haploidentical or cord blood transplants may increase somewhat due to urgent situations when a patient's primary diagnosis would not allow deferring transplant for later.

Blood banks play a vital role to ensure the efficient functioning of any transplant center. However, the current COVID-19 pandemic has decreased the nationwide volunteer blood donations. Blood product shortage needs to be anticipated before and an effective communication with the other local blood banks as a source of blood products should be in place [2]. These blood shortages are probably the result of nonpharmacological interventions such as home sheltering, social distancing, home quarantine, etc. which are being promoted in order to suppress the community transmission of SARS-CoV-2 spread [3]. Unfortunately, this has led to an unprecedented cancellation of blood donation drives. This adds an additional responsibility on the transplant team to keep coordinating with the blood bank colleagues to ensure blood products are available 24×7. Pagano et al. in their report discussed the measures taken to defend blood shortage at the University of Washington, Seattle. Based on their observation, steps such as canceling the elective surgeries and procedures, requesting one unit of red blood cells at a time, rechecking on the indications of blood product order requests, and calling for more blood donation drives could help the blood centers and hospitals to tide over the COVID-19 crisis (https://fda.gov/news-events/press-announcements/coronavirus-covid-19-update-blood-donations) [4]. To spare the scarce resources (regular and ICU beds, personnel, blood products, etc.) that are expected to be in high demand during the COVID-19 surge, transplant centers have been postponing stem cell transplants whenever clinically possible [5].

In conclusion, given the limited experience with the SARS-CoV-2 virus, we anticipate more modifications in the interim recommendations. As COVID-19 is an evolving disease, for decision-making, paying attention to reports from local health authorities, reviewing the latest data, and following interim guidelines is essential to ensure uniformity in the approach to transplant patients.

Author contributions All authors have seen the manuscript and agree to the content and data. All the authors played a significant role in the paper.

Compliance with ethical standards

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

Ethics statement The article does not contain the participation of any human being and animal.

Publisher's note Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

References

1. Sahu KK, Mishra AK, Lal A. Novel coronavirus (2019-nCoV): update on 3rd coronavirus outbreak of 21st century. QJM. 2020.Mar 3. pii: hcaa081.
2. Ueda M, Martins R, Hendrie PC, McDonnell T, Crews JR, Wong TL, et al. Managing cancer care during the COVID-19 pandemic: agility and collaboration toward a common goal. J Natl Compr Cancer Netw. 2020;20:1–4.
3. Sahu KK, Lal A, Mishra AK. Latest updates on COVID-2019: a changing paradigm shift. J Med Virol. 2020. Mar 20.
4. Pagano MB, Hess JR, Tsang HC, Staley E, Gernsheimer T, Sen N, et al. Prepare to adapt: blood supply and transfusion support during the first 2 weeks of the 2019 Novel Coronavirus (COVID-19) pandemic affecting Washington State. Transfusion. 2020 Mar 21.
5. Sahu KK, Jindal V, Siddiqui AD. Managing COVID-19 in Patients With Cancer: A Double Blow for Oncologists. JCO Oncol Pract. 2020 Apr 17:OP2000167.