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Personalized at-home autologous hematopoietic stem cell transplantation during the SARS-CoV-2 outbreak

Severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) reached Spain presumably in February 2020. On March 13th, the Spanish government ordered a national lockdown to control the spread of the virus and prevent the healthcare system from collapsing. At the end of May 2020, 239 429 cases had been reported nationwide and 27 127 people had died. This health crisis forced institutions to place a hold on most non-priority healthcare activities, and reallocate hospital and human resources to address the overflow of patients with SARS-CoV-2. At Hospital Clinic of Barcelona, a 750-bed public university hospital [1], 70 % of its facilities were designated for the treatment and management of patients with coronavirus disease 2019 (COVID-19). The unusual scenario presented, as well as the fragile state of our immunocompromised patients due to hematological diseases and administered treatments [2] obligated us to cease and delay cancer treatments and procedures.

Our hospital transplant unit includes eight beds, with a median (range) of 11 (7–15) patients admitted daily. It forms part of the total 32 beds assigned to hematological patients. Since November 2000, 419 at-home autologous stem cell transplants (ASCT) have been performed, with a median of 32 ASCT per year within the last ten years. These transplants include patients with multiple myeloma (MM) and lymphoma. The program experience and its improvements have been published elsewhere [3–7], showing its feasibility and safety, as well as reproducibility in other hematological centers.

As such, when the national lockdown took place in Spain, at-home ASCT continued. However, new policies and adjustments were introduced to personalize the procedure in such a state of affairs. Herein we describe our experience and optimization strategies undertaken in our "home transplant unit" to uphold patient safety during the procedure. Although SARS-CoV-2 continues to pose a burden on many health systems worldwide, our model may provide insight on how to improve transplant units without compromising patient care.

1. Procedure optimization and outcomes

During Spain's lockdown from March 13th to May 25th, 2020, the basic reproduction number or R0 of COVID-19 was 2.2 (1.4–3.9). In this period, we performed 14 hematopoietic stem cell transplants (HSCT) (six allogeneic and eight autologous), like in the previous year when compared (Fig. 1). None of the patients who received a transplant were infected with COVID-19. Of the eight ASCT, seven were performed at home (six in MM and one in Hodgkin lymphoma), while one patient with systemic AL amyloidosis was excluded from the homecare program. The eligibility criteria for the at-home transplantation program included ECOG performance status $\leq$2; travel time from home to the hospital $<$30 minutes and permanent caregiver availability. All patients signed an informed consent form before the beginning of the transplant. Even though most hospital beds were occupied by patients with COVID-19, including 14 (44 %) beds usually assigned to hematological patients, we were able to keep a hematology floor with 18 beds for those patients who were either already undergoing conditioning regimens for ASCT and allo-HSCT or were diagnosed with de novo acute leukemia. Additionally, a nasopharyngeal swab (NPS) for RT-PCR detection of SARS-CoV-2 was performed on all patients 24 h prior to admission. Patients with MM were conditioned with high-dose melphalan (200 mg/m^2) and patients with Hodgkin Lymphoma, with carmustine, etoposide, cytarabine, and melphalan (BEAM) at standard doses, followed by a peripheral blood stem cell infusion in the hospital. All of them were discharged home on day +1.

Similarly, extensive and rigorous health education was provided to both patient and caregiver before admission to the at-home ASCT program.

In cases in which patients had only one caregiver, a mandatory NPS was required before the patient could be discharged to a residence. Caregivers were advised to quarantine after negative NPS results and during the entirety of the procedure. To avoid caregiver exposure, logistical support was integrated by either a patient's relatives or volunteers offered by our unit.

Patients with more than one co-inhabitant were advised to be confined alone in one bedroom and adopt protective, necessary measures (a FFP2 face mask without exhalation valve, hand hygiene, and protective reverse isolation) when sharing common household areas.

Hematology nurses followed patients on a daily basis, either at home or by phone. They verified patient's vital signs, oral intake, central venous catheter status and the presence of extramedullary toxicities; they further managed intravenous medications and collected blood samples [8]. In this scenario, protection measures were established, including the use of personal protective equipment (PPE) during patient visits. Nurses in the at-home unit were available from 8:00 AM to 10:00 PM, in two shifts, 7 days a week. A median of 150 min/day $\times$ 7 days/week were required for patient care, including medication preparation, travel time and visit to the patient. Platelet transfusion was administered at home.

Due to the high risk of possible infection, patients were not allowed to leave their residence, except in cases when medical attention was necessary.

Only one patient with MM required a hospital visit for medical evaluation, as fever appeared on day +5 in association with a catheter-related bloodstream infection by *Pseudomonas aeruginosa*. The catheter was therefore removed and replaced with a new one. Piperacillin and tazobactam 4.5 g/6 h IV were started, rapidly controlling the fever and preventing readmission of the patient to the hospital. None of the patients developed oral mucositis WHO grade $\geq$ 2. Two of the seven patients developed gastrointestinal WHO grade 2 toxicity, but none required electrolyte or IV fluid. Also,

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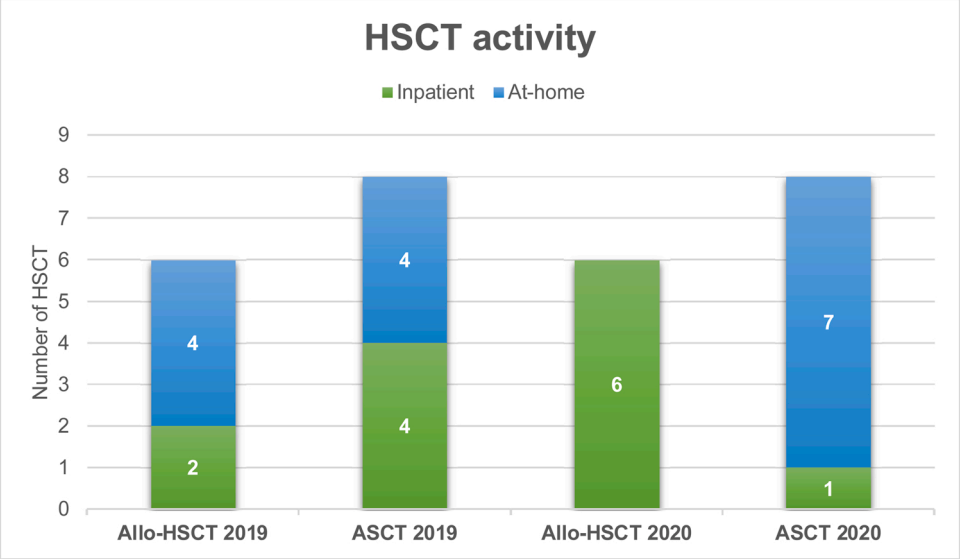

Fig. 1. HSCT activity. March 13th to May 25th (2019 and 2020).
Abbreviations: Allo-HSCT: allogeneic hematopoietic stem cell transplant; ASCT: autologous hematopoietic stem cell transplantation.

none of the patients developed grade 3 or 4 adverse events according to the Common Terminology Criteria for Adverse Events (CTCAE), Version 5.0, November 2017.

Our cohort comprised three males and four females, with a median age of 57 (range 36–66) years at the time of transplant. Four (57 %) patients presented with an HCT-CI score ≥ 3. Median number of days to platelet engraftment (PLT) $> 20 \times 10^9$/L was 12 days (range 11–13). Two patients preserved PLT above 20×10^9/L during the whole procedure. No other complications related to at-home ASCT or COVID-19 were present. The median (range) length of the procedure was 15 (14–17) days. Lack of a caregiver did not pose as an issue, as the lockdown was in effect.

During the 30-day follow-up period of an at-home ASCT, a patient with Hodgkin lymphoma required hospital readmission on day +18 due to septic shock by *Serratia marcescens*-producing AmpC enzymes encoded by resident chromosomal genes (cAmpCs). The patient required vasopressors and broad-spectrum antibiotics but was able to fully recover and return home ten days after admission.

Finally, none of the patients presented with disease progression or relapse during the follow-up period. One patient with MM did undergo a second at-home ASCT due to a high-risk cytogenetic disease, while four patients began maintenance therapy.

2. Present and future challenges

This study addresses the different challenges in performing at-home ASCT during Spain's lockdown due to the first outbreak of SARS-CoV-2, while highlighting improvements in such procedures. Our main goal focused on the safety of the patient, as well as caregivers and healthcare workers involved with the ASCT.

In March 2020, the European Society for Blood and Marrow Transplantation (EBMT) and the American Society of Transplantation and Cellular Therapy (ASTCT) published early recommendations and statements [9,10]. These guidelines included specific recommendations for cellular therapy candidates and donors, as well as changes in logistical elements before and during HSCT procedure. Examples of the latter comprised at-home isolation for 14 days prior to beginning the transplant process and SARS-CoV-2 detection by NPS before conditioning. Further, the recommendation to delay HSCT procedure was made if feasible in some cases when the prevalence of SARS-CoV-2 was high [9,10].

Evidently, the increase of patients with SARS-CoV-2 in its varying disease severity has imposed a significant burden on already saturated hospitals, including a shortage of hospital beds and staff for scheduled procedures. Changes and delays in oncological treatments have consequently occurred. For example, when assessing the impact of the SARS-CoV-2 pandemic on treatments in oncological patients, Albiges et al. [11] reported a median length of adjournment of 20 (interquartile range (IQR): 12–30) and 28 (IQR: 22–44) days for systemic therapy and surgery or ablative techniques, respectively. For most cancers, data suggests that treatment postponement is associated with worst overall survival [12], even though no specific data is present concerning hematological patients or cellular therapy recipients. We believe, as some other publications already confirm, that patients with hematological malignancies receiving HSCT or cellular therapy cannot experience a delay in therapy [13]. Our main goal was to avoid patient and caregiver exposure, by reducing hospital visits. Our at-home transplant program was already stablished to reduce patient exposure by decreasing visits to the hospital; also we have a specific support unit where patients are rapidly evaluated by a hematologist in case of an adverse event, allowing us a rapid intervention that prevents patient readmission and further medical complications.

We acknowledge that many medical, logistical and social elements must be taken into account before an HSCT can be performed, especially in a state of pandemic. However, we also believe that the ability to perform at-home ASCT guarantees that treatment times are respected to some extent, while upholding patient safety.

This study has some limitations, including that it was carried out in a single center with a low number of patients. We were aware of the existing risk of developing bacteremia or sepsis during the procedure in a period where Intensive Care Unit (ICU) beds were highly restricted, nevertheless in our experience of 434 patients managed at-home, only three (0.7 %) patients required ICU admission. As published before [5,6], our febrile neutropenia rate and readmission rate among MM patients was 24 % and 2 % respectively, and even though 41 % of lymphoma patients presented neutropenic fever during follow up, the readmission rate was only 1 %. The observed therapy related mortality in patients with MM and lymphoma is 0.9 % and 2 %, respectively [5,6]. We recognize that our ability to continue with at-home ASCT was in part due to our vast, 20-year experience of

performing such a procedure.

Currently, as we face continous SARS-CoV-2 waves across Europe, with growing numbers of hospitalized patients once again, our main challenge will be to maintain scheduled hematological treatments and procedures and ensuring patient care. That stated, the at-home ASCT could serve as a safe and reproducible option to perform.

Author contributions

A.M–R., L.G.R.L., and F.F-A., designed the study, collected and analyzed data, wrote and reviewed the paper. N.B.D. and C.G.M. treated patients and reviewed the paper. All the authors approved the final version of the manuscript.

Declaration of Competing Interest

The authors report no declarations of interest.

References

[1] J.M. Pericàs, D. Cucchiari, O. Torrallardona-Murphy, J. Calvo, J. Serralabós, Alvés, et al., Hospital at home for the management of COVID-19: preliminary experience with 63 patients, Infection (2020), 0123456789, https://doi.org/10.1007/s15010-020-01527-z.
[2] G.L. Shah, S. DeWolf, Y.J. Lee, R. Tamari, P.B. Dahi, J.A. Lavery, et al., Favorable outcomes of COVID-19 in recipients of hematopoietic cell transplantation, J. Clin. Invest. (2020) 0–47, https://doi.org/10.1172/JCI141777.
[3] F. Fernández-Avilés, E. Carreras, A. Urbano-Ispizua, M. Rovira, C. Martínez, A. Gaya, et al., Case-control comparison of at-home to total hospital care for autologous stem-cell transplantation for hematologic malignancies, J. Clin. Oncol. 24 (30) (2006) 4855–4861, https://doi.org/10.1200/JCO.2006.06.4238.
[4] G. Gutiérrez-García, M. Rovira, N. Arab, C. Gallego, J. Sánchez, M. Ángeles Álvarez, P. Ayora, et al., A reproducible and safe at-home allogeneic haematopoietic cell transplant program: first experience in Central and Southern Europe, Bone Marrow Transplant. 55 (5) (2020) 965–973, https://doi.org/10.1038/s41409-019-0768-x.
[5] L.G. Rodríguez-Lobato, A. Martínez-Roca, D.F. Moreno, G. Gutiérrez-García, M. Suárez-Lledó, et al., Impact of intensifying primary antibiotic prophylaxis in at-home autologous stem cell transplantation program for lymphoma patients, Leuk. Lymphoma 61 (7) (2020) 1565–1574, https://doi.org/10.1080/10428194.2020.1742901.
[6] L.G. Rodríguez-Lobato, A. Martínez-Roca, S. Castaño-Díez, A. Palomino-Mosquera, G. Gutiérrez-García, A. Pedraza, et al., The avoidance of G-CSF and the addition of prophylactic corticosteroids after autologous stem cell transplantation for multiple myeloma patients appeal for the at-home setting to reduce readmission for neutropenic fever, PLoS One 15 (11) (2020), e0241778, https://doi.org/10.1371/journal.pone.0241778.
[7] F. Fernandez-Avilés, G. Gutiérrez-García, At-home HSCT, in: E. Carreras, C. Dufour, M. Mohty, N. Kröger (Eds.), The EBMT Handbook: Hematopoietic Stem Cell Transplantation and Cellular Therapies [Internet], 7th ed., Springer, Cham (CH), 2019. Chapter 63. PMID: 32091789.
[8] N. Martínez-Cibrian, L. Magnano, G. Gutiérrez-García, X. Andrade, J.G. Correa, M. Suárez-Lledó, et al., At-home autologous stem cell transplantation in multiple myeloma with and without G-CSF administration: a comparative study, Bone Marrow Transplant. 51 (4) (2016) 593–595, https://doi.org/10.1038/bmt.2015.287.
[9] European Society for Blood and Marrow Transplantation (EBMT), Coronavirus Disease COVID-19: EBMT Recommendations, 2020. Update March. 2020;16. Available at: https://www.ebmt.org/sites/default/files/2020-03/EBMT%20COVID19%20guidelines%20v.3.2%20%282020-03-16%29.pdf.
[10] American Society of Transplantation and Cellular Therapy, Interim guidelines for COVID-19 management in hematopoietic cell transplant and cellular therapy patients, 2020. Version 1.2. Available at: https://higherlogicdownload.s3.amazonaws.com/ASBMT/a1e2ac9a-36d24e23945c45118b667268/UploadedImages/COVID19_Interim_Patient_Guidelines_3_18_20.pdf.
[11] L. Albiges, S. Foulon, A. Bayle, B. Gachot, F. Pommeret, C. Willekens, et al., Determinants of the outcomes of patients with cancer infected with SARS-CoV-2: results from the Gustave Roussy cohort, Nature Cancer 1 (October) (2020), https://doi.org/10.1038/s43018-020-00120-5.
[12] H.E. Hartman, Y. Sun, T.P. Devasia, E.C. Chase, N.K. Jairath, R.T. Dess, et al., Integrated survival estimates for cancer treatment delay among adults with cancer during the COVID-19 pandemic, JAMA Oncol. 48109 (2020) 1–9, https://doi.org/10.1001/jamaoncol.2020.5403.
[13] Z. Mahmoudjafari, M. Alexander, J. Roddy, et al., American society for transplantation and cellular therapy pharmacy special interest group position statement on pharmacy practice management and clinical management for COVID-19 in hematopoietic cell transplantation and cellular therapy patients in the United States, Biol. Blood Marrow Transplant. 26 (6) (2020) 1043–1049, https://doi.org/10.1016/j.bbmt.2020.04.005.

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