blood advances

Bridging the gap using telemedicine: optimizing an existing autologous hematopoietic SCT unit into an allogeneic hematopoietic SCT unit in Paraguay with the help of the WBMT

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Background

Paraguay used to be one of the countries in Latin America that was not consistently performing allogeneic stem cell transplantations (allo-SCTs). An SCT program was started in 1995, and 114 SCTs were performed during the next 22 years. Only 18 of them were allogeneic, and the results were dismal. As a consequence, only a few (n = 3) allo-SCTs were performed in the last 10 years. Patients had to go outside the country for treatment or not receive the only curative treatment for their disease.

The Worldwide Network for Blood and Marrow Transplantation (WBMT) was founded in 2007 as a network of several societies worldwide with the intention of promoting excellence in SCT, stem cell donation, and cellular therapies. In addition to their annual global survey, their most important activities were to help establish new SCT programs and to optimize existing ones.

In 2017, the Institute of Social Welfare (IPS [Instituto de Previsión Social]), which provides health insurance for national workers, was the only center with an SCT program, and thus it was chosen by the WBMT as a WBMT twinning program that would use the newest technologies with help from the World Health Organization (WHO). The program needed to be optimized to include allo-SCTs, considering that Paraguay was identified in the WBMT survey as one of the countries that lacked such therapy. At that point, mainly autologous SCTs were performed for patients with multiple myeloma (MM), and the SCTs used melphalan 200 (Mel 200) or Mel 140; a few patients with lymphoma received Mel 140 plus etoposide. The few allo-SCTs from matched related donors (MRDs) had a treatment-related mortality (TRM) rate of 55% at day 100 after transplantation.

The Hospital de Clínicas and the Niños de Acosta Ñu General Paediatric Hospital were just starting their SCT programs at the time, and 5 autologous SCTs were performed between the 2 of them. Dietger Niederwieser, MD, from the WBMT invited a hematologist from IPS to train for 6 months under his tutelage at the University of Leipzig (Leipzig, Germany), which performs around 220 SCTs per year.

Results

From the January 2, 2018, to May 2019, 28 SCTs have been performed at our center: 11 allo-SCTs (8 MRD and 4 haploidentical) (Figures 1 and 2). All patients have engrafted, although 2 of the patients who received haploidentical SCTs died, 1 as a result of complications after pericardial effusion and the other as a result of septicemia from a multiresistant *E. coli* infection (metallo-beta-lactamase [MBL]) from a previous admittance to the intensive care unit during induction. TRM at 100 days after transplantation for the whole cohort was 7%, mostly for haploidentical SCTs. Overall survival and progression-free survival for patients who had passed the 180-day mark after transplantation were 81% and 75%, respectively. Of the patients who received allo-SCTs, 5 patients had grade 1, 1 patient had grade 2, and 1 patient had grade 4 acute graft-versus-host disease (GVHD).

The list of drugs essential for performing SCTs was checked, and the list of drugs licensed for use in the county was updated. D. Niederwieser was involved with all patients on a daily basis by using telemedicine to view the patient's charts, laboratory test results, and imaging studies, by sharing his expertise regarding medications, and sometimes by speaking directly to patients to assure them that all international precautions and standards were being followed.

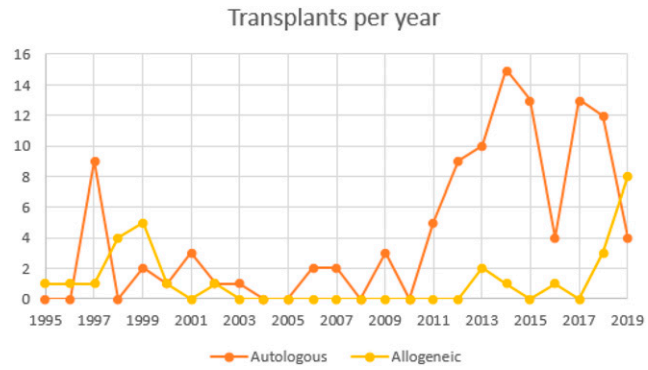

Figure 1. Number of autologous and allogeneic transplantations per year, 1995-2019.

The program also requested medications deemed essential by the SCT team, including carmustine, liposomal amphotericin, intravenous fludarabine, intravenous paracetamol, anti-thymocyte globulin, and oral and intravenous voriconazole. These drugs are now available at the hospital and will serve not only the SCT Program but all patients who require those drugs. However, there is still a problem with drugs such as busulfan, melphalan, and intravenous cyclosporine. Because those drugs are not sold in Paraguay, the hospital will not cover their cost, so patients have to pay for the drugs themselves and buy them from other countries (melphalan mostly from Argentina and busulfan mostly from Chile). Alternatively, they can use oral formulations of drugs such as cyclosporine, which is available in Paraguay.

The SCT Program at IPS started with 2 regular beds at the beginning of 2018. The SCT Unit now has a total of 7 beds: 4 have high-efficiency particulate air (HEPA) filters, 1 has a HEPA filter and positive pressure, and there are 2 regular beds. Growth is slow because going from 2 to 7 beds requires more on-call physicians

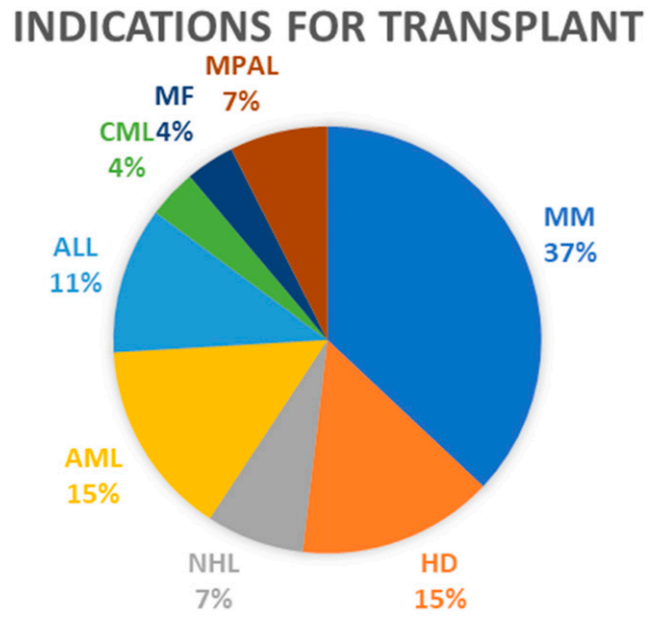

Figure 2. Indications for transplantation. ALL, acute lymphoblastic leukemia; AML, acute monoblastic leukemia; CML, chronic myeloblastic leukemia; HD, Hodgkin disease; MF, myelofibrosis; MM, multiple myeloma; MPAL, mixed phenotype acute leukemia; NHL non-Hodgkin lymphoma.

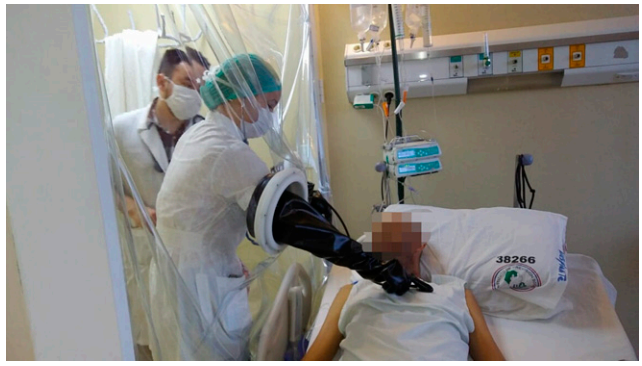

Figure 3. HEPA-filtered room with positive pressure where patient is examined through a plastic separator.

Figure 4. Apheresis machine used for collecting stem cells for autologous and allogeneic SCTs from peripheral blood.

and trained nurses; medical professionals with the required training are being added to the SCT Program at a steady pace. The SCT Unit now makes SCTs available for patients with MM.

Drugs available in Paraguay's SCT Program include Mel 200 and Mel 140; carmustine, etoposide, cytarabine, and melphalan (BEAM) with or without rituximab for lymphomas; busulfan plus cyclophosphamide for acute leukemias in younger patients; sequential mitoxantrone, fludarabine, cytarabine, and granulocyte colony-stimulating factor plus 2 days of busulfan plus cyclophosphamide for acute leukemias for patients who have achieved partial response; and busulfan plus fludarabine as reduced-intensity conditioning for patients older than age 50 years. All SCTs have been performed with fresh cells except for one because the hospital does not have the necessary equipment for cryopreservation. GVHD prophylaxis includes cyclosporine and methotrexate for transplants for patients with MRDs and also included tacrolimus plus mycophenolate mofetil plus posttransplant cyclophosphamide for patients with haploidentical SCTs.

Furthermore, because of the high success rate of the SCT Program and because IPS is the only center that performs allo-SCTs in Paraguay, a Cooperative Agreement has been signed between IPS and the Ministry of Health by which any Paraguayan citizen or any citizen of another nationality living in Paraguay may receive an SCT at IPS regardless of whether they are insured by Social Security. The Ministry of Health will reimburse IPS for the cost of the transplant (IPS does not make a profit from this transaction, it is merely to prevent loss of insured patient's money). Two patients have already received transplants in this modality.

Conclusion

International cooperation through telemedicine is one way to bridge the gap between experienced specialized centers thousands of kilometers away and smaller centers located in developing countries. A high level of involvement is required from both local and distant experts in the field who understand the limitations and constraints of centers in developing countries. The Cooperative Agreement between the IPS and the Ministry of Health has made SCTs available for everyone in Paraguay. The SCT Program is still limited because it needs medications that are not available in Paraguay (eg, melphalan, busulfan, and intravenous cyclosporine) and equipment that is not available at IPS (for cryopreservation), but the SCT Unit is planning to acquire equipment for cryopreservation in the near future.

Authorship

Conflict-of-interest disclosure: D.N. served on a speaker's bureau for Daiichi Sankyo and served as a consultant for Cellectis. The remaining authors declare no competing financial interests.

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