Conquering Blood Diseases – From Research to Patient Care

Late Critical Problems in Transplantation: An Historical Perspective

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The American Society of Hematology (ASH) is 50 years old this year. In 1968, when ASH was 10 years old, the first successful allogeneic transplant procedures were performed, marking the start of clinical hematopoietic cell transplantation (HCT). Three children with immunodeficiency disorders were cured using sibling bone marrow. These three patients became the field's first long-term survivors, and all were alive and well when last reported in 1994, 25 years after their transplants.

The field of HCT has grown rapidly over the last 40 years and it has benefited greatly from clinical and laboratory advances in supportive care, infectious diseases, and human leukocyte antigen (HLA) typing. In the 1970s half of procedures used bone marrow from matched siblings to treat nonmalignant diseases. Transplants for malignant diseases used radiation-based, myeloablative conditioning regimens and usually were applied in the setting of advanced disease. In the 1980s the number of allogeneic and autologous transplants for malignant disease increased. Cyclosporine, the first calcineurin inhibitor, became available. Use of unrelated donors allowed transplantation when suitable family members were not available, although the HLA typing methods used to select unrelated donors were primitive compared to today's standards. The 1990s brought additional transplantation options. Use of peripheral blood stem cells, unrelated donors, and umbilical cord blood increased. Development of less intensive conditioning regimens, so called "mini" or "nonmyeloablative" or "reduced intensity" procedures, allowed transplantation of older and sicker patients and the ability to transplant patients multiple times. The number of transplants for high-risk and metastatic breast cancer increased dramatically and then plummeted. The 2000s have seen continued advances in supportive care, a sharp decline in the number of transplants for chronic myeloid leukemia due to the development of tyrosine kinase inhibitors, increasing use of autologous transplantation for multiple myeloma and the ability to infuse two cord blood units for allogeneic transplantation.

Yet, the HCT field thus far has focused most of its attention on the early post-transplant period. Forty years and several hundred thousand procedures later, we are facing a growing survivor population with many late treatment-related complications. Greater success in overcoming the early risks of transplantation, application of HCT to a broader set of diseases, and the aging of survivors have resulted in many late complications, which take their toll in morbidity and premature mortality. Interest in studying late adverse effects of HCT has blossomed in the last 10 years and mirrors a broader cancer survivorship agenda in clinical care and research. From highly experimental roots and in the face of continuing therapeutic innovations, HCT now is established enough as a field not only to focus on disease-free survival, but also to ask the important questions about how our curative treatments affect the quality and duration of that survival.

See the related ASH 50th Anniversary Review articles under the MOBILIZATION AND TRANSPLANTATION section of the publication ASH 50th Anniversary Reviews: A Salute to the American Society of Hematology.