The Ende brothers and the arcane history of the first umbilical cord blood hematopoietic stem cell transplant

Dr Eliane Gluckman presented her work on umbilical cord blood (UCB) hematopoietic stem cell (HSC) transplantation in a session on pioneers in transplantation at the American Society of Hematology's 50th Annual Meeting. She is to be congratulated for historical accuracy, acknowledging that the first UCB hematopoietic transplant was published by Milton and Norman Ende in 1972.[1] Dr Milton Ende was an internist who gave 139 ABO-compatible fetal cord blood transfusions to 15 patients after noting unexpected improvement in some of his patients with malignancy. Dr Norman Ende is a pathologist and began to investigate the scientific basis for the improvement. One patient was a 16-year-old male with acute lymphoblastic leukemia who received eight transfusions of cord blood over a period of 17 days. One unit that consisted of 45 mL of cord blood engrafted, increased the hematocrit, and showed a change in the recipient's blood type from a phenotype of Jka+/M– to Jka–/M+. The donor's blood group antigens were not detectable immediately after the infusion but were detected on Day 6 postinfusion and by Day 27 comprised 75% of all red blood cells (RBCs). Donor cells continued to be detectable for 2 months. Although the engraftment was transient, it allowed time for establishment of normal hematopoiesis and a marrow in remission.

The history of the first UCB HSC transplant recapitulates much of the history of bone marrow transplantation (BMT) where the initial attempts were generally unsuccessful but demonstrated transient engraftment in some patients.[2] Sustained marrow engraftment was first documented in 1965, also in a patient with acute lymphoblastic leukemia.[3] Engraftment was also demonstrated by a change in RBC phenotype and the donor also received intravenous infusions of marrow from multiple donors. Detection of chimerism after the infusion of UCB by the Ende brothers in 1970 is remarkable in retrospect since it was only in the latter 1980s that more sophisticated cytogenetic and molecular tests evolved for the detection of chimerism.

Developments of successful protocols for BMT were established. They included immunosuppressive therapy, histocompatibility testing, treatment of graft-versus-host disease, and infection control; thus, by the late 1970s BMT had become an accepted therapeutic modality. These protocols provided the necessary framework for transplantation of HSCs from other sources, initially from peripheral blood followed by UCB.

In 1989 Ende and colleagues[4] and Broxmeyer and colleagues[6] simultaneously published papers advocating the use of UCB as a source of progenitor cells for BMT and Gluckman and colleagues[6] successfully treated a patient with Fanconi's anemia with a transplant of HSC from UCB. The Ende brothers are to be congratulated for their astute clinical observation, establishing the scientific basis of that observation and performing the first transplant of HSCs from UCB. Dr Broxmeyer is to be congratulated for his studies on the characteristics and storage of UCB hematopoietic progenitor cells and Dr Gluckman for her efforts that subsequently established UCB HSCs as an accepted therapeutic modality.

CONFLICT OF INTEREST

The author declares no conflict of interest.

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