

Parathyroid and Thymus Transplantation in Complete DiGeorge Syndrome

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Purpose/Background: DiGeorge syndrome is a heterogeneous condition in which infants are born with variable deficiencies of the thymus, parathyroid, and heart and often have other anomalies as well. In complete DiGeorge syndrome infants are athymic and are born with a profound T cell deficiency. Approximately 20% have profound hypoparathyroidism. Although thymus transplantation results in reconstitution of T cells, the ongoing hypoparathyroidism is a significant problem. The infant must take daily calcium replacement and is at risk of nephrocalcinosis and hypocalcemic seizures. Infants with no T cells should not be able to reject a parathyroid transplant when given at the same time as a thymus transplant. However, it is unknown if T cells that develop in a thymus transplant will tolerate or reject a parathyroid transplant. The purpose of this study was to ask if simultaneous transplantation of parental parathyroid tissue and unrelated thymus tissue can result in T cells tolerant of the parathyroid graft such that both the parathyroid and immune problems can be corrected.

Methods: A female infant was diagnosed with DiGeorge syndrome based on hypoparathyroidism associated with a hypocalcemic seizure on day 11, ventricular septal defects requiring surgery at 1 month, and absence of T cells noted at 5 weeks of age. The 22q11 FISH test was normal. An unrelated postnatal thymus was obtained for transplantation. The thymus shared an HLA-DR allele with the mother and the infant. Rabbit anti human thymocyte globulin was used as pre transplant conditioning. Thymus slices were inserted into the quadriceps of the recipient in an open procedure after a 2-week culture period. Concurrent parathyroid transplantation was performed at the time of the thymus transplant. Donor parathyroid tissue was obtained from the mother in an open operative procedure. The parathyroid was minced into small pieces and inserted into the quadriceps at a site distinct from the thymus graft. Parathyroid graft function was assessed by monitoring serum calcium and intact PTH.

Results: There were no adverse events associated with the transplantation or parathyroid donation. The patient required total parental nutrition (TPN) beginning 2 weeks after transplantation because of ongoing malnutrition and diarrhea. The patient rapidly gained weight and is currently half on TPN and half on oral feedings. The parathyroid hormone level which had been undetectable prior to transplantation rose to 18 pg/ml on day 17 post transplantation and to 40 pg/ml on day 66. The patient when last tested on day 73 after transplantation had only 5/cumm T cells. A biopsy of the thymus graft on day 80 showed thymopoiesis. Based on previous patients, T cells should appear in the periphery at approximately day 90. It is unknown if the T cells will be tolerant of the parathyroid when they appear in the periphery.

Summary: This is the first reported case of thymus and parathyroid transplantation in an infant with complete DiGeorge syndrome. There were no adverse events associated with the transplants or living-related donor parathyroidectomy. Parathyroid function was established initially. The patient is being monitored for T cell development and continued parathyroid function.