Human Islet Allotransplantation Under FK 506

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C. Ricordi, A. Tzakis, P. Carroll, Y. Zeng, H.L.R. Rilo, R. Alejandro, R. Shapiro, J.J. Fung, D.H. Mintz, and T.E. Starzl

SHORT-term[1] and prolonged[2-5] insulin independence has been recently reported following human islet allotransplantation in diabetic patients, indicating that it is possible to replace the endocrine function of the pancreas by an islet transplant in man. Nevertheless, rejection remains the major problem limiting the clinical applicability of islet transplantation in patients with type 1 diabetes mellitus (DM).

This report documents our initial experience on human islet intrahepatic allotransplantation using FK 506 as main immunosuppressive agent.

Twenty-two intrahepatic islet allografts were performed in 21 patients: 10 patients, aged 8 to 58 years, underwent combined liver-islet allotransplantation following upper-abdominal exenteration for tumors too extensive to be removed with less drastic procedures.[6,7] Preliminary results on these patients have been reported previously.[2] Four type I diabetic patients, aged 22 to 56, years received a combined liver-islet allograft (the indications for liver transplantation were cirrhosis secondary to hepatitis C, alcoholic cirrhosis, and cryptogenic cirrhosis). Eight patients, aged 28 to 42 years, received nine combined cadaveric kidney-islet grafts (one retransplant) for end-stage renal disease secondary to type I DM. One patient had detectable c-peptide before the islet transplant and was excluded from analysis.

The human islets were obtained by a modification[8] of the automated method for human islet isolation[9] and infused into the liver via the portal vein.

Immunosuppression was performed with FK 506 (clusters) and FK 506 plus steroids (type 1 DM). Supplementary steroids or OKT3 was given if rejection was suspected clinically or diagnosed by biopsy.

Six patients who received a combined liver-islet allograft following the cluster resection did not require insulin for 5 to over 19 months. The first patient, who received the islet allograft on January 10, 1990, is still insulin independent over 19 months postoperatively. Since the first report,[2] three patients died for cancer recurrence.

All patients with type 1 DM who received either a combined liver-islet or a kidney-islet allograft still require insulin therapy. Nevertheless, basal and stimulated c-peptide production is present in all patients, and 10% to 90% reduction in insulin requirement has been observed.

Our results indicate that simultaneous allotransplantation of a liver may constitute a favorable factor for islet allograft survival in cluster patients. Rejection is still a major problem in patients with type 1 DM, although adverse factors such as steroids, FK 506, and type 1 DM itself, may have contributed to impair islet engraftment and/or function in these patients.

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From the Transplant Institute, University of Pittsburgh School of Medicine, Pittsburgh, Pennsylvania; and the Diabetes Research Institute, University of Miami, Miami, Florida.

Supported by research grants from the Juvenile Diabetes Foundation International (No. 1911421), New York, New York.

Address reprint requests to Camillo Ricordi, MD, Transplant Institute, University of Pittsburgh School of Medicine, 5C Falk Clinic, 3601 Fifth Avenue, Pittsburgh, PA 15213.

0041-1345/91/$3.00/+0