Human Islet Allotransplantation in 18 Diabetic Patients


REPORTS of short-term\(^1\) and prolonged\(^2-5\) insulin independence following human islet allotransplantation indicate that it is possible to replace the endocrine function of the pancreas by an islet transplant in humans. This article discusses our initial experience with islet isolation and intrahepatic allotransplantation in 18 patients.

MATERIALS AND METHODS

Nineteen intrahepatic islet allografts were performed in 18 patients. In group 1, nine 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.\(^2\) In group 2, three type 1 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. All patients had an absent C-peptide response to glucagon or Sustacal challenge test. In group 3, six patients aged 28 to 42 years received seven combined cadaveric kidney-islet grafts (one retransplant) for end-stage renal disease secondary to type 1 diabetes mellitus.

The human islets were obtained by a modification\(^8\) of the automated method for human islet isolation.\(^9\) The preparation was infused into the portal vein catheter over 20 to 30 minutes. Immunosuppression was with FK-506 (group 1) and FK-506 plus steroids (groups 2 and 3). Supplementary steroids or OKT3 was given if rejection was suspected clinically or diagnosed by biopsy.

RESULTS AND DISCUSSION

Patients in groups 2 and 3 received a number of islets that was significantly higher (\(P < .05\)) compared to the cluster-islet patients of group 1 (data not shown). In group 1, six patients did not require insulin for 5 to over 16 months. The first patient, who received the islet allograft on January 10, 1990, is still insulin independent over 16 months postoperatively. Since the first report,\(^2\) two patients died for cancer recurrence. In group 2, one patient is alive 7 months after transplantation. She had a 100% positive cytotoxic crossmatch and a rejection episode during the first postoperative week. Approximately an 80% decrease in her insulin requirement was observed over the first 6 postoperative months (from 70 to 15 units of insulin per day). HbA1c has been within the normal range (<5.95%). In addition, C-peptide response (>2 pmol/L) to Sustacal challenge tests 2, 3, and 6 months after transplantation has progressively improved. The second patient, who died 6 months after transplantation from hepatitis B and sepsis, also demonstrated significant islet function (basal and stimulated C-peptide levels of 0.76 and 1.59 pmol/L, respectively). A third patient died 36 hours following combined liver-islet allotransplantation from primary nonfunction of the liver due to humoral (hyperacute) rejection. The crossmatch was 100% positive. In group 3, none of the patients became insulin independent. One patient died from aspiration pneumonia 5 days following surgery.

In the present report, prolonged (5 to >16 months) insulin independence was observed in six patients who underwent upper-abdominal exenteration and liver-islet replacement.\(^2\) Four of them received islets from two donors. In contrast, in our experience none of the type 1 diabetic patients who received either a liver-islet or a kidney-islet allograft are insulin independent. Although our best result in type 1 diabetic patients was obtained in a case of positive crossmatch (100%), we currently consider a positive crossmatch as an absolute contraindication to human islet allotransplantation because of the increased risk of morbidity and mortality in this group.

In conclusion, our results indicate that rejection is still a major factor limiting the clinical application of islet transplantation in patients with type 1 diabetes mellitus, although other factors, such as steroid treatment, may contribute to impaired islet engraftment and/or function.

REFERENCES


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

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

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