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Histologic Finding of Pancreatic Islet Tissue Following Intraportal Human Islet Allotransplantation

C. Ricordi, **C.E. Sever**, **P. Carroll**, **A. Tzakis**, **Y. Zeng**, **H.L.R. Rilo**, **A.J. Demetris**, **R. Alejandro**, and **T.E. Starzl**
Transplant Institute, University of Pittsburgh School of Medicine, Pittsburgh, Pennsylvania, and the Diabetes Research Institute, University of Miami School of Medicine, Miami, Florida.

THE ultimate test of viability of separated human islets is functional activity after transplantation into a diabetic recipient. Morphologic identification of insulin-containing transplanted islets could provide important correlative data and eventually confirm the functional results. The present report describes identification of intrahepatic islet tissue following human islet allotransplantation.

MATERIALS AND METHODS

Human islets were obtained and transplanted into the liver via portal vein injection following upper-abdominal exenteratton and liver replacement,[1] or following liver or kidney transplantation in type I diabetic patients. Liver tissue was examined from needle biopsy (n = 1), wedge biopsy (n = 2), or at autopsy (n = 2). Immunohistochemical stains were performed on formalin-fixed, paraffin-embedded tissue using the avidin-biotin complex method.[2] A panel of antibodies directed against insulin, glucagon, mononuclear cells, and class II antigens was used.

RESULTS AND DISCUSSION

In all patients, islet tissue was mostly found in subcapsular location. In patients who underwent upper-abdominal exenteration and liver-islet replacement, islets were found in several sections from two patients (17 and 109 days after transplantation). No significant surrounding inflammatory reaction was demonstrated. The insulin and glucagon stains unequivocally demonstrated beta and alpha granulation in the majority of the islet cells. In type I diabetic patients who received a combined liver-islet (n = 1, biopsy on postoperative day 15) or kidney-islet (n = 2, days 2 and 5 posttransplant) allograft, the islet tissue was often associated with a mild, predominantly lymphocytic infiltrate. In one patient who received a liver-islet transplant, the needle biopsy obtained 15 days after transplantation revealed a mixed portal infiltrate surrounding an islet, which reflected hypoperfusion injury of the liver allograft. In a patient who died 5 days following combined kidney-islet transplantation from aspiration pneumonia, intrahepatic islet tissue was often associated with a dense mixed infiltrate of lymphocytes and macrophages. Most of the lymphocytes stained positive with T-cell markers, and several of them were also positive for HLA-DR, suggesting T-cell activation. HLA-DR stain was also strongly positive in histiocytic cells with dendritic morphology, possibly representing antigen-presenting cells. Interestingly, the islet cells remained HLA-DR negative, despite the surrounding inflammatory reaction.

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

A wedge liver biopsy that was taken from a type I diabetic patient who required reexploration for evacuation of a perinephric hematoma 2 days after combined kidney-islet transplantation revealed a mild reactive mononuclear infiltrate around the intrahepatic islet tissue.

In summary, mononuclear cell infiltrate charactenzed intrahepatic islets following allotransplantation in type I diabetic patients. In contrast, in patients receiving a combined liver-islet allograft following upper-abdominal exenteration, no significant inflammatory response was observed.

The mononuclear cell infiltrate observed in type I diabetic patients indicates that a specific inflammatory reaction and/or rejection is most likely to occur in these patients. Alternatively, the different finding could reflect a difference in the time of evaluation. In fact, liver tissue was analyzed earlier in type I diabetic patients who received a combined kidney-islet allograft (2 and 5 days posttransplant) compared to patients undergoing upper-abdominal exenteration and liver-islet replacement (17 and 109 days posttransplant).

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