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Effect of Intraportal Human Islet Transplantation on Kidney Graft Survival in Simultaneous Kidney–Islet Allografts

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AN increased frequency of acute kidney rejection episodes has been observed following simultaneous kidney and pancreas transplantation.[1–4] This has not been noted in all series.[5,6] The mechanism of how the pancreas graft might induce rejection in the transplanted kidney is not known. We examined the frequency of kidney rejection episodes in patients who underwent combined kidney–islet transplantation.

METHODS

Eight patients aged 29 to 38 years with long-standing insulin-dependent (type I) diabetes mellitus received nine combined cadaveric kidney–islet grafts (one retransplant), with one (n = 6), two (n = 2), or three (n = 1) islet donors. The cadaveric donor ABO types were all compatible with recipient types and HLA matching was random, the antigen match being 0 to 2 for the kidney and 0 to 3 for islets. All patients had a negative crossmatch. One patient who underwent the procedure died on the fifth postoperative day of aspiration pneumonia. This was not included in the analysis of frequency of rejection, but data are included in the calculation of mortality and graft survival.

Human islets were obtained as previously described.[8] The islets were transplanted by infusion into a branch of the portal vein.

All patients received a 1000-mg bolus of methylprednisolone during the operation, followed by a decreasing prednisone dose from 200 to 20 mg over the course of the first week posttransplant. FK 506 was given at a dose of 0.1 mg/kg intravenously administered as a continuous infusion over 24 hours, beginning immediately following transplantation. When patients resumed a solid diet, an oral dose of 0.15 mg/kg/BID was started. Patients 6 to 8 also received imuran 200 mg/d during the first postoperative week in addition to the previously mentioned immunosuppression.

Data were analyzed by χ^2 test with continuity correction. Significance of difference was considered as $P \leq .05$.

RESULTS AND DISCUSSION

Six-month graft survival was 86%, 76%, and 78% in diabetic recipients of a kidney graft (DK), nondiabetic kidney transplant recipients (NDK), and diabetic recipients of kidney and islets (DKI), respectively. One-year graft survival was 82% (DK), 73% (NDK), and 78% (DKI). Mortality rates were not different in the groups. The unexpected finding was the frequency of kidney rejection episodes, 55.1% in DK, 65% in NDK, and 100% in DKI patients ($P < .02$). Most rejection episodes were mild and easily treated with corticosteroids. Only one graft was lost to refractory recurrent rejection episodes. After rejection episodes, five patients still have demonstrable islet cell function but all patients still require exogenous insulin. The best results were obtained in patients who received more than one donor.

Although the number of patients in our kidney islet group is small, the frequency of rejection episodes seems out of proportion to what was expected for islet transplantation. As with kidney and pancreas grafts, these rejection episodes are largely manageable. There were no significant differences in HLA matches in the three groups.

The immunogenicity of the islet preparations or the intravascular route of administration (portal vein) could be determining factors in the increased frequency of kidney rejection observed. Despite the small volume and relative purity of the islet preparations, significant contaminating cells are still present.[7] These cells, which include lymphoid and dendritic cells, could be responsible for an increased immunogenicity of the islet graft.

Our data also indicate that a single mild rejection episode, even in a patient who receives islets from multiple donors, may be enough to compromise the ability to achieve complete insulin independence, although diabetes control may be stabilized.[8]

In conclusion, an increased frequency of kidney rejection episodes was observed after combined kidney–islet allotransplantation. However, most of these rejection episodes were mild and did not produce any significant difference in patient and kidney graft survival.

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