The Impact of Positive T-Cell Lymphocytotoxic Crossmatch on Intestinal Allograft Rejection and Survival

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A POSITIVE antidonor T-cell lymphocytotoxic cross-match (X-M) has been shown to have a deleterious effect on graft survival after solid organ transplantation.[1–3] This is the first report to address the impact of preformed antidonor IgG lymphocytotoxic antibodies on intestinal allograft rejection and survival.

MATERIALS AND METHODS

Over a 9-year period, 124 consecutive patients received a total of 130 intestinal allografts at our center: 51 isolated intestines and 79 composite visceral grafts (62 liver/intestine and 17 multivisceral). Of these, 51% were male and 58% were children. All donors were cadaveric and ABO identical. The HLA match was random and no attempts were made to immunomodulate the graft. The baseline immunosuppression was tacrolimus and steroids. Daclizumab was used as an induction therapy for the last 17 patients and OKT3 was utilized to treat steroid-resistant rejection. In 27 allografts (4 positive X-M, 23 negative X-M), a single dose (3 to 5 × 10⁸ cells/kg body weight) of unmodified donor bone marrow cells were infused intravenously within 24 hours after graft implantation. The X-M test was performed in all patients by obtaining recipient sera immediately before transplantation that tested for cytotoxic antibody activity against donor T lymphocytes as previously described.[2] To shorten the cold-ischemia time, the recipient operation was often started before the results of the X-M were available. The X-M was positive with dithiothreitol (DTT) in 23 (18%) grafts. All were primary grafts with 7 (30%) isolated intestines and 16 (70%) composite visceral grafts that contained liver. Twelve were children and 11 were adults with a relative predominance of adult females (39%). The clinical features of both positive and negative X-M recipients were similar, including number of previous abdominal operations, operative time, cold-ischemia time, donor/recipient CMV status, and median follow-up period. The donor and recipient operations as well as the perioperative management strategy were the same in both groups as described elsewhere.[4,5] The Kaplan–Meier method was used to calculate survival rates. Chi-square and standard t tests were used for statistical analysis.

RESULTS

With a mean follow-up of 27 months, 10 (2 isolated intestine, 8 composite visceral) of the 23 positive X-M allografts were lost, with an overall survival of 57%. The causes of the 10 graft (patient) losses were opportunistic infections in 5 (PTLD = 3, CMV = 1, fungal sepsis = 1), rejection in 3 (acute = 2, chronic = 1), and dissection of the ascending thoracic aorta in 1. The remaining graft (liver/intestine) was transplanted across a high-lymphocytotoxic antibody titer (1:512) to a black pediatric recipient who died of primary graft failure 4 days after transplantation. Hyperacute rejection could not be excluded in such a case despite failure of the conducted immunohistochemical and pathologic studies to confirm the diagnosis. Using the negative X-M grafts as control, the presence of preformed lymphocytotoxic antibodies did not significantly affect the 5-year actuarial (Kaplan–Meier) patient and graft survival.

Intestinal allograft rejection occurred in 91% of the positive and 84% of the negative X-M (control) grafts. The mean (SD) number of rejection episodes per graft was also higher for the positive compared with the negative X-M grafts (5.4 ± 5 vs 4.0 ± 4) as was the need to use OKT3 (43% vs 33%). Such differences between positive and negative X-M grafts were significantly higher among the isolated intestine cases, with a mean frequency of 7.3 ± 8 vs 4.1 ± 4 and an OKT3 use of 86% vs 45% ($P = .05$). Within the positive X-M grafts, the mean number of intestinal rejection episodes per graft was significantly less for composite visceral (4.5 ± 3) compared with isolated intestinal (7.1 ± 7) allografts. The need for OKT3 was also significantly ($P = .03$) less, with an incidence of 27% and 75%, respectively.

CMV disease developed with a higher incidence among the positive (58%) compared to the negative X-M (27%) group. However, PTLD occurred with equal frequency (22%) among both cohorts. None of the positive X-M recipients developed GVHD.

DISCUSSION

In this series, 18% of our intestinal recipients were harboring preformed antidonor IgG lymphocytotoxic antibodies. This relatively high rate, compared with other solid organ transplant recipients,[1–3] could be attributed to the multiple abdominal operations that these patients received before

transplantation with the frequent need for multiple blood transfusion.

Similar to other solid organ allografts, positive T-cell lymphocytotoxic X-M increased the frequency and severity of intestinal rejection. Such a risk was significantly higher among patients who received intestine only. The simultaneously transplanted liver as part of a composite visceral allograft seemed to ameliorate the negative effect of the preformed antibodies and X-M reactivity. These data further support our previous observation that the liver is significantly protective of concomitantly engrafted intestine.[5]

In conclusion, positive T-cell lymphocytotoxic X-M increases the frequency and severity of rejection after intestinal transplantation, particularly with isolated intestine.

Therefore, our current recommendation, until better immunomodulation strategies can be established, is to avoid transplanting positive X-M allografts to patients who are not in urgent need of an isolated intestine.

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