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Adverse impact of high panel-reactive antibody (PRA) and positive cytotoxic crossmatch in liver transplantation

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Abstract Of 91 liver transplants (LTX) performed from October 1988 to December 1992, 13 (14.2%) of the patients received a liver from a lymphocytotoxic-positive crossmatch (CM) donor. Severe early rejection resulting in graft floss occurred in seven positive CM patients. Three of the remaining positive CM patients suffered several rejection episodes leading to chronic rejection and FK 506 was required as rescue treatment. A significant difference in mean panel-reactive antibody (PRA) of 8.6% and 56.9% was found in negative and positive CM patients, respectively ($P = 0.012$). A higher mean PRA (67.7%) was found in positive CM patients with rejection compared with positive CM patients without rejection (PRA 38%). Overall graft and patient survival were 31.9% and 35% in positive CM patients compared with 57.0% and 61.9% in negative CM patients. These differences were statistically significant ($P = 0.023$). In our experience the risk of developing severe acute rejection with graft failure and chronic rejection is related to PRA > 60% and positive CM. We recommend that in patients with PRA > 60%, the result of CM should be awaited before proceeding to LTX.

Key words Lymphocytotoxic crossmatch · Panel reactive antibody · Liver transplantation

Introduction

Human liver transplants (LTX) are usually resistant to antibody-mediated rejection and can be successfully performed with positive antidonor crossmatches [3]. Recently, Starzl et al. reported a significant decrease in patient and graft survival when LTX was performed with a positive IgG lymphocytotoxic crossmatch [4].

The aim of this study was to ascertain the impact of a positive panel-reactive antibody (PRA) and a positive crossmatch in LTX.

Materials and methods

From October 1988 to December 1992, 91 LTX were performed in 81 adult patients. Of these, 13 patients (12 women and 1 man) received a liver from a lymphocytotoxic-positive crossmatch donor (14.2%). A crossmatch test was interpreted as positive when more than 20% of donor lymphocytes were killed by recipient serum. Two cases were retransplantations.

Immunosuppression

Standard postoperative immunosuppression consisted of cyclosporin A (CsA) and steroids, and OKT3 was added when the result of

a positive crossmatch was known or renal failure precluded the use of CsA. Rejection episodes were treated with a 1 g bolus of methylprednisolone. If rejection persisted, a 14-day course of 5 mg/day OKT3 was given.

Crossmatch test

Pretransplant serum was drawn immediately before LTX and used for crossmatching. All sera were treated with dithiothreitol (DTT) to inactivate IgM antibodies. Donor T lymphocytes were isolated from lymph nodes using nylon wool. The cytotoxicity test was performed according to the NIH standard technique. Briefly, 1 µl of 2×10^6/ml T lymphocytes was added to 1 µl of serum for 1 h at room temperature. Rabbit complement (5 µl) was added for an additional 1 h at room temperature and eosin blue was added to stain dead cells. Cells were fixed with formol.

Panel-reactive antibody

PRA was assessed by testing recipient serum against a selected panel of 30 cells, including all frequent antigens, in a Caucasian population. PRA above 10% was considered positive.

Results

Rejection (Table 1)

Severe early rejection resulting in graft loss occurred in 7 of the 13 positive crossmatch patients (53.8%). Two underwent successful retransplant despite a positive crossmatch donor in one, and five died. The remaining six positive crossmatch patients suffered no early acute rejection (46.2%). Three of them experienced several rejection episodes some months after LTX leading to chronic rejection, and were converted to FK506. Two were successfully rescued and the third died from chronic rejection. The remaining three patients experienced no rejection, although two died at 14 and 23 months, respectively, post-LTX from unrelated causes.

Table 1 Rejection in positive CM patients

	No. of cases
Early severe rejection; graft loss	7
Several rejection episodes	3
No rejection	3

Table 2 Crossmatch and PRA in LTX

	Crossmatch negative (78)	Crossmatch positive (13)	*P* value
Mean PRA (%)	8.6	56.9	0.012

Table 3 PRA and rejection in positive CM patients

	Mean PRA (%)	Mean PRA (%)
Early severe rejection; graft loss	67.5	
Several rejection episodes	41.1	62.7
No rejection		38
P	NS	NS

Panel-reactive antibody (Tables 2 and 3)

A significant difference in mean PRA of 8.6% and 56.9% was found in negative and positive crossmatch patients, respectively, ($P = 0.012$), but no significant differences in mean PRA were found in positive crossmatch patients with early rejection (PRA 67.5%) or without early rejection (PRA 41.1%). The mean PRA in positive crossmatch patients with rejection (62.7%) was higher than in positive crossmatch patients with no kind of rejection (38%), although this difference was not statistically significant. Only three of the negative crossmatch patients (4%) with positive PRA developed severe rejection, and no differences were found in PRA when compared with patients without rejection.

Survival (Fig. 1)

Overall graft and patient survival were 31.9% and 35% in positive crossmatch patients compared with 57.0% and 61.9% in negative crossmatch patients. These differences were statistically significant ($P = 0.023$).

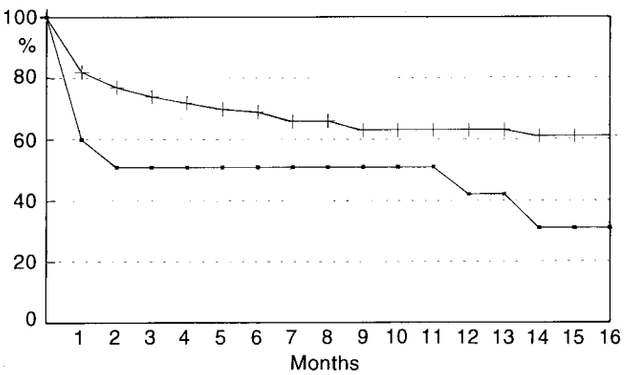

Fig. 1 Survival in CM-positive (■) and CM-negative (+) grafts ($P = 0.023$)

Discussion

Three different patterns were seen in patients with positive lymphocytotoxic crossmatch. Graft loss due to severe early rejection was observed in approximately 54% of cases. In three patients (23%), no evidence of rejection was observed after at least 1 year of follow-up, and in the remaining three patients (23%) changes in chronic rejection were detected by biopsy. The ten patients with some kind of rejection during follow-up presented high levels of anti-HLA antibodies (mean PRA 62.7%) compared with patients without rejection (PRA 38%), which suggests that antibodies may have persisted after LTX in these patients [2]. Our results show that positive crossmatch and high PRA are associated with decreased liver graft survival. This finding is similar to the results of other studies [1, 4].

In our experience the risk of developing severe acute rejection with graft failure and chronic rejection is related to PRA > 60% and positive lymphocytotoxic crossmatch. We recommend that in patients with PRA > 60%, the result of crossmatch should be awaited before proceeding to LTX.

References

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