Effect of OKT3 on Survival and Rate of Retransplantation

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WE HAVE previously reported the results of our pilot randomized trial[1,2] and our later extended series of 157 liver allograft recipients[3,4] treated with the mouse antihuman T cell antibody OKT3 (Orthoclone OKT3, OrthoPharmaceutical Corporation, Raritan, NJ) for treatment of acute hepatic allograft rejection. An additional 93 liver transplant patients have been treated with OKT3 since the last investigation and were included in this study.

METHODS

Between November 1984 and June 1986 250 hepatic allograft recipients received a course of OKT3. Follow-up data were available in all 250 patients until the beginning of March 1987, with a mean follow-up time of 432.9 ± 302.7 days. Baseline immunosuppression consisted of cyclosporine (Cs) and steroids. Clinical and histologic criteria leading to OKT3 therapy as well as principles of OKT3 therapy in conjunction with Cs and steroids have been extensively described previously.[1,3,4]

Analysis was performed using the previously described grouping scheme for allograft recipients.[1] Briefly, in group 1 patients OKT3 treatment was started less than ten days postoperatively; in group 2 patients treatment was started ten days to three months postoperatively; and in group 3 patients treatment was started at greater than three months postoperatively.

RESULTS

The average age of the 250 OKT3-treated patients was 28.4 ± 18.3 years. Eighty-seven patients were children (mean age, 6.3 ± 5.4 years), and 163 were adults (mean age, 40.2 ± 11.2 years). Two hundred twenty-one (88.4%) patients had their first graft, and the other 29 (11.6%) had undergone retransplantation before receiving OKT3 (Table 1).

The response to OKT3 therapy was determined as survival of the allograft. At the beginning of March 1987, 146 (58.4%) patients treated with OKT3 had functioning allografts with an actuarial 1-year survival of 62.0%. Sixty-three patients (25.2%) needed retransplantation, and 41 patients (16.4%) died. Group 2 patients had superior results: 79 (71.8%) had functioning allografts, and the 1-year survival reached 74.3%. For comparative purposes additional data for all liver transplant recipients from August 1983 to June 1986 not treated with OKT3 were determined. Of 362 grafts 181 (50.0%) were functioning at the beginning of March 1987 with an actuarial 1-year survival of 53.3% (Table 1).

DISCUSSION

In agreement with our previous study this investigation showed the efficacy of OKT3 in reversing acute hepatic allograft rejection. Our initial findings have also been verified by another center.[5] The optimal response to OKT3 occurred in group 2 patients in whom cell-mediated rejection was the primary cause of postoperative liver allograft dysfunction. The less than optimal response rate in groups 1 and 3 reflects concomitant processes, ie, an element of coexisting ischemic injury and renal failure in group 1 and a degree of chronic rejection in group 3.

An important benefit of this drug was observed in patients who have historically done poorly. These patients typically present with hepatic allograft dysfunction in the early

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Table 1. Graft Status at the Beginning of March 1987 and One-Year Survival in Liver Transplant Recipients Treated With OKT3

Group	No. of Grafts	Graft Status		1-Year Survival		
		Functioning (%)	ReTx (%)	Died (%)	% Graft	% Patient
1	119	57 (47.9)	38 (31.9)	24 (20.2)	48.4	62.4
2	110	78 (71.9)	17 (15.5)	14 (12.7)	74.3	82.2
3	21	10 (47.6)	8 (38.1)	3 (14.3)	71.4	87.5
1-3	250	146 (58.4)	63 (25.2)	41 (16.4)	62.0	73.4
No OKT3*	362	181 (50.0)	90 (24.9)	91 (25.1)	53.3	71.5

*For comparative purposes data for all liver transplant recipients not receiving OKT3 from August 1983 to June 1986 are added.

posttransplant period and usually have additional metabolic derangements, generally reflecting a precarious preoperative status. Such patients, especially if they present with an additional element of cellular rejection, appeared to benefit by a normalized graft function from OKT3 therapy.

Rejection is a major factor influencing the need for retransplantation.[6] During the extended follow-up period the retransplantation rate appeared to diminish greatly in group 2 patients presenting primarily with cell-mediated rejection. The higher rate of retransplantation seen in group 1 and group 3 patients possibly reflects the inability of OKT3 to reverse the signs of concomitant disease disorders.

The decreased need for retransplantation is reflected in the survival of hepatic allografts. A significant increase in allograft survival was demonstrated. The major benefit was seen in group 2 patients, who had a superior 1-year graft survival (Table 1). In group 1 patients allograft survival approximated that in the historic control group.

These findings suggest that OKT3 has affected the overall success of liver transplantation with respect to allograft survival in patients with documented liver rejection. The normalization of survival curves in group 1 patients suggests that OKT3 also has a role in these critically ill patients as an added treatment for early rejection and/or prophylaxis in patients in whom Cs therapy must be handled cautiously. Thus OKT3, in conjunction with Cs and steroids, has improved the treatment of hepatic allograft rejection.

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