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The use of OKT3 in steroid-resistant rejections following cadaveric kidney transplantation

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OKT3 has been proved to be effective in the treatment of steroid-resistant rejection after renal allograft transplantation [1]. We investigated the clinical course of OKT3 recipients to find out in which cases of steroid resistance OKT3 therapy might be ineffective.

Key words: Renal transplantation – Rejection – OKT3

Material and methods

From December 1986 to October 1990, 380 consecutive cadaveric kidney transplantations were performed. Routine immunosuppression consisted of CsA and prednisone. In cases of high immunological risk, azathioprine was additionally given. If an acute cellular rejection occurred and was confirmed histologically, steroid therapy was administered. Until June 1989 two courses of steroid pulses (3 × 0.25 g IV) were given, and from then on only one course. In 54 of the 380 patients the rejections were steroid resistant. In all of these cases persisent rejection was confirmed histologically and then treated with OKT3 (5 mg per day for 7–14 days). With regard to age, sex, HLA mismatches and number of transplantations, this group of patients showed no significant differences compared with a group of 326 patients not treated with OKT3. The mean follow-up time was 18 months for the OKT3 recipients and 23 months for the other group. The cases in which rejection was reversed after OKT3 therapy were compared with those with organ loss (Table 1). Patient and graft survival were calculated using the life-table method.

Results

In 54 (17%) of 380 patients, steroid-resistant rejection occurred and was treated with OKT3. In 28 of these patients the graft was rescued (52%) and in 26 cases (48%) the graft was lost. Six patients (11%) of the OKT3 group died within 18 months after transplantation, three of these due to enforced immunosuppression (EBV sepsis; CMV sepsis plus reactivated tuberculosis; enterococcus pneumonia plus peritonitis plus sepsis). One patient died from aortic dissection developing on top of an iliacal occlusion which occurred under OKT3 therapy. Two other patients died from cardiac failure in generalized sepsis with pre-existent diabetes and from gastrointestinal bleeding subsequent to pre-existing chronic hepatitis plus chronic rejection. In nine cases (17%) OKT3 therapy had to be withdrawn for the following reasons: stomatitis (two), HSV meningitis, somnolence, psychosis and exhaustion (three). Eight of these patients lost their graft, and one graft was rescued later with ATG therapy and showed good function.

In 13 of the cases with organ loss (50%) histological findings showed predominantly perivascular infiltration, endothelial proliferation and/or epithelial necrosis. In the group with good organ function, six biopsies (21%) gave the same result. The number of kidneys preserved in Collins solution was significantly higher in the group with graft loss.

In the OKT3-treated group, 1-year graft survival was 58% ±7% versus 85% ±2% in the patients not treated with OKT3. In the OKT3 group, 1-year patient survival was 90% ±4% versus 95% ±1% in the other patients. The 1-year survival for the patients with restored renal function ($n = 28$) was 100% compared with 81% for the OKT3 recipients ($n = 26$) with graft loss.

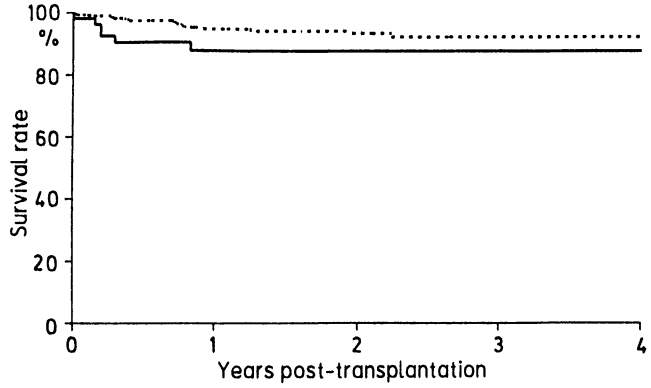

Fig. 1. Actuarial patient survival of OKT3 recipients ($n = 54$) (—) vs. patients not treated with OKT3 ($n = 322$) (----). $P = 0.1$

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Table 1. Comparison of OKT3-treated patients: rescued vs. lost grafts

	Good function (> 3 months)	Graft loss (< 3 months)	*P*
Number of patients	28	26	
Recipient age (years)	41.9 ± 1.9	42.8 ± 2.3	n.s.
Sex (male: female)	17:11	16:10	n.s.
Transplantation number			
First	26 (93%)	23 (88%)	n.s.
Second/third	2 (7%)	3 (12%)	n.s.
Cold preservation (h)	23.14 ± 1.37	22.65 ± 1.35	n.s.
Donor age (years)	37.79 ± 3.42	38.08 ± 4.27	n.s.
Preservation solution			
Collins	13 (46%)	19 (73%)	0.046
UW/HTK	15 (45%)	22 (41%)	
Panel reactive antibodies (%)	3.53 ± 1.9	8.19 ± 4.03	n.s.
Mismatch			
HLA-A	0.82 ± 0.12	0.69 ± 0.12	n.s.
HLA-B	0.78 ± 0.1	0.69 ± 0.12	n.s.
HLA-DR	0.50 ± 0.12	0.53 ± 0.09	n.s.
Withdrawal of OKT3	1 (4%)	8 (31%)	
Start of OKT3 treatment (weeks post-transplantation)	4.6	3.5	
Predominant histological findings			
Perivascular infiltration and/or endothelial proliferation and/or epithelial necrosis	6 (21%)	13 (50%)	0.028
Cellular rejection	22 (79%)	13 (50%)	

Values are means ± SEM

Discussion

The high efficacy of the monoclonal antibody OKT3 for steroid-resistant rejection is well known. On the other hand, during clinical use severe side-effects and even a fatal outcome directly related to OKT3 administration have been observed. The combination of previous high-dose steroid anti-rejection therapy with OKT3 is not recommended because of the high risk of infection [2]. Therefore we reduced steroid treatment to one course. In all cases of steroid resistance the use of OKT3 should be considered carefully, taking into account individual patient risk and histopathological findings. Pre-existent chronic diseases ought not to be underestimated. ATG or triple therapy are alternatives in the treatment of steroid-resistant rejection.

Conclusion

There are alternatives to OKT3 in the treatment of steroid-resistant rejection. In cases of high risk of morbidity and histopathological findings that indicate probable ineffectiveness of OKT3, alternative therapy is used in Essen.

References

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