

Prediction of Rejection in Renal Transplantation by Immune Parameters

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ABSTRACT

Background: Monitoring of phenotypic characteristics of T-lymphocytes in peripheral blood is commonly performed to give the clinical parameters in the management of kidney transplant recipients. **Objective:** To predict rejection in renal transplantation by immune parameters. **Methods:** 16 non-diabetic kidney transplant candidates (4 females and 12 males, age = 20-65 yr, first time transplant) were selected. The transplanted patients were divided into two groups based on the rejection during 3 weeks post transplant: group I (n = 9) without rejection and group II (n = 7) with a rejection episode. Immune parameters including lymphocytes subpopulations (by flow-cytometry) and immunoglobulin classes (IgM, IgG, IgA and IgE by nephelometric assay) before and 45 days after transplantation were determined. **Results:** The results of this investigation showed that the level of immunoglobulin IgG, IgM, IgA and IgE decreased post transplantation due to immunosuppressive drugs. CD3, CD4, CD8 T cells count, CD56 NK cells count and CD20 B cells count pre- and post-transplantation did not show any significant differences. The amount of IgE (220 vs. 462 IU/ml), CD3 (62% vs. 69.7%) and CD4 (35% vs. 41.3%) cells increased in group II during rejection episode pre-transplantation. In addition, IgA increased pre-transplantation in group I those without rejection episode in comparison with group II with a rejection episode. Forty five days post transplantation IgA (209 vs. 152 mg/dl), IgG (1009 vs. 703 mg/dl) and CD20 (15% vs. 10%) increased in group I patients. **Conclusion:** It is suggestive that pre-transplantation increases IgE, CD3 and CD4 are predictive of acute rejection.

Keywords: Cytokine, Rejection, Renal Transplantation

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INTRODUCTION

Acute rejection, a major cause of morbidity in renal transplant recipients, is considered as an important risk factor for the development of chronic allograft nephropathy (1-3). Initial studies on immunologic monitoring of T cell subsets using MAbs suggested a correlation between changes of T cell subsets and clinical events such as acute rejection and viral infection (4-5). Valeri et al. reported that increment of the CD3/CD25 T subset, especially, seems to be a peculiar immunologic activation sign of acute rejection and it was observed before any decrement in graft function (6). Weimer et al. showed that pre-transplant CD4 T cell function and IL-10 responses of recipient cells were predictive of acute rejection (7). A decrease T cell subpopulation one month post transplantation in rejecting group of recipients has also been reported (8). Although numerous studies have been carried out, the precise mechanism and pathogenic role of peripheral T-cell subpopulations and cytokines in acute allograft rejection remains controversial. High serum IgA level in pre-transplant recipients is associated with better graft function after transplantation (9-10). In the present study, we compared the pre-transplant and post-transplant immunoglobulin levels and T cells subpopulations, B and NK cells in patients with or without rejection.

SUBJECTS AND METHODS

Patient selection: in order to evaluate risk factors, and predict the acute rejection episode, 16 non-diabetic kidney transplant candidates (4 females and 12 males, age = 20-65 yr, first time transplant) were selected. The transplanted patients were divided in two groups based on the rejection episode during 3 weeks post-transplant: group I (n = 9) without rejection and group II (n = 7) with a rejection episode. The immune parameters including serum immunoglobulins, IgG, IgM, IgA determined by nephelometric assay and IgE have been detected by ELISA method and T lymphocyte subpopulation, B cell and NK cell count were determined by flow-cytometry one day before transplantation and 45 days post-transplantation.

RESULTS

The results of this study (Table 1) in pre-transplant samples showed that the mean of serum IgE in group I patients is lower than that for group II of patients with rejection episode (220 ± 317 vs. 462 ± 464 IU/ml). However, serum IgA (282 ± 114 vs. 244 ± 108 mg/dl) and IgG (1361 ± 374 vs. 1201 ± 460 mg/dl) were higher in group I patients. The mean percentages of CD3 (62 ± 8 vs. 69 ± 12 , $P = 0.08$) and CD4 (35.8 ± 8.1 vs. 41.3 ± 3.2 , $P = 0.05$) in group I patients decreased in comparison to group II transplantation. The mean percentages of CD8, CD56 and CD20 in group I and II did not show significant differences.

The results of this study in post-transplant samples showed that the mean of serum IgE in group I patients without rejection episode is lower than that for patients in group II with a rejection episode (33 ± 29 vs. 166 ± 364 IU/ml). Serum IgA (209 ± 91 vs. 152 ± 54 mg/dl, $P = 0.08$) and IgG (1009 ± 364 vs. 703 ± 291 mg/dl, $P = 0.04$) in group I patients were higher than those for group II patients. The differences between percentages of CD3, CD4, CD8 and CD56 cells in group I and group II patients were not significant. CD20 cells increased significantly in group I patients compared to those for group II patients post transplantation ($15\% \pm 10\%$ vs. $10\% \pm 4\%$, $P = 0.03$).

Table 1. Immunological markers pre- and post-kidney allograft transplantation in rejecting and non-rejecting groups of recipients

Markers	Pre-transplantation			Post-transplantation		P value
	Group I N= 9	Group II N= 7	P value	Group I N= 9	Group II N= 7	
IgE IU	220 ± 317	462 ± 464		33 ± 29	166 ± 36	
IgG mg/dl	1361 ± 374	1201 ± 460		1009 ± 364	703 ± 291	P= 0.04
IgM mg/dl	106 ± 54	99 ± 79		143 ± 76	131 ± 95	
IgA mg/dl	282 ± 114	244 ± 105	P= 0.08	209 ± 91	152 ± 54	P= 0.08
CD3%	62 ± 8	69 ± 12	P= 0.08	62 ± 13	68 ± 11	
CD4%	35 ± 8	41 ± 3	P= 0.05	35 ± 12	40 ± 12	
CD8%	30 ± 6	31 ± 7		29 ± 8	30 ± 11	
CD56%	22 ± 12	23 ± 8		20 ± 10	19 ± 14	
CD20%	12 ± 3	12 ± 7		15 ± 5	10.6 ± 4.1	P= 0.03

DISCUSSION

Acute rejection is a well known complication of renal transplantation. In order to predict acute rejection post transplantation, T cell subsets, B cell and NK cell and serum immunoglobulin levels (IgE, IgG, IgM and IgA) have been evaluated in 16 patients pre-transplant and 45 days post-transplant in two groups of recipients. Group I (n = 9) without acute rejection and renal dysfunction and group II (n = 7) with an episode of acute rejection post transplantation. We found that pre-transplant high serum IgE level in recipient is probably associated with acute rejection episode; however it is necessary to work up with a larger sample size. In addition, serum IgA in pre-transplant samples of group I recipients was higher than that of group II which suggests that high level of pre-transplant IgA is associated with better graft outcome. This is similar to data presented by Susal et al. (9-12) and Susskind et al. (13). Most of the rejection episodes occurred during the first 2 weeks after transplantation. There were no significant differences in CD3 and CD4 T cells before and after transplantation, but CD3 and CD4 T cells increased in group II patients in pre- and post-transplant samples (P = 0.08 and P = 0.05, respectively). There were no significant differences in the percentages of CD8 T cells and CD56 NK cells in pre- and post-transplant samples in group I and group II patients. In our study the CD3 and CD4 T cells increased in group II recipients and it is suggested that elevated numbers in pre-transplantation predicts acute post transplantation rejection. In this regard, Valeri et al. reported a significant increase in CD4 T cell subsets in group II versus group I (6). Data reported by Shabtai et al. indicate that pre-transplant levels of activated CD4 significantly correlates with the time of onset of acute rejection after transplantation (14). A decrease in all T-cell subpopulations as well as NK cells has been reported in both groups (rejecting and non-rejecting), the decrease was more pronounced in rejecting patients than in stable patients (8). Olausson et al. reported that patients with rejection episodes had significantly lower levels of T helper cells than recipients without rejection (15). Although numerous studies have been carried out, the precise mechanism and pathogenic role of peripheral T-cell subpopulations in acute renal allograft rejection remains controversial. In conclusion our data showed that immunological monitoring including immunoglobulins and immunophenotyping of lymphocytes by CD markers could be valuable in prediction of rejection. Nevertheless for better clarification of this issue further studies should be carried out with larger sample sizes.

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