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Review Article

Should the First Rejected Kidney Implant be Removed?

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Abstract

Renal transplantation (TX) is widely used as a definitive therapy for chronic, end-stage organ failure. T cells are pivotal in rejection (RX), and RX is a process whereby donor tissue is recognized and destroyed by the host immune system. Within a rejecting graft it is likely that high concentrations of IL-2 are present. The binding of interleukin 2(IL-2) to its receptor (IL-2R) on human T cells constitutes the key regulatory event in the initiation and maintenance of the immune response.

The receptor, IL-2R, is found in two forms: cellular and soluble. The surgical removal of a transplanted kidney following RX or failure can be hazardous. Two surgical techniques were applied: extracapsular and intracapsular removal. The technique of kidney transplant removal by either the intra- or extra-capsular route of the exact timing of the operation are important features for safe treatment of patients with end-stage graft failure.

The results of the report are a prospective study on 21 renal TX recipients, and show that nephrectomy of previous TX kidney will reduce the levels of four markers in serum and urine.

Keywords: Transplant; Renal transplant; Therapy; Immune response; Kidney; Immunology.

Abbreviations

sIL-2R:Soluble Interleukin 2 Receptor; CRP:C-Reactive Protein; TX:Transplant; RX:Rejection; INFX:Infection; Cys. C:Cystatin C; UCRE:Urine Creatinine; S/creat:Serum Creatinine; ELISA:Enzyme Linked Immuno-Sorbent Assay; GFR:Glomerular Filtration Rate.

Introduction

Renal transplantation (TX) is widely used as a definitive therapy for chronic, end-stage organ failure. Improved survival rate for transplanted kidneys has been attributed to better immune-suppression techniques [1]. However, not all renal TX are successful as

they become RX, necrotic, and not functional. The question whether the rejected TX should be removed or not is discussed.

Patients and methods

Six or more consecutive serum and urine samples were taken from 21 renal TX patients at the Sheffield Kidney Institute (SKI). Samples were divided into three groups (15-1st time TX recipients, 2-2nd TX recipients with first TX removed, and 4-2nd TX recipients with 1st TX in situ).

Samples were analyzed by the following:

1. Roche CREA Unimate 5.
2. IDS Diaclone sIL-2R ELISA kit.
3. Roche CRP.
4. Dako Cystatin C PET Kit.

Serum creatinine levels were taken directly from patients' notes.

The effect of nephrectomy on serum and urine markers of a previous implant prior to TX was analyzed regardless whether TX patients were treated for RX or infection (INFX).

All of the 21 TX patients were divided into three categories:

a) TX recipients who have their 1st TX in situ.
b) TX recipients who have had their 1st TX removed prior to receiving the new TX.
c) Those who are receiving a renal TX for the first time.

Geometric means (GM) were used in all calculations for skewed data and it was achieved by calculating the Log10 for each data group. Marker levels were analysed using Student t-test, and the significance level was taken at $p<0.05$.

Results

Comparisons of Log_{10} transformed GM results Table 1, between groups A and B, and between A and C indicated that all markers levels, except for CRP levels in group B ($p>0.05$), were significantly increased in TX recipients who received a new TX but had their previous TX in situ ($p<0.001$ for UCRE and U/sIL-2R, and $p<0.0001$ for the rest of markers).

Samples		U/sIL-2R (pg/ml)	S/sIL-2R (pg/ml)	CRP (mg/L)	S/creat. (mg/L)	Cys. C (mmol/L)	UCRE (mmol/)
A	2nd TX, 1st in situ n=4	12491 ± 2830	13139 ± 1592	33 ± 11	554 ± 59	4.66 ± 0.48	10673 ± 1480
B	2nd TX, 1st out n=2	5906 ± 839 <0.0001	8136 ± 809 <0.001	22 ± 27 >0.05	233 ± 104 <0.0001	1.85 ± 0.81 <0.0001	6377 ± 1272 <0.001
C	First TX recipient n=15	6767 ± 657 <0.001	8134 ± 449 <0.0001	13 ±3 <0.0001	258 ± 43 <0.0001	1.53 ± 0.30 <0.0001	5655 ± 664 <0.0001

Table 1: Geometric mean (GM) ± 1.96 SEM results of log10 transformed data of 1st and 2nd transplant (TX) recipients–Effect of leaving 1st TX in situ on markers levels. *Comparisons between groups A vs. B and A vs. C were done using student t-test; and the significance level p values are shown.

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All GM values in group A were outside the normal TX ranges. TX recipients who had a nephrectomy of their 1st TX show levels similar to those recipients who had a TX for the first time. Statistical analysis between groups B and C showed no significant difference between markers levels ($p>0.05$) except for CRP ($p<0.05$).

Discussion

TX patients with previously rejected implants have increased markers levels that may be disadvantageous in that they may obscure diagnosis of increases in the markers' levels post-TX. Continuous CRP synthesis (when groups A and C were compared) may have an effect in acute RX through its activity on complement activation, which leads to tissue injury and graft loss [2]. Increased levels of creatinine due to low GFR has a life-limiting effect [3]. Some workers argued that leaving a previous transplant in situ in the asymptomatic patient will not have a harmful effect [4-6], but all preferred to remove previous rejected transplants when complications arise [4-7]. One study result showed that chronically rejected renal allografts, even calcified, maintained some endocrine activity in the absence of any excretory function [7].

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