Pre-Transplant Donor Specific Unresponsiveness in a Kidney Retransplant Recipient

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ABSTRACT
A living related kidney transplant recipient, who showed very characteristic findings in immunologic study, was reported. This patient was a retransplant recipient. First graft of this patient was his mother's kidney, and the second graft was his older sister's kidney. HLA compatibility between the patient and the second donor was one haplotype identical. Although the patient was responsive in mixed-leukocyte-culture (MLC) against the second donor before first transplantation, MLC and cell-mediated-lympholysis (CML) tests before retransplantation showed specific unresponsiveness to the second donor. During 36 months after retransplantation, no rejection episodes nor any complications have been observed.

INTRODUCTION
According to previous reports, survival of the second graft in kidney recipients was almost the same or relatively lower than that of first graft. However, almost of them were cadaveric transplant patients. Prognosis of the second graft from a living related donor was not yet well known due to the small number of reported cases. In this study, we reported on a kidney retransplant recipient grafted from a living related donor. This patient showed specific unresponsiveness in CML against the donor before second transplantation, and he has been maintaining very good graft function.

PATIENT
The patient was a 35 years old male. He had received a kidney allograft from his mother in 1974. In the ensuing 3 years and 4 months, the renal function of this graft gradually deteriorated due to chronic rejection, with onset of renal failure and returned to hemodialysis at 5 years and 8 months. The patient then was given a kidney from his older sister. In a

Fig. 1. HLA family study of the patient

HLA family study, this second donor shared the same mismatched haplotype detected in the first donor, and her other haplotype was shared with the recipient (Fig. 1). From this results, the risk of hyperacute rejection was suspected. However, the serum of the patient had no cytotoxic antibodies against the second donor's T or B cells. Although MLC response of the patient against the second donor was high (S. I.: 33.9) before first transplantation, it decreased to very low response (S. I.: 2.4) before the second transplantation. CML reactivity against the second donor was also extremely low (-4.1%), whereas the reactivity against unrelated cells was 23.7% (Table 1). This suggest that spe-
Table 1. MLC and CML reactivity of the retransplant patient before the first and second transplantation

<table>
<thead>
<tr>
<th>Cell mixture</th>
<th>1st transplant</th>
<th>2nd transplant</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>MLC (S. I.)</td>
<td>MLC (S. I.)</td>
</tr>
<tr>
<td>R·D1m</td>
<td>61.8</td>
<td>2.0</td>
</tr>
<tr>
<td>R·D2m</td>
<td>33.9</td>
<td>2.4</td>
</tr>
<tr>
<td>R·Um</td>
<td>26.3</td>
<td>17.9</td>
</tr>
</tbody>
</table>

R: recipient  
D1: first donor (mother)  
D2: second donor (elder sister)  
U: unrelated person  
m: mitomycin C treatment  
S. I: stimulation index

Specific unresponsiveness to the second donor in generation of cytotoxic lymphocyte exist in this recipient. The second transplant was therefore performed at 6 months after the reinsitution of hemodialysis. During the 36 months following retransplantation, no rejection episodes nor any complications have been observed. CML reactivity against the second donor remained at less than 10\%, while the reactivity against third-party cells has ranged from 23.3\% to 49.8\% (Fig. 2).

**DISCUSSION**

In organ retransplantation, presensitization by the first graft is one of the most important risk factors associated with acceptance of the second graft. If the patient, who is going to receive the second transplant, has cytotoxic antibodies against the donor by sensitization following the first graft, the possibility of hyperacute rejection will be very high. Conversely, if the sensitization brings about enhancing effect such as
that associated pretransplant blood transfusion, successful prognosis will be expected. Casali\(^1\) reported that graft survival of the patients receiving both transplants from living related donors was better than that of the patients receiving both grafts from cadavers. The patient presented in this study received both of the first and the second graft from living related donor, and showed donor specific unresponsiveness in MLC and CML tests. Moreover he had no cytotoxic antibody against the second donor. The second donor had the same mismatched haplotype (A9, Bw59, Cw1 and DRw9) as that of the first donor. The specific unresponsiveness against the second donor before retransplantation therefore must be brought about by this mismatched haplotype.

We had previously demonstrated that many successful kidney transplant recipients showed donor specific CML unresponsiveness\(^2\). Several authors\(^3,7\) reported the same results. This phenomenon indicates that generation of cytotoxic T lymphocytes against donor cells specifically decreased. Such immunologic unresponsiveness must be one of the most important mechanisms for successful organ transplantation for HLA incompatible recipients. Our patient had already obtained specific unresponsiveness in CML against the second donor prior to the grafting from the donor. This unresponsiveness greatly contributed to successful retransplantation. CML is very good indicator to know the cellular immune response against donor, and it must be very useful to test specific immune response prior to retransplantation from living related donor.

**REFERENCES**