Hiroshima Journal of Medical Sciences
Vol. 33, No. 4, 775-777, December, 1984
HIJM 33-111

Pre-Transplant Donor Specific Unresponsiveness in a Kidney Retransplant Recipient*)

Kiyohiko DOHI, Eiji ONO, Yasuhiko FUKUDA,
Toshimasa ASAHARA, Hiroshi YAHATA and Haruo EZAKI

The Second Department of Surgery, Hiroshima University School of Medicine, 1-2-3, Kasumi, Minami-ku, Hiroshima 734, Japan

(Received September 25, 1984)

Key words: Kidney transplantation, Mixed leukocyte culture, Immune tolerance

ABSTRACT

A living related kidney transplant recipient, who showed very characterstic 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[4-6], survival of the second graft in kidney recipients was almost the same[4,5] or relatively lower[6] 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 tranplantation, 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 ensuring 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 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 aginst 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 aginst the second donor was also extremely low (−4. 1%), wherease the reactivity against unrelated cells was 23. 7% (Table 1.). This suggest that spe-

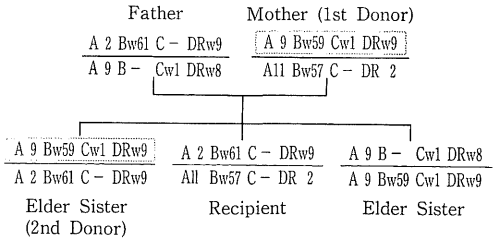

Fig. 1. HLA family study of the patient

*) 土肥雪彦, 小野栄治, 福田康彦, 浅原利正, 八幡浩, 江崎治夫：ドナー特異的 unresponsiueness を呈した腎再移植症例

Table 1. MLC and CML reactivity of the retransplant patient before the first and second transplantation

cell mixture	1st transplant	2nd transplant	
	MLC (S. I.)	MLC (S. I.)	CML (% cytotoxicity)
$R \cdot D_{1m}$	61.8	2.0	−10.2
$R \cdot D_{2m}$	33.9	2.4	−4.1
$R \cdot U_m$	26.3	17.9	23.7

R : recipient
D_1 : first donor (mother)
D_2 : second donor (elder sister)
U: unrelated person
m: mitomycin C treatment
S. I : stimulation index

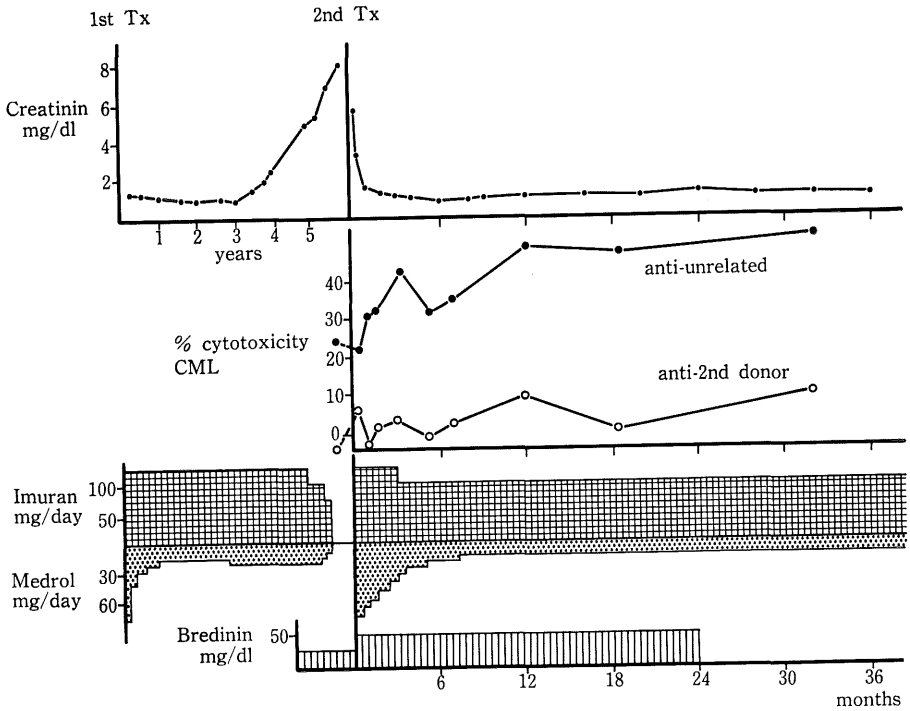

Fig. 2. Clinical course of the retransplant patient

cific 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 reinsituation 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 suvival 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

1. **Casali, R., Simmons, R. L., Ferguson, R. M., Mauer, M. and Najarian, J. S.** 1976. Factors related to success of failure of second renal transplants. Ann. Surg. **184** : 145-154.
2. **Dohi, K., Ono, E., Fukuda, Y., Asahara, T., Yahata, H. and Ezaki, H.** 1984. Immunological characteristics of recipients with long-term-functioning kidney graft of more than three years. Hiroshima Journal of Medical Science **33** :
3. **Goulmy, E., Persijin, G., Blockland, E. and van Rood, J. J.** 1981 Cell mediated lympholysis in renal allograft recipients. Transplantation **31** : 210-217.
4. **Marni, A., McMaster, P., Evans, D. B. and Calne, R. Y.** 1979. Ts ti really worth re-transplanting patients? Proc. EDTA **16** : 352-358.
5. **Opelz, G. and Terasaki, P. I.** 1978. Absence of immunization effect in human-kidney retransplantation. New Eng. J. Med. **229** : 369-374.
6. **Rook, A., Prichard, S., Morehouse, D. D., Guttman, R. D. and Huchinson T. A.** 1979. Results of retranplantion in individuals who received two successive cadaver kidneys. Canadian Journal of Surgery **22** : 519-522.
7. **Wonigeit, K. and Pichlmayr, R.** 1977 Specific defect in the capability to *p*enerate cytotoxic effector cells in vitro after organ transplantation in man. Dialysis and Transplantation **6** : 58-61.