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GENERATION OF CML NEGATIVITY AFTER PLANNED BLOOD TRANSFUSION IN RENAL ALLOGRAFT RECIPIENTS

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INTRODUCTION

Kidney graft survival can be improved by blood transfusion (1, 2, 3) and by HLA-DR matching (4, 5, 6, 7). Since cell mediated lympholysis (CML) reactivity against the donor may be a good in vitro correlation of the homograft reaction, we have investigated the influence of blood transfusion and HLA-DR matching on CML reactivity. In this study CML activity of the kidney recipients against the splenocytes of the specific kidney donor was studied serially at various times before and after blood transfusion and renal allografting.

METHODS AND MATERIALS

We used a standard CML assay, by which peripheral blood lymphocytes of the recipients were sensitized in vitro against the splenocytes of the specific donor, and against HLA-A, -B, -C and DR incompatible control cells of unrelated healthy individuals. We measured the percentage of the donor specific and non-specific lysis against PHA stimulated blast cells.

Longitudinal and single sample studies were performed. For the longitudinal studies serial samples of peripheral blood lymphocytes were taken from the recipients at several time intervals, as follows: a. before blood transfusion b. at different times after blood transfusion c. on the day of transplantation d. after different times after transplantation and e. in the case of rejection, after transplantectomy. All those samples, including the spleen cells of the specific donor were frozen and stored in liquid nitrogen. All the combinations with one particular patient were tested on the same day in the same experiment.

RESULTS

Of a total of 50 donor-recipient combinations: 23 were studied longitudinally and 27 singly. Figure 1 shows an example of a long-term study of a

patient who was immunized with one blood transfusion at 91 days before transplantation. We showed that the donor-specific CML reactivity changed from 39% before transplantation, to 14% two weeks after transplantation. This CML activity was donor-specific, because the anti-control cells lysis stayed at a constant level. In figure 2 another example is given in which the specific anti-donor lysis comes back to the pre-transfusion level. These two examples have been taken from a total of 23 donor-recipient combinations studied longitudinally. Both patients have a good functioning graft for more than one year. The relationship between CML non-reactivity and renal allograft survival can be more readily studied by calculating the decrement (or increment) in the % CML in relation to the baseline level prior to blood transfusion.

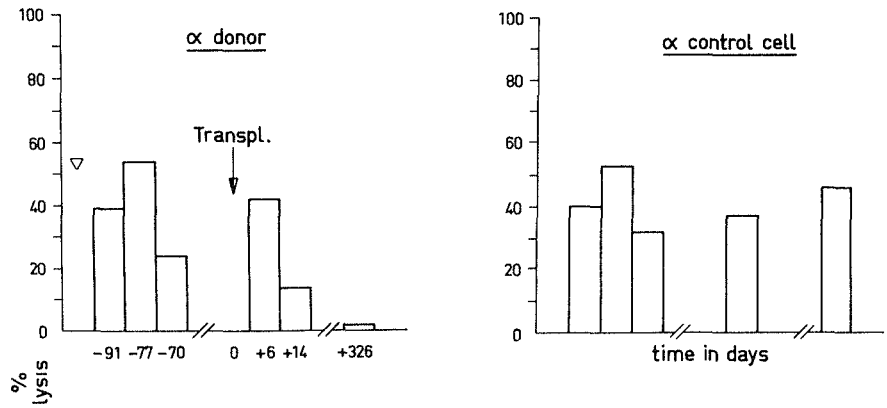

Fig. 1. Donor specific C.M.L. reactivity before and after transplantation.

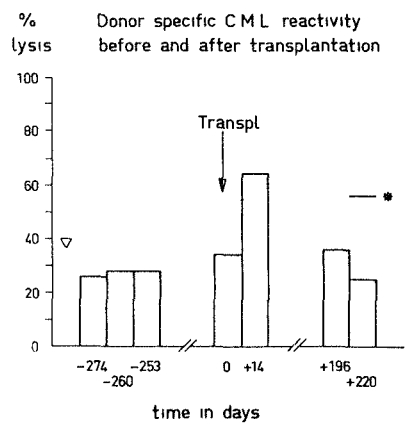

Fig. 2. — * = anti-control cell lysis.

This data is summarized in figure 3 for 23 patients studied longitudinally. The increment of decrement is only shown for the most recent sample in the longitudinal study.

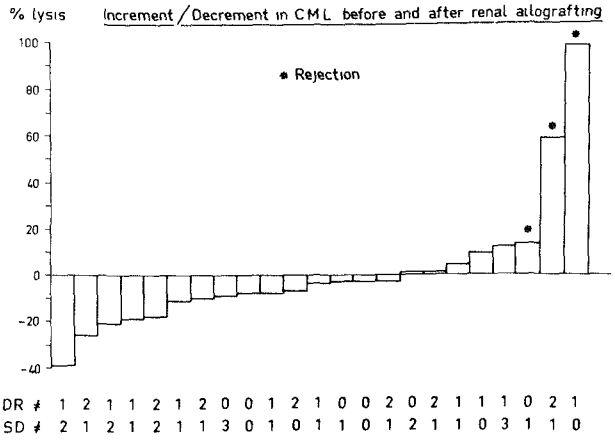

Fig. 3. The 3 cases in which the kidney was rejected, CML activity was tested after transplantectomy.

In view of the blood transfusion policy, we investigated (in the total group of 50 patients) whether there was a relationship between the number of blood transfusions given and the occurence of CML in the most recent sample. In this case non-reactivity was defined as a CML kill equal to or below 10%. We found CML non-reactivity more frequently in multi-transfused patients, however the data which are given in table 1 are not significant. An incidental observation was that there was a transient non-specific rise in CML reactivity following a single transfusion in non sensitized recipients (observed in 7 out of 23 cases)

TABLE 1

RELATION BETWEEN THE NUMBER OF BLOOD TRANSFUSIONS AND THE OCCURENCE OF CML NON-REACTIVITY

Blood transfusions			
		1	more than 1
CML	+	7	7
	-	8	22

(functioning grafts only)

TABLE 2

RELATION BETWEEN HLA-DR MATCHING AND CML NON-REACTIVITY

HLA-DR mismatches				
		0	1	2
CML	+	3	7	4
	-	5	13	13

(functioning grafts only)

The important role of the HLA-DR matching between donor and recipient and its in vitro relevance has been studied in the total group of 50 patients. The results given in table 2 in which only the functioning grafts are presented indicate, that there is no clear cut relationship between HLA-DR matching and CML negativity.

CONCLUSIONS

The importance of an in vitro correlation with the cadaveric kidney graft survival has become a major immunological topic. Many groups have already investigated the occurence of direct and indirect CML activity in renal allograft donor-recipient combinations. With special regard to our longitudinal studies, the change in CML activity (e.g. decrement in lysis from pretransfusion to post-transplantation level, figure 3) shows similarity to the observations of Wonigeit (8) and Thomas (9). An important point is that the CML non-reactivity could already be demonstrated within a short period after grafting (figure 1). The correlation between the number of blood transfusion and the absolute % lysis against the donor is so far not significant, but if the same trend continues in a more extensive study, a significant association might arise.

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