LITERATURE CITED


Received 25 April 1984. Accepted 11 July 1984.

OCCURRENCE OF POSTTRANSPLANT DONOR-SPECIFIC CELL-MEDIATED LYMPHOLYSIS NONREACTIVITY IN RENAL ALLOGRAFT RECIPIENTS WITH PERIOPERATIVE TRANSFUSIONS ONLY

Lymphocytes from renal allografted patients can display specific cell mediated lympholysis nonreactivity (CML-NR) in vitro toward the splenocytes of the specific kidney donor (1–7). Findings by others and by our group indicate clearly that occurrence of donor specific CML-NR, as manifested in vitro by patients’ posttransplant lymphocytes, correlate significantly with good renal function. Our studies (4, 8) included a group of patients receiving only one planned blood transfusion before kidney transplantation and another group receiving more than one blood transfusion before kidney transplantation. In both groups of pretransplant transfused patients donor-specific CML-NR posttransplant was observed (4); the occurrence of CML nonreactivity did not significantly correlate with the difference between one, or more than one, pretransplant blood transfusion.

Numerous reports have been published concerning the beneficial effect of pretransplant blood transfusions on cadaveric kidney graft survival (9). Moreover, a prospective study by Fassbinder et al. (10) demonstrated that the graft survival in patients transfused only perioperatively did not differ significantly from that in patients transfused preoperatively and perioperatively. The latter in vivo results actually prompted us to investigate whether or not absence of cytotopic activity of patients’ posttransplant lymphocytes toward the specific kidney donor splenocytes occurred also in perioperative transfused patients. Furthermore, we analyzed whether the occurrence of CML-NR in each patient could be correlated with renal function.

Twelve kidney recipients, 10 male and 2 female patients, received their first cadaveric renal allograft. They were only transfused 0–6 hr before transplantation, and they had never been transfused previously (10). Both female patients had a history of previous pregnancies. The mean age of the patients was 42 years (range: 30–54 years). The 12 male donors, 9 male and 3 female donors, had a mean age of 25 years (range: 16–47 years). All recipients were treated with a standard immunosuppressive regimen—i.e., prednisone and azathioprine. Rejection episodes were treated with high doses of methylprednisolone i.v. A retrospective analysis, in which these 12 unrelated donor-recipient combinations were tested in CML, was carried out without prior information concerning their clinical status. Beside the measurements of specific cytotopic activity of the patient’s posttransplant lymphocytes toward the splenocytes of their specific kidney donor (Table 1), two additional control combinations were performed. First, in order to control the cytotopic capacity of recipient cells, the latter cells were sensitized in vitro with irradiated HLA-A, -B, -C, and -DR-incompatible cells of an unrelated healthy subject as stimulator cells; second, in order to determine whether or not CML nonreactivity could have been caused by a defect of the stimulatory capacity of the kidney donor splenocytes, lymphocytes of healthy blood donors selected at random were used as responder cells and cultured with the irradiated splenocytes as stimulator cells.

The CML technique used has been described previously in detail (11). Percentages equal to or below 10% specific 51Cr release were considered to be negative.

Table 1 shows the results of the CML assays carried out with the lymphocytes from 12 patients who had been transfused perioperatively only. They were studied between 8–41 months posttransplantation.

Eleven of the 12 patients with functioning grafts were found to be CML nonreactive toward the splenocytes of the specific kidney donor, although they were positive with the lymphocytes
from random donors (Table 1). The occurrence of CML-NR in patients 1–9 appeared to correlate with successful function of the kidney graft.

Two patients (10 and 11) with a functioning graft still showed a positive CML, 19 and 28 months posttransplantation respectively, toward the specific kidney donor splenocytes. These two patients had been suffering repeatedly from severe rejection crises, but so far had not lost their grafts. The observed positive CML values in these patients indicate that antidonor specific CTLs were still circulating.

Among the 12 perioperative transfused patients studied, one (patient 12) rejected his graft 6 weeks posttransplant. An extremely high level of antidonor lysis was observed even 33 months after rejection.

Additionally, the lymphocytes of the latter patient displayed a high cytolytic capacity against control cells (Table 1). Increased levels of cytotoxicity against random control cells by lymphocytes from patients who rejected their kidney were also observed previously (4).

We have investigated the influence of perioperative transfusions on the occurrence of posttransplant donor-specific CML-NR in a group of renal allografted patients who were transfused perioperatively only.

Our results indicate that development of posttransplant donor-specific CML-NR also occurs in patients who have been transfused perioperatively only, and that CML-NR is associated with good renal function. The results are comparable with those found in the pretransplant transfused group of patients described earlier (4). Thus, lymphocytes from renal allografted patients with good functioning grafts, whether they have been transfused perioperatively only or pretransplantation, display donor-specific CML-NR in vitro.

The tolerant state observed in vivo—as well as in vitro by CML—in the perioperatively transfused group of patients leads us to question the exact role of the blood transfusion on the development of donor-specific CML-NR. With regard to the study presented here, it seems unlikely that suppression of the cytolytic activity specifically towards the kidney donor splenocytes, as observed in CML, could be an effect of the blood transfusion, from a donor selected at random, given 0–6 hr before transplantation. If that were so, suppressor cells would have to be generated within a very short period. Of the three patients who remained CML-reactive, one had rejected his graft before testing and the two others had repeated rejection crises. We have previously shown that such CML reactivity can increase during rejection crises (4). Longitudinal studies were not performed on this clinical material, however. It is not known whether nontransfused allografted patients with good renal function also exhibit CML nonreactivity in vitro.

Acknowledgments. We wish to thank the staff and administrative personnel of the Eurotransplant Organization for their organizational help and support.

E. GOULMY
E. BLOKLAND

1 Department of Immunohaematology, University Hospital, Leiden.