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Retrospective Tests of B-Cold Lymphocytotoxins and Transplant Survival at a Single Center

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IN A PREVIOUS study we showed that patients who have antibodies reactive to B lymphocytes in the cold have a higher kidney transplant survival rate than patients with no preformed cytotoxins.¹ This result is of potential importance because antibodies to B lymphocytes may possibly be detecting enhancing antibodies. Such antibodies that help a transplant are particularly relevant because of the recent finding that immunization by transfusion results in higher transplant survival rates.² In order to reexamine this finding, sera from over 203 patients from a single transplantation center were tested. The previous study had been based on patients accumulated from 27 centers. It was hoped that a more uniform treatment of these patients and the increased numbers of cases would either confirm or refute the earlier findings.

MATERIALS AND METHODS

Frozen serum samples stored at -80°C for periods up to 7 years from 203 recipients were investigated. The samples were taken within 1 week prior to transplantation. Of the transplants, 129 were grafts from cadaver donors, and 74 were one-haplotype-identical related transplants. Transplants from HLA-identical sibling donors were disregarded for this study.

The isolation and testing of B and T lymphocytes have been described.³ All sera were tested under three conditions: that is, B lymphocytes at 5°C and B and T lymphocytes at 37°C .

The sera were divided into three types of reaction patterns (Table 1). The B-cold pattern consisted of reactions of B lymphocytes at 5°C and negative reactions for B and T lymphocytes at 37°C . The B-warm pattern was defined as reactions of B lymphocytes at both temperatures with no reactions of T lymphocytes at 37°C . The T-warm pattern was defined as a reaction with B lymphocytes at both temperatures and T lymphocytes at 37°C .

RESULTS

Of the 203 sera tested, 21 (10.3%) showed the B-cold pattern, 29 (14%) showed the

B-warm pattern, and 15 (7%) showed the T-warm pattern; the remaining 138 patients (68%) did not react with either T or B lymphocytes. These percentages of distribution for the four different categories of patients are quite similar to those obtained in two earlier studies.^{1,4} Thus there is some assurance that storing sera in different ways over fairly long periods of time did not significantly change the types of antibody detectable in the sera. It should be noted, however, that our earlier study also dealt with sera stored as long as 3 years.

As shown in Fig. 1, patients who had antibodies to B lymphocytes in the cold had a higher transplant survival rate at 1 year (80%) than patients with no antibodies (69%). The difference is admittedly small, and the number of patients with the B-cold antibody pattern is limited.

The differences among the four categories of patients with cadaver-donor transplants were marked (Fig. 2). Those patients with the B-cold pattern had a 1-year survival rate of 82%, as compared with 58% for patients with no antibodies ($p < 0.07$). Those with the B-

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Supported in part by Grants AM-02375, AM-17260, and AM-07772 from the National Institute of Arthritis and Metabolic Diseases, Contract N01 CM 02092 from the National Cancer Institute, research grants from the Veterans Administration, and Grants RR-00051 and RR-00069 from the General Clinical Research Centers Program of the Division of Research Resources, National Institutes of Health.

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0041-1345/79/1101-0203\$01.00/0*

Table 1. Three Reaction Patterns and Their Specificities

| Pattern | Reaction | | | Specificity |
|---------|----------|--------|--------|--------------------|
| | B 4°C | B 37°C | T 37°C | |
| B-cold | + | — | — | Non-HLA |
| B-warm | + | + | — | HLA-A, -B, -C, -DR |
| T-warm | + | + | + | HLA-A, -B, -C |

warm and T-warm patterns had 37% and 36% survival, respectively, at 1 year.

DISCUSSION

In comparison with our previous study, the general results of this study from a single center are quite similar. In this series the patients with antibodies reactive to B lymphocytes only in the cold had higher transplant survival rates. Among related-donor transplants the difference in survival rate was not significant in either study. With the cadaver-donor transplants a significant difference was found in this study as well as in the study reported previously. It should be noted that an independent study of patients from the Mayo Clinic also confirmed the original observation.⁵ In that study the B-cold pattern was found to be significantly associated with prolonged survival in the recipients with related donors but not in the recipients with cadaver donors.

In the current investigation the patients who had preformed warm cytotoxins to either

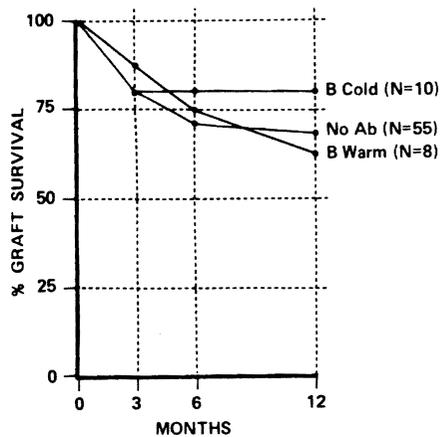


Fig. 1. Actuarial graft survival for one-haplotype-matched related transplants according to type of preformed cytotoxins.

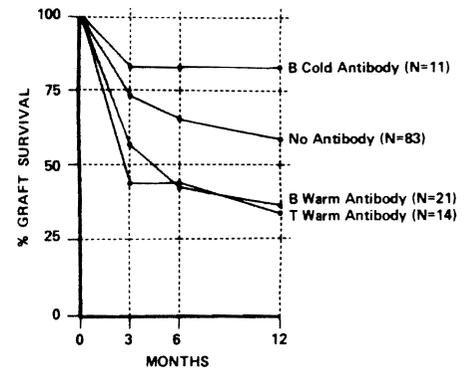


Fig. 2. Actuarial graft survival for cadaver-donor transplants according to type of pretransplant cytotoxins.

B or T lymphocytes were noted to have a lower graft survival rate than those with no cytotoxins. This lower survival rate can be attributed either to the fact that those patients who make antibodies were more responsive or to the fact that weak positive cross-matches or latent positive cross-matches were not detected in these patients.

It is also important to note that positive cross-matches to B lymphocytes should be divided into the two categories⁶ for cytotoxins active in the cold that are not deleterious, whereas those reactive in the warm appear to be associated with low transplant survival rates. It seems now that warm B-cell cytotoxins are directed against HLA-DR, or in many instances against HLA-A, -B, and -C specificities.⁷ HLA-A, -B, and -C antibodies that are too weak to react against T lymphocytes have now been shown to react to B lymphocytes. Thus a positive cross-match to B cells reactive in the warm would be assumed to be a contraindication to transplantation. Many of the transplants with positive B-cell cross-matches that have functioned may have been in patients with non-HLA antibodies reactive in the cold.⁸⁻¹¹

The present retrospective studies suggest that the cold antibodies to B lymphocytes can be monitored, particularly after such treatment as transfusions, to determine the ideal state prior to transplantation. Following blood transfusions, the monitoring of patients with antibodies to B and T lymphocytes may be

important in knowing when to stop the immunization and when to continue it.

SUMMARY

Sera from 203 recipients prior to transplantation were examined against a panel of 30 T and B lymphocytes at 5°C and 37°C. Those patients classified as having B-cold cytotoxins only had higher 1-year transplant survival rates from cadaver donors (82%) than

patients with no antibodies (58%) or patients with antibodies reactive to T and B lymphocytes in the warm (37%). These results based on transplants from a single center confirm earlier studies derived from patients in 27 centers.

ACKNOWLEDGMENT

The authors wish to acknowledge the excellent technical assistance of Simon Prince, Mark Hermes, Larry Cardman, and Yoshi Arai.

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