Changes in Cell Surface Markers in Human Small Bowel Transplantation With FK 506

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GRAFT-VERSUS-HOST disease (GVHD) and allograft rejection in human small bowel transplantation (SBT) are not yet fully described. These complications may prevent successful SBT. Immunohistochemical as well as histologic studies could be valuable to interpret these biologic processes. Therefore, in this study, we monitored the replacement of donors' lymphocytes by recipients' in the small bowel and the migration of donor lymphocytes in the peripheral circulation (PC), and characterized the cell surface markers of the graft-infiltrating cell, endothelial cell, and epithelial cell using a variety of monoclonal antibodies (MAb).

MATERIALS AND METHODS

The subjects of this study were five SBT patients treated with FK 506. One patient received the small bowel allograft alone, and the others received the liver and small bowel allografts from the same donor. Blood samples were collected daily for 60 days and lymphocytes were separated by the Ficoll gradient centrifugation. Serial biopsies of allografts were taken from the patients. The immunostaining was performed using the MAb against the mismatched HLAs between donor and recipient (One Lambda, Los Angeles, Calif): anti-CD3, CD4, CD8, δT, CD19, macrophage, HLA-ABC, HLA-DR, and ICAM-1 (Dako, Santa Barbara, Calif).

RESULTS

Clinical GVHD was not observed in our first five patients within 6 months. Replacement of donors' lymphocytes by recipients' in the small bowel was completed within 12 weeks in all cases. The percentage of donor lymphocytes in PC revealed 9% to 12% at the peak; however, they disappeared at 54 days after SBT at the longest.

$CD3^+DR^+$ cells increased significantly in the lamina propria and epithelial glands during the rejection. $CD8^+$ cells were also predominant, and macrophage infiltration was significant. $CD19^+$ cells were not detected in lamina propria. In contrast, $CD3^+$ cell increase was minimal in lamina propria and epithelial glands during the nonrejection period. Partial T cells expressed DR antigen. The expression of HLA-DR in the epithelium and ICAM-1 in small vessel and lamina propria was enhanced during both rejection and nonrejection episodes.

DISCUSSION

It was reported that GVHD was well-controlled in SBT in the rat[1] and bone marrow transplantation in humans[2] treated with FK 506. Although transitional donor lymphocytes were seen in PC, our patients did not develop clinical GVHD after SBT. These results suggest that, under appropriate immunosuppression, the immunosurveillance system in the host could eliminate donor lymphocytes resulting in the absence of clinical GVHD.

The main effector cells found during rejection in SBT patients seem to be macrophages and $CD8^+$ lymphocytes. The expression of HLA-DR and ICAM-1 in the epithelium did not reflect the magnitude of rejection episodes. Therefore, to characterize graft-infiltrating lymphocytes, particularly activated T lymphocytes and macrophages in conjunction with cytokine monitoring,[3] may be of great importance in understanding rejection after SBT.

REFERENCES

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