1350

Histologic Monitoring of Human Small Bowel Allografts With Clinical Correlation

K. Nakamura, S. Todo, K. Abu-Elmagd, J. Reyes, A. Tzakis, J.J. Fung, T.E. Starzl, and A.J. Demetris

ADVANCES in surgical techniques and the introduction of the newer, more powerful immunosuppressants have resulted in the successful clinical application of small bowel transplantation.[1-3] This study focused on the routine histologic monitoring of small bowel allografts using serial endoscopic biopsies. Histopathologic findings, effectiveness, and the limitations of mucosal biopsies as a monitoring tool are discussed.

MATERIALS AND METHODS

Between May 2, 1990 and August 21, 1991, a total of nine patients underwent small bowel plus liver (n = 8) or small bowel transplantation alone (n = 1) at the University of Pittsburgh. There were three adults (ages 21 to 31 years) and six children (ages 1 to 4 years) comprised of four males and five females. All patients were treated with FK 506 and steroid therapy.

Routine H&E sections of serial endoscopic biopsies of the allograft small bowel and liver were examined in all patients. Histological parameters assessed included: the degree and type of inflammation above that normally present; inflammatory gland or crypt infiltration and damage; pericapillary or perivenular lymphocyte cuffing and subendothelial infiltration; architectural distortion; ulceration of the epithelium, villous blunting, mucous, and parietal cell loss; fibrosis; and regenerative epithelial changes (ie, nuclear stratification, increased N:C ratio). Histological evaluation of liver allograft biopsies was according to previous publications.[4]

RESULTS

Discordance between rejection of the small bowel and liver was occasionally seen, with rejection of the small bowel allograft preceding that of the liver, in the early periods. The sole patient treated with a small bowel allograft alone experienced more frequent and more severe episodes of rejection than those who were also given a liver.

Specimens near the stoma opening often showed acute and chronic inflammation with fibrosis, which at times was difficult to differentiate from rejection.

Previous experience with animal small bowel allografts had suggested that rejection may manifest clinically as mucosal ulcerations and sepsis.[5,6] A similar scenario was observed to various degrees in three of the five patients, most frequently in the early (<100 days) posttransplant period. However, organisms were not uniformly cultured from the peripheral blood.

Histopathologically, during the above episodes, biopsies revealed an increase in mononuclear cells in the lamina propria and submucosa (when present). The infiltrate consisted primarily of blastic and smaller lymphocytes cuffed around small veins and infiltrating glands and crypts. Epithelial cell necrosis and reparative epithelial changes such as irregularly shaped lumens, mucous cell depletion, nuclear stratification, and an increased N:C ratio were also seen. When severe, architectural distortion with villous blunting and focal ulceration with resultant neutrophil plugging of capillaries and pseudomembranes were seen. Treatment of such patients with bolstered immunosuppressive therapy resulted in resolution of the clinical symptoms and a normalization of the endoscopic appearance of the small bowel mucosa. Resolution of the infiltrate and reparative changes were noted in follow-up biopsies.

In later biopsies, changes interpreted as ongoing immunologic damage (ie, lymphocytic cryptitis and infiltration of glands) were less frequently accompanied by clinical symptoms, making pathologic diagnosis less certain. Detailed histologic findings will be presented elsewhere.[7]

DISCUSSION

This early study showed that endoscopic biopsy monitoring was able to correctly identify rejection as a cause of graft damage after human small bowel transplantation. More severe episodes, which tended to occur earlier, were more often accompanied by clinical symptoms and were easier to diagnose by biopsy. Later, presumed pathologic evidence of rejection was less often accompanied by clinical symptoms, and an unequivocal pathologic diagnosis of rejection was more difficult. Other animal and human studies, including the one presented here, have shown that potent immunosuppression in the early posttransplant period fosters orderly replacement of the graft mucosal lymphoid tissue by cells of the recipient.[2,6] The donor lymphoid cells released from the graft are capable of producing GVHD.[8] Recipient cells coming into the graft were capable of recapitulating the local immune architecture or causing rejection. Recognition of the latter was accomplished by detecting evidence of an infiltrate associated with tissue damage, repair, and architectural abnormalities in the mucosa. Deeper levels of the intestine wall (ie, submucosa, muscularis propria) were not usually present in biopsy samples.[9] More detailed results will be presented elsewhere.[7]

From the Pittsburgh Transplant Institute, Departments of Pathology and Surgery, Pittsburgh, Pennsylvania.

Address reprint requests to A.J. Demetris, Department of Pathology, Division of Transplantation, Presbyterian University Hospital, Pittsburgh, PA 15213.

© 1992 by Appleton & Lange

0041-1345/92/$3.00/+0

REFERENCES

1. Grant D, Wall W, Mimeault R, et al: Lancet 335:181, 1990
2. Iwaki Y, Starzl TE, Yagihashi A, et al: Lancet 337:818, 1991
3. Todo S, Tzakis A, Abu-Elmagd K, et al: Transplantation (in press)
4. Demetris AJ, Lasky S, Van Thiel DH, et al: Am J Pathol 188:151, 1985
5. Murase N, Demetris AJ, Kim DG, et al: Surgery 108:880, 1990
6. Murase N, Demetris AJ, Matsuzaki T, et al: Surgery 110:87, 1991
7. Nakamura K, Todo S, Abu-Elmagd K, et al (in preparation)
8. Abu-Elmagd K, Fung JJ, Reyes J, et al (in preparation)
9. Banner B, Dean P, Williams J: Transplantation 46:665, 1988