Morphological Monitoring of Human Small Bowel Allografts

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RECENT introduction of the powerful new immuno-suppressant, FK 506, has resulted in successful clinical application of small intestinal transplantation.[1,2] The following report summarizes the routine histopathologic monitoring of graft function and rejection after orthotopic small intestinal transplantation, alone or in combination with the liver.

MATERIALS AND METHODS

Between May 2, 1990 and February 4, 1992, a total of 14 patients underwent small bowel plus liver (n = 8), small bowel transplantation alone (n = 5), or multivisceral transplantation (n = 1) at the University of Pittsburgh. Baseline immunosuppression consisted of FK 506 and steroids. Eleven patients are alive with the allograft in place at 147 to 707 days posttransplant. Three patients died at 23 days of graft-versus-host disease (GVHD), at 380 days of lymphoproliferative disease, and at 776 days of sepsis. Perioperative graft specimens and serial endoscopically guided biopsy specimens were reviewed in order to assess the preservation injury, acute or chronic rejection, and infectious disease of the intestinal grafts.

RESULTS

Although intestinal specimens with cold ischemic time less than 5 hours had no significant damage, those stored more than 7.5 hours revealed focal epithelial denudation of the villi and hemorrhage/congestion in the lamina propria, which healed within 10 days posttransplant.

During early (<1 month) rejection episodes, biopsies revealed an increased mixed cellular infiltrate of the lamina propria, consisting primarily of lymphocytes with focal venulitis and cryptitis. Epithelial cell necrosis and reparative epithelial changes such as irregularly shaped lumens, mucous or Paneth cell depletion, and nuclear stratification were also seen. When the rejection was severe, architectural distortion with villous blunting, focal ulceration with resultant neutrophil plugging of capillaries, and pseudomembranes with bacterial colonies were encountered. These findings were more evident in specimens from the ileum, and less often encountered in biopsies obtained after 30 days posttransplant, and resolved with additional immunosuppressive treatment. It is important to note that histological features of rejection can be focal.

One case represented chronic rejection with scattered mucosal abscess, obliterative arteriopathy, and prominent cryptitis in the failed graft at 668 days posttransplant.

Three patients suffered from cytomegalovirus (CMV) infection 20, 48, and 53 days posttransplant, histologically and immunohistochemically confirmed by the presence of intranuclear or cytoplasmic inclusion bodies in the mucosa as well as villous atrophy, apoptosis of crypt cells, and mixed cellular inflammatory infiltrate, which was sometimes difficult to differentiate from rejection.

Using the mismatched HLA class I antibodies, immunohistochemistry revealed gradual replacement of the donor hematolymphoid cells of the intestinal wall and mesenteric lymph nodes with those of the recipient which recapitulated the usual mucosal immune system architecture.

DISCUSSION

This study showed endoscopic biopsy monitoring was able to correctly identify rejection as a cause of graft damage after human small bowel transplantation with histological findings of mucosal architectural distortion, including villous blunting, increased mixed cellular or blastic lymphocytic infiltration, venulitis of the deep lamina propria, and depletion of mucous and Paneth cells with reparative change and mucosal ulceration. More severe episodes were more often accompanied by endoscopic findings, clinical symptoms, and were easier to diagnose by biopsy. The phenomenon of the lymphoreticular repopulation of the intestinal graft peripheral seeding of donor hematolymphoid cells is important in studying the evolution of early and late rejection and GVHD.[3-5]

Cytomegalovirus enteritis was the most common infectious complication in the graft and histologically may be difficult in some cases to differentiate from rejection.[6] Early detection and proper therapeutic adjustment are needed to assume graft function and patient well-being. Histological monitoring should be done in conjunction with clinical correlations, serology, and microbiological culture. Multiple mucosal biopsies and comparison with previous biopsy samples to monitor the effect of therapy is extremely important.

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