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Gastrointestinal Motility in the Immediate Postoperative Period After Intestinal Transplantation, With Special Reference to Acute Rejection

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WITH the advent of a new immunosuppressive agent, FK 506, intestinal transplantation has become feasible, but with problems and complications. Gastrointestinal (GI) dysmotility has been a problem after intestinal transplantation.[1] However, its characteristics and mechanism are largely unknown, especially dysmotility developing during the immediate postoperative period. We studied the changes in GI motility in dogs for 2 weeks after intestinal autotransplantation and allotransplantation. The results were compared between both groups and correlation between intestinal dysmotility and histologic rejection was examined.

MATERIALS AND METHODS

Sixteen adult mongrel hound dogs of both sexes, weighing 18 to 25 kg, were used. Animals were given oral neomycin (1 g/d) and metronidazole (0.5 g/d) for 5 days before the operation. Animals were divided into three groups: group 1 (n = 4), sham operation; group 2 (n = 6), intestinal autotransplantation; and group 3 (n = 6), intestinal allotransplantation.

After overnight fasting, intestinal transplantation was performed by a modified Lillehei technique routinely applied in our laboratory.[2] The intestinal graft was transplanted orthotopically. A 20-cm segment of Thiry–Vella loop using the distal end of the graft ileum was made at the left lower abdomen as double stomas for postoperative mucosal biopsy. Control animals (group 1) received laparotomy and intestinal manipulation. Strain gauge transducers (SGTs; Star Medical, Tokyo) was fixed on the serosa of the GI tract from the stomach to the terminal ileum. No immunosuppressive therapy was given to any of the animals.

Motility measurements were performed in conscious animals on postoperative days 1, 3, 7, and 14 for groups 1 and 2, and every day for group 3. During each motility measurement, fasted motility was recorded for 6 hours in each animal. Octreotide, a somatostatin analogue, was injected intravenously, at a dose of 0.25 μg/kg in group 1 and group 2 animals and 1 μg/kg in group 3 animals after 6 hours of spontaneous fasted motility recording. GI motility changes were recorded for 30 minutes after octreotide injection. One hour after the completion of recording, bethanechol, a muscarinic acetylcholine receptor agonist, was given at 200 μg/kg per hour for 30 minutes. GI motility changes were recorded throughout the bethanechol infusion.

Mucosal biopsies were taken daily for 2 weeks from the Thiry–Vella loop of group 2 and group 3 animals. All of the animals were killed after 14 days postoperatively. Animals unable to eat or drink or became too weak to stand were killed before 14 days. Tissue samples were obtained at killing.

RESULTS

All control animals recovered immediately after surgery. The animals were healthy, without diarrhea, for 14 days. Average body weight loss was 6.4 ± 1.1% at 1 week and 3.4 ± 1.7% at 2 weeks. Sham operation animals regained normal GI motility by 7 days. All autotransplantation animals ate well from the next morning. However, all of them had watery diarrhea that continued for the duration of study. Average weight loss was 11.2 ± 2.0% at 1 week and 14.7 ± 1.0% at 2 weeks. Phase III contractions appeared in the graft of autotransplantation animals the next day, but were delayed in the native GI tract until day 3. No migrating motor complex (MMC) cycle was regained in this group until 14 days. However, contractile response of the autograft to both agents was active, and was similar to that seen in control animals by day 3. In the allotransplantation animals, one dog was excluded from the study because of peritonitis. The remaining 5 animals were killed at 5, 7, 9, 9, and 12 days. All of them had watery diarrhea. The animals appeared as healthy as the autotransplanted animals until they became lethargic 2 to 3 days prior to killing. Mean weight loss was 9.8 ± 1.0% at 1 week and 12.9 ± 1.4% at 2 weeks. No MMC pattern was seen. Phase III contractions were weakly and transiently detected in the allografts of only two animals, and disappeared 1 to 2 days before killing due to rejection. Spontaneous phasic contractions were observed from day 1 and continued until 1 to 2 days before animal killing. Decrease of contractile activity was more prominent in the ileum than proximal intestine. Giant migrating contractions were frequently seen along the entire intestine. Response of the allograft to pharmacological stimulation was greatly inhibited from the outset, long before histological rejection developed. Histopathology of rejected intestine at killing revealed destruction of mucosal architecture, as well as dense infiltration of inflammatory cells into the submucosal layer, muscle layer, and the nervous system. Drastic decrease of contractile activity from rejection was found only at an advanced stage where the graft had significant damage in the entire structure of the intestinal wall.

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DISCUSSION

GI dysmotility of allografts at an early postoperative period may be caused by immune responses other than cellular rejection, since no evident cellular infiltration was seen. There is a controversy whether monitoring of intestinal motility is useful for detection of early graft rejection.[3,4] From this study, monitoring of basal GI motility for detection of rejection is not reliable, because significant dysmotility develops only as a final event of graft rejection.

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