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## Major Colonic Complications of Hepatic Transplantation\*

LAWRENCE J. KOEP, M.D., THOMAS G. PETERS, M.D., THOMAS E. STARZL, M.D., PH.D.

THE SERIES of orthotopic hepatic transplants at the University of Colorado Medical Center now includes 157 patients. In this series there have been eight major colonic complications, providing an incidence of 5 per cent. Of this group of eight patients, only three survived, yielding a hospital mortality rate of 63 per cent for those patients in whom colonic complications developed.

Earlier reports from both this center and Cambridge-Kings College have identified the biliary tract as the most frequent source of complications in hepatic transplantation.<sup>2-14</sup> As our experience increases, however, colonic complications are assuming a more identifiable position in the postoperative period. The colon's contribution to renal-transplant morbidity is now well established. The incidences of colonic complications associated with renal transplantation, 1-5 per cent, are similar to the incidence in our series of hepatic transplantations.<sup>1,8,10,11</sup> Case material is summarized in Table 1.

### Report of Eight Cases

**Patient 1.** A 2½-year-old girl underwent hepatic transplantation for biliary atresia. Despite good hepatic function, a bile leak necessitated biliary revision at two weeks. This was accompanied by a brief period of rectal bleeding, which ceased spontaneously. On her sixty-fifth post-transplant day the patient underwent negative exploratory laparotomy because of suspicion that an abdominal abscess was present. Four days later, massive hematochezia recurred. Laparotomy revealed bleeding from a cecal ulcer, necessitating right hemicolectomy with ileotransverse colostomy. Bleeding ceased but pulmonary and hepatic failure rapidly developed. Diffuse cytomegalovirus inclusion disease of the lung, liver, and brain was found.

**Patient 2.** A 16-year-old girl received an orthotopic hepatic transplant for chronic active hepatitis. Despite an initially benign course, rejection occurred on the forty-seventh post-transplant day, necessitating increased steroid administration. Five days later, hepatic function was again normal, but the following day free intraperitoneal air was seen on chest x-ray. Exploration of the abdomen disclosed a freely perforated diverticulum of the right colon with diffuse peritonitis. Hemicolectomy with ileostomy and mucous

From the Department of Surgery,  
University of Colorado Medical Center,  
Denver, Colorado, and the  
Denver Veterans Administration Hospital,  
Denver, Colorado

fistula was performed. Pulmonary and renal failure ensued, and the patient died four days later of severe *Pneumocystis carinii* pneumonia.

**Patient 3.** A 5½-year-old boy with biliary atresia received an orthotopic hepatic transplant following a particularly difficult hepatectomy. Operative trauma to the right colon produced serosal tears, which were repaired. Six days later, laparotomy for intra-abdominal bleeding disclosed a free perforation at the previous colonic repair site. This perforation was closed and widely drained; however, three days later it again disrupted, necessitating right colonic resection, ileostomy, and mucous fistula. Initial recovery was good, but biliary obstruction and later rejection intervened. Three weeks after colonic resection the patient died of pneumonia and hepatic failure.

**Patient 4.** A 29-year-old man experienced severe encephalopathy following a portacaval shunt, necessitating an orthotopic hepatic transplant. Two early episodes of rejection abated in response to increased steroid administration. A month after transplantation, a wound infection was opened, exposing the transverse colon. Two months later a small erosion produced a colcutaneous fistula. Two initial repair attempts were unsuccessful but, a year after transplantation, a segmental colonic resection and primary anastomosis healed the fistula. The patient remains well two years following transplantation.

**Patient 5.** A 3½-year-old boy underwent hepatic transplantation for biliary atresia. The hospital course was unremarkable, and the patient was discharged with normal hepatic function after 10 weeks. One and a half years after transplantation, he was admitted for vomiting and melena. An upper-gastrointestinal tract barium study demonstrated a duodenal ulcer, and gastroscopy revealed gastric distention with a tight pylorus that could not be passed. Despite appropriate antacid therapy, melena recurred and became massive two weeks later. Laparotomy was hindered by extensive abdominal adhesions, but no ulcer was seen through a gastroduodenostomy. Further exploration revealed pneumatosis cystoides intestinalis confined to the colon. Because bleeding was massive, a colectomy with ileoproctostomy was performed. The colon, though completely covered with mucosal petechiae, had no ulcerations. Recovery was uneventful, and mild diarrhea resolved within a month. Six months later the patient died suddenly of varicella meningitis; there was no colonic abnormality at autopsy.

**Patient 6.** A 15-year-old boy with alpha<sub>1</sub>-antitrypsin deficiency had severe cirrhosis that necessitated orthotopic hepatic transplantation. His recovery was complicated by two episodes of rejection. The first evidence of rejection was seen a month after transplantation, and was readily reversed by increased steroid administration. The second episode of rejection developed a month later and was more resistant to steroids. At this time, massive lower-gastrointestinal-tract bleeding suddenly occurred. Although hepatic function was impaired at this time, clotting was corrected with fresh plasma. Continued hematochezia necessitated laparotomy, which revealed pneumatosis cystoides intestinalis and intraluminal blood confined to the

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Address reprint requests to Dr. Koep: Box C-305, Department of Surgery, University of Colorado Medical Center, 4200 East Ninth Avenue, Denver, Colorado 80262.

TABLE 1. Clinical Summary

	Age (years)	Days after Transplant	Colonic Complication	Procedure	Results
Patient 1	2½	69	Hematochezia from cecal ulceration	Right hemicolectomy with ileotransverse colostomy	Died 3 days later
Patient 2	16	52	Right colonic perforation at probable diverticulum	Right hemicolectomy with ileostomy and mucous fistula	Died 5 days later
Patient 3	5½	6	Right colonic perforation at traumatic repair site	1) Closure colonic perforation 2) Right colectomy with ileo- and mucous fistula	Died 17 days later
Patient 4	29	94	Transverse colocolocutaneous fistula	1) Closure colonic perforation 2) Limited colonic resection and anastomosis	Well after 2 years
Patient 5	3½	512	Massive hematochezia with pneumatosis cystoides intestinalis of colon	Colectomy with ileoproctostomy	Died 6 months later
Patient 6	15	56	Massive hematochezia with pneumatosis cystoides intestinalis of colon	Colectomy with ileoproctostomy	Well after 2 years
Patient 7	44	65	Hematochezia with cecal ulceration	1) Colectomy with ileosigmoidostomy 2) Ileostomy with mucous fistula	Died 6 weeks later
Patient 8	22	19	Hematochezia with cecal ulcerations	Right hemicolectomy with ileotransverse colostomy	Died 1 day later

## Discussion

These patients sustaining colonic complications following hepatic transplantation were considerably younger than those reported to have had similar complications following renal transplantation. The age range of this group of eight patients was 2.5 to 44 years, with a mean of 17.1 years. This probably reflects the younger age distribution of all the hepatic transplant recipients, mean 21 years. The 5:3 male predominance of this group may have been influenced by transplant recipient selection in which males have enjoyed an 85:72 advantage.

These eight complications appear to fall into four general categories: trauma, diverticula, infections, and pneumatosis cystoides intestinalis of the colon. Those two patients who had colonic trauma sustained it either during transplantation (Patient 3) or later, as a result of an open wound (Patient 4). One colonic operative injury during hepatic transplantation had been reported earlier.<sup>9</sup> This injury was repaired during transplantation and healed well; this patient is not included in this report.

Diverticular perforation occurred only once, and then in the right colon (Patient 2). This differs from the more frequent left-colonic diverticulum perforation observed in renal transplantation. Since many of our patients are severely constipated, stercoraceous erosion in the right colon may have been a contributing factor.<sup>7</sup>

colon. Colectomy with ileoproctostomy terminated the bleeding, although examination of the specimen revealed only petechiae, without mucosal ulcers. Following colectomy liver function initially deteriorated, then gradually improved until the patient's discharge from the hospital two months later. There has been no further bleeding, and bowel habits are normal two years following hepatic transplantation.

**Patient 7.** A 44-year-old man with sclerosing cholangitis described an untreated episode of colitis many years previously. Prior to hepatic transplantation, barium-enema examination, colonoscopy, and biopsies revealed no abnormality. Following transplantation, at one and two months, the patient experienced episodes of rejection responding to increased steroid administration. During the second episode, sudden, massive, lower-gastrointestinal-tract bleeding occurred. Laparotomy revealed an otherwise normal colon distended with blood. Colectomy and ileosigmoidostomy controlled the bleeding. Examination of the specimen revealed cecal ulcers with cytomegalovirus changes. Hepatic function continued to deteriorate, and the patient died two weeks later. At autopsy both cytomegalovirus pneumonia and massive hepatic necrosis with cytomegalovirus were present.

**Patient 8.** A 22-year-old woman who had chronic active hepatitis experienced several episodes of encephalopathy following a distal splenorenal shunt. She then received a hepatic transplant, complicated by air embolism. Her post-transplantation course was further complicated by persisting hepatic failure, hepatorenal syndrome, and coma. Two months following transplantation she began to have melena following dialysis. Gastroduodenoscopy twice revealed only gastritis with slight erosions but without bleeding. The serum urea nitrogen was kept below 125 mg/dl. A week later, massive lower-gastrointestinal-tract bleeding occurred, and persisted despite correction of the depressed hepatic clotting factors. Mesenteric angiography was nondiagnostic. Laparotomy confirmed colonic bleeding and right hemicolectomy with ileotransverse colostomy terminated the bleeding. Examination of the specimen revealed *Candida enteritidis* with numerous ulcerations of the right colon. The patient died a day later of pulmonary and hepatic failure. Autopsy confirmed disseminated candidiasis.

Infectious ulceration of the right colon occurred in three patients. Patient 1 died with diffuse cytomegalovirus infection and, though not originally identified in the resected colon, cytomegalovirus was probably the cause of the cecal ulcers. In Patient 7 cytomegalovirus was identified in the colonic ulcers. Both patients had multiple-organ involvement with cytomegalovirus.<sup>3, 6, 12, 16</sup> The other infection, also producing cecal ulcers, was fungal. In addition to cecal ulcers, many other organs were involved by disseminated candidiasis. Nystatin is customarily given orally to prevent fungal overgrowth once bowel function returns.<sup>4</sup> Unfortunately, a prolonged ileus precluded this prophylaxis. Each of these patients was found to have right-colonic lesions that necessitated resection for massive hematochezia. No other enteric pathogen was identified, and no evidence of pseudo-membranous colitis was present.

Pneumatosis cystoides intestinalis confined to the colon was found in Patients 5 and 6. Both patients were explored emergently for rectal bleeding, and the diagnosis was not suspected preoperatively. Colectomy with ileoproctostomy was performed in either case, and petechiae were present in much of the colon in both patients, though in neither were ulcers identified. There was no clotting defect in either patient. Both patients had no identifiable pulmonary disease, neither patient was receiving respiratory assistance, and, following resection, there was no evidence of any gastrointestinal bleeding in either patient. Conservative therapy has been effective when pneumatosis cystoides intestinalis is identified roentgenographically.<sup>5</sup> When sepsis or bleeding suggests further disruption of mucosal integrity, as occurred in these patients, resection is necessary.<sup>13</sup>

The etiology of the perforations resulting from trauma or diverticula is apparent. The etiology of those episodes of massive gastrointestinal bleeding resulting from either cecal ulcers or diffuse petechiae is less obvious. All patients were immunosuppressed, and four had recently had steroid administration increased because of transplant rejection (Patients 2, 4, 6 and 7). Hepatic function was severely depressed in three patients (Patients 6, 7 and 8). Patients 7 and 8 probably had sepsis. All patients, however, bled in the presence of completely normal clotting.

Diagnostic maneuvers were restricted by the precipitous nature of the complications, particularly bleeding. In only two patients (Patients 6 and 8) were clotting defects found, and both defects were corrected well before operation. Occult bleeding is quite common during periods of impaired clotting secondary to hepatic dysfunction. Sigmoidoscopy was always performed and, despite profuse bleeding,

permitted inspection of mucosa below the peritoneal reflection. Gastroduodenoscopy was performed in the last four patients; the one error in diagnosis occurred because the pediatric gastroscope could not negotiate the tight pylorus in Patient 5. Angiography was attempted in Patient 8 only. The results were nondiagnostic and the delay nearly fatal. Angiography remains a desirable diagnostic tool if the delay can be tolerated.

Nonoperative management consists of correction of clotting defects and administration of vasopressin, although the route remains controversial.<sup>15</sup> Operative management has consisted of resecting and exteriorizing perforations. Bleeding has been managed by resection and primary anastomosis. Patient 7 had a re-exploration for sepsis and, although the ileosigmoidostomy appeared intact, it was converted to an ileostomy and mucous fistula.

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