Nonobstructing Colonic Dilatation and Colon Perforations Following Renal Transplantation

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• **Nonobstructing colonic dilatation has not been commonly reported following renal transplantation, and colon perforations carry a high morbidity and mortality in this population. During a 7-year period, nonobstructing colonic dilatation developed in 13 adults 1 to 13 days after renal transplantation. Twelve (92%) of the 13 had poorly functioning allografts. Five (83%) of the 6 with and 2 (29%) of the 7 without colonoscopy had resolution of nonobstructing colonic dilatation. Of the seven right-sided colon perforations during this period, six were associated with nonobstructing colonic dilatation. An additional 4 patients had diverticular perforations in the left colon. Of a total of 11 patients with colon perforation, 7 had surgery within 24 hours of the perforation and 6 (86%) of these survived. Only 1 (25%) of the 4 having surgery more than 24 hours later survived. Six of the survivors retained functioning allografts. Nonobstructing colonic dilatation seems to be a potential complication of poor graft function after renal transplantation, and colonoscopy is effective in its treatment. In patients with colon perforations, early surgery and reduced immunosuppression are essential in decreasing mortality.**
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Mortality following renal transplantation has decreased remarkably in the last 15 years. However, colonic perforations following renal transplantation continue to have a high morbidity and mortality.[1] In the literature, a majority of colonic complications reported are a result of diverticular disease and are in the sigmoid colon.[1] Increased incidence of diverticular disease[2,3] and increased tendency to constipation[4,5] in patients with end-stage renal disease were some of the proposed reasons. Nonobstructing colonic dilatation (NCD; Ogilvie's syndrome), which occurs in association with several medical and surgical conditions,[6] has been reported only rarely following renal transplantation.[7] Similarly, right-sided colon perforations have formed only a small group of the overall colon perforations.[1] A preponderance of cases with NCD and right-sided perforations among those patients in whom colon perforations developed at the University of Pittsburgh (Pa) has prompted us to review our experience with colonic perforations and NCD following renal transplantation.

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SUBJECTS AND METHODS

A retrospective review of 1050 adult (≥19 years) recipients of cadaveric kidneys at the Presbyterian-University Hospital, Pittsburgh, between January 1981 and December 1987 was done to identify patients with colon perforation, NCD, or both. A total of 18 patients were identified; they form the basis of this study. Charts were reviewed for age, sex, primary renal disease, graft function, duration from transplantation to the onset of complications, interval between onset of symptoms and surgery, type of intestinal surgery, and patient and graft survival. In the pretransplantation evaluation, contrast enemas were done only in patients with symptoms of active or past colonic disease. Pretransplantation bowel cleaning was done by a sodium phosphate (Fleet's), tap water, and/or milk and molasses enema.

All patients received a pretransplantation oral dose of cyclosporine of 17.5 mg/kg and an intravenous dose of 1 g of methylprednisolone sodium succinate in the operating room. After transplantation, cyclosporine was administered intravenously at 4 mg/kg per day. When oral intake was resumed, 17.5 mg/kg per day of cyclosporine was given orally to overlap reducing doses of intravenous cyclosporine. Whole blood cyclosporine levels of 700 to 1000 ng/mL by radioimmunoassay or 200 to 300 ng/mL by high-performance liquid chromatography were sought. The dose of prednisone was tapered to 20 mg/d by posttransplantation day 6. Aluminum-containing antacids were given four to six times per day. Acute rejection was treated with bolus steroids, increased oral prednisone, or both. Steroid-resistant rejection was treated in the earlier period by antilymphocyte globulin, and in the later period by monoclonal antibody orthoclone OKT3 (Ortho Pharmaceuticals, Raritan, NJ).

RESULTS

In four patients, left-sided colon perforations developed secondary to diverticular disease. Their clinical characteristics and treatment are given in Table 1. The salient pathological findings were typical of diverticulitis with perforations. Two had localized abscesses. Three of the four survived perforation and retained functioning allografts.

In 13 patients, NCD developed soon after transplantation. But for one exception, NCD was associated with poor allograft function due to posttransplant acute tubular necrosis (9 patients), hyperacute rejection (2 patients), or marked acute cellular rejection (1 patient). Patients with NCD devel-

Age, y/Sex
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50/F
62/F
69/M

Age, y/Sex
40/M
51/M
44/F
64/M
42/M
45/F
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53/M
37/M
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Table 1.—Clinical Characteristics of Patients With Left-Sided Colon Perforations

Age, y/Sex	Cause of Renal Failure	Days After Transplantation	Interval From Perforation to Surgery, h	Surgical Treatment	Patient and Graft Status
42/F	Chronic glomerulonephritis	283	24	Perforation exteriorized with colostomy	Alive; graft lost to chronic rejection 4 y later
50/F	Polycystic kidneys	31	24	Sigmoid resection, colostomy, and mucous fistula	Alive; creatinine level, 160 μmol/L
62/F	Hypertension	7	24	Sigmoid resection, Hartman's procedure, and colostomy	Alive; creatinine level, 110 μmol/L
69/M	Unknown	14	48	L-sided colon resection, Hartman's procedure, and colostomy	Died 6 wk after transplantation

Table 2.—Clinical Features of 13 Patients With NCD Following Renal Transplantation*

Age, y/Sex	Cause of Renal Failure	Onset of NCD Following Transplantation, d/ Maximum Cecal Diameter, cm	Colonoscopy	Course of NCD†	Patient and Graft Status
40/M	Unknown	1/12	Yes	Resolved	Alive; graft lost to renal artery stenosis, 4 mo
51/M	Buerger's disease	2/11	No	Resolved	Alive; creatinine, 310 μmol/L
44/F	Hypertension	13/12	Yes	Resolved	Alive; graft lost to rejection, 3 wk
64/M	Glomerulonephritis	3/9	Yes	Resolved	Alive; creatinine, 210 μmol/L
42/M	Polycystic kidneys	1/14	Yes	Resolved	Alive; graft lost to hyperacute rejection, 3 d
45/F	Interstitial nephritis	2/9	No	Resolved	Alive; creatinine, 220 μmol/L
51/F	Polycystic kidneys	5/12	Yes	Resolved	Alive; kidney lost to chronic rejection, 64 mo
53/M	Hypertension	3/12	No	R-sided colon perforation (4 d)	Died
37/M	Hypertension	2/12	No	R-sided colon perforation (36 h)	Alive; graft lost to chronic rejection 18 mo later
60/M	Unknown	2/11	No	R-sided colon perforation (24 h)	Died
54/M	Hypertension	2/11	Yes	R-sided colon perforation (24 h)	Alive; creatinine level, 250 μmol/L
34/M	IgA nephropathy	2/9	No	R-sided colon perforation (24 h)	Alive; creatinine level, 220 μmol/L
52/M	Lupus nephritis	2/14	No	R-sided colon perforation (24 h)	Alive; graft lost to rejection 1 mo later

*NCD indicates nonobstructing colonic dilation.
†Duration in parentheses refers to the interval between the onset of perforation and right-sided colon resection.

oped marked abdominal distention within a few days after transplantation. Abdominal roentgenograms in all patients revealed marked distention of the large intestine with gas. The cecum and the ascending colon were particularly distended (Fig 1). The cecal diameter ranged from 9 to 14 cm (Table 2). All patients were initially treated with nasogastric suction and enemas. Colonoscopy was performed in 6 patients. At the conclusion of endoscopic decompression, a colonic catheter was left in the right colon in 4 patients to help in deflating the colon further (Fig 2). In a total of 7 patients (5 following endoscopy, 2 without endoscopy), the colonic dilatation resolved within a 2- to 8-day period without recurrence (Table 2).

Six patients with NCD (one following colonoscopy) went on to suffer right-sided colon perforation 3 to 9 days after the onset of NCD. An additional patient without NCD developed cecal perforation 8 days following renal transplantation. This patient also did not have early graft function and required

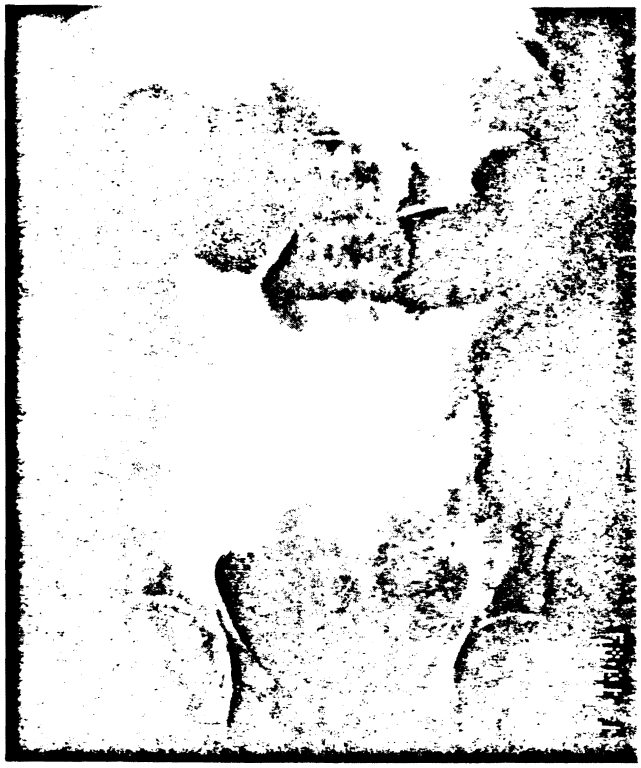

Fig 1.—Abdominal roentgenogram of a 40-year-old man 2 days after a cadaveric renal transplantation showing dilated cecum (12 cm) and ascending and transverse colon.

Fig 2.—Abdominal roentgenogram of the same patient shown in Fig 1 two days after colonoscopic decompression and placement of a catheter. Colonic dilatation completely resolved, and the catheter was removed 3 days later.

hemodialysis. The indications for surgery were any one or a combination of the following: increasing abdominal tenderness, presence of intramural colonic gas, free peritoneal air, and presence of systemic gram-negative sepsis. All had right-sided colon resections, ileostomy, and a colonic mucous fistula (except one with primary anastomosis) from less than 1 day to 4 days after the onset of features of perforation.

The resected specimens showed thin-walled and dilated colon with areas of ulceration and ischemic necrosis as well as single or multiple perforations. The specimen in the seventh patient without NCD revealed a perforation in the indurated posterior wall of the cecum with several ulcers surrounding it. Histological examination was nonspecific. Three of the seven patients who suffered right-sided colon perforation died.

Sepsis with multiple organ failure was the cause of the 4 deaths in the 11 patients with colon perforation. Three of the 4 patients who died had surgery more than 24 hours after the apparent onset of features of perforation. Clinical confusion with rejection, ileus, and perigraft hematoma led to delay in operating on these patients. In comparison, 6 of the 7 patients who had surgery within 24 hours survived. Immunosuppression therapy was stopped in 8 of the 11 patients in whom colon perforation developed and was not resumed for periods varying from 7 to 35 days. This suspension of immunosuppression did not seem to affect allograft function adversely. Six of the 7 survivors went on to have fully functioning allografts. One survivor lost his graft 1 month after transplantation secondary to rejection. However, 2 patients subsequently lost their allografts to chronic rejection 18 and 38 months later.

COMMENT

The majority of the colon perforations following renal transplantation that were reported in the literature were on the left side, the leading cause being diverticulitis.[1] Higher incidence of diverticulosis and onset of its symptoms at an earlier age have been reported in patients with end-stage renal disease, especially those with polycystic kidney disease.[2,3] However, in our patients diverticular perforations accounted for only 36% of all colon perforations. The interval from transplantation to perforation was highly variable in our patients (7 to 283 days), as was the experience reported by the others.[1] Steroids have been postulated to cause lymphoid atrophy with thinning of the bowel wall,[5] decreased rate of epithelial turnover,[6] and decreased ability to resist bacterial translocation in all types of patients.[9] In immunocompromised patients these perforations are also detected at an advanced stage because of the failure of the peritoneal defenses to limit the perforation.[10]

Ogilvie[11] first described massive colonic dilatation without obstruction in 1948. Since then, this syndrome of NCD has been described in association with several conditions,[4,7,12-14] including pelvic and abdominal surgery as well as uremia. Bauer and Overgaard[7] described the occurrence of NCD in a renal transplant recipient 5 days after transplantation in association with poor allograft function. The graft was subsequently lost. This patient had another episode of NCD almost a year later, 3 days after his second transplantation, which did not appear to function. All of our patients with NCD had a common clinical presentation. Colonic distention occurred within a short time following a transplantation that was associated with poor allograft function due either to ischemia or rejection.

The pathogenesis of NCD is unknown. Ogilvie,[11] in his initial description, speculated an inhibition of sympathetic stimuli to the colon. Electrophysiological studies have described arrest of normal spike and motor activity of the colon in response to distention.[15] The use of high doses of cyclosporine in our patients is an unlikely explanation as we have not encountered this problem in liver transplant recipients with

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similar dosage schedules of cyclosporine. Even though electrolyte abnormalities have been reported to cause NCD,[12] one of our patients had any extensive electrolyte imbalances. Extraperitoneal dissection during the placement of the kidney could be another causative factor by disturbing the retroperitoneal autonomic network. Infusions of papaverine and prostaglandin E_1, both known smooth-muscle relaxants, were administered to two patients with hyperacute rejection and may have contributed to the onset of NCD.

Kukora and Dent[16] first described colonoscopic decompression of NCD, and subsequently Bernton and coworkers[17] reported the endoscopic placement of a decompression catheter to treat recurrent NCD. Other similar experiences have been reported.[6,13,14] In our experience, colonoscopic decompression was successful in five of six patients.

Right-sided colon perforations following renal transplantation have been reported only in a few patients.[18-21] Ischemic and nonischemic colitis, right-sided fecal impaction, and nonspecific cecal ulcers have all been implicated. Unrelieved NCD leads to cecal perforation and its reported mortality is high.[22] In six of the patients in this series, right-sided colon perforations associated with NCD developed. Their pathogenesis might be explained by Laplace's law of relating wall tension to the radius of a hollow viscus.[22,23] In a distended colon, the cecum by nature of its larger diameter than the remainder of the large intestine has the highest wall tension and thereby is more susceptible to distention-induced ischemia. Van Zwalenburg[24] showed that gradual increase of intraluminal pressure from 30 to 130 mm Hg caused cessation of capillary, venous, and eventually all circulation in the bowel wall. Wangensteen[25] estimated that an intracecal pressure of 26 cm H_2O was necessary for cecal perforation. The pathological findings of mucosal hemorrhage, necrosis, ulceration, and submucosal venular thrombosis in the resected specimens of our patients with NCD and right-sided colon perforation would suggest that cecal distention led to ischemia and perforation.

Once colon perforation has occurred, early and adequate surgery is an essential factor in protecting these patients from uncontrolled sepsis.[1,20] In our series of 11 colon perforations, 6 of the 7 patients who had surgery within 24 hours of onset of features of perforation survived. Only 1 of the 4 patients operated on more than 24 hours after the onset of perforation survived. The other 3 died of unremitting generalized sepsis. As reported in the literature, primary anastomosis following colon resection has had disastrous consequences in these immunocompromised patients and should be avoided.[1,20,26] The only patient with primary anastomosis in our experience suffered an anastomotic leak but survived after further surgery.

It was gratifying to observe that six of the seven survivors managed to keep functioning allografts despite colon perforation and peritonitis. It seems prudent to drastically reduce or temporarily stop immunosuppression in patients when a colon perforation develops.

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