CASE RECORDS of the MASSACHUSETTS GENERAL HOSPITAL

Case 26-2009: A 34-Year-Old Man with Cystic Fibrosis with Abdominal Pain and Distention

Steven D. Freedman, M.D., Ph.D., Raul N. Uppot, M.D., and Mari Mino-Kenudson, M.D.

PRESENTATION OF CASE

Dr. David M. Dudzinski (Medicine): Fever and abdominal pain and distention developed in a 34-year-old man with cystic fibrosis during an admission to this hospital for pulmonary care.

The patient was awaiting lung transplantation for end-stage lung disease due to cystic fibrosis. Cystic fibrosis had been diagnosed at birth, and he was homozygous for the F508 mutation in the cystic fibrosis transmembrane conductance regulator gene (*CFTR*). He had been hospitalized at least annually for complications of the disease, most recently 1 year earlier because of pneumonia caused by *Pseudomonas aeruginosa* and methicillin-resistant *Staphylococcus aureus*. His daily pulmonary care included albuterol and hypertonic saline by nebulizer, followed sequentially by physical therapy with the vest system of high-frequency chest-wall oscillation and colistin by nebulizer. Other medications included trimethoprim–sulfamethoxazole twice daily; during the 2 months before admission, ciprofloxacin and tobramycin aerosol treatments were administered because of worsening cough, declining pulmonary function, and sputum cultures that were positive for *P. aeruginosa*.

Three days before admission, the patient was seen in the pulmonary clinic of this hospital. He reported persistent cough, increased dyspnea, and moderate sputum production. On examination, he appeared dyspneic, and inspiratory crackles were heard in both upper lobes. Oxygen saturation was 93% while he was breathing ambient air. Measurement of forced expiratory volume in 1 second (FEV_1) was 0.74 liter (21% of the predicted value). A specimen of sputum was obtained, which grew *P. aeruginosa*, with intermediate resistance to fluoroquinolones; it was susceptible to cefepime, ceftazidime, aztreonam, gentamicin, and piperacillin–tazobactam. He was admitted to the hospital for pulmonary care and additional antibiotic therapy.

An operation had been performed on the bowel when the patient was an infant. He had insulin-dependent diabetes mellitus and osteoporosis. Approximately 3.5 years before admission, during evaluation for lung transplantation, mild elevations in serum aminotransferase levels were noted. Pathological examination of a biopsy specimen of the liver revealed biliary scarring and inflammation, mild fibrosis without cirrhosis, and mild-to-moderate steatosis. Nineteen months before admission,

From the Department of Medicine, Beth Israel Deaconess Medical Center (S.D.F.); the Departments of Radiology (R.N.U.) and Pathology (M.M.-K.), Massachusetts General Hospital; and the Departments of Medicine (S.D.F.), Radiology (R.N.U.), and Pathology (M.M.-K.), Harvard Medical School — all in Boston.

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the distal intestinal obstruction syndrome was treated with intravenous fluids and oral polyethylene glycol at another hospital. He also had psoriasis, poor dentition, and a past traumatic wrist fracture. He had no known allergies. He was single and lived with his father and stepmother, who owned a bird and fish. He worked in the food industry, drank alcohol rarely, and had smoked briefly more than 15 years earlier; he did not use illicit drugs. He had no exposure to tuberculosis or sick persons and had not traveled recently. There was no family history of cystic fibrosis, heart disease, diabetes mellitus, or cancer. His mother had reportedly died at a young age from an unknown cause. Medications on admission included hypertonic saline by nebulizer, ursodiol, trimethoprim–sulfamethoxazole, pancrelipase, neutral protamine Hagedorn (NPH) insulin with meals and lispro human analogue insulin as needed, alendronate weekly, and vitamins.

On examination, the patient appeared relatively well nourished but was thin and weighed 54.2 kg. He was able to converse without dyspnea or tachypnea. The blood pressure was 138/57 mm Hg, the pulse 73 beats per minute, the temperature 36.2°C, and the respiratory rate 18 breaths per minute; oxygen saturation was 91% while he was breathing ambient air and 97% while he was breathing 2 liters of oxygen by nasal cannula. Excursion of the chest was symmetrical and measured 2 to 3 cm; breath sounds were coarse bilaterally, with inspiratory crackles at the left middle and upper posterior lung fields, the right upper posterior lung field, and the bilateral upper anterior lung fields. The abdomen was soft, with no tenderness or distention. Bowel sounds were present. There was a transverse, healed surgical scar, 15 cm in length, on the abdomen, and the liver edge was palpated 1 cm below the costal margin; there was no tenderness or rebound. There was clubbing of the fingers and toes; the remainder of the examination was normal. The prothrombin time was 16.9 seconds (reference range, 11.1 to 13.6); measurement of other tests of coagulation and plasma levels of bilirubin, total protein, albumin, globulin, magnesium, amylase, and lactic dehydrogenase were normal; other laboratory-test results are shown in Table 1. A chest radiograph showed hyperexpanded lungs and architectural distortion consistent with cystic fibrosis; the findings were unchanged as compared with previous studies.

A percutaneous central venous catheter was placed and its position confirmed by chest radiography. Tobramycin, ceftazidime, and trimethoprim–sulfamethoxazole were administered. On the second hospital day, a sputum culture grew *P. aeruginosa*, two types of candida, and one colony of *Aspergillus fumigatus*.

On the afternoon of the fifth hospital day, the temperature rose to 38.7°C; the pulmonary and abdominal examinations were unchanged. Specimens of blood, sputum, and urine were cultured. A chest radiograph showed a catheter extending from the right arm with the tip projecting over the right shoulder and was otherwise unchanged. Acetaminophen was administered, and the antibiotics were continued. The next morning, the temperature was 36.8°C, and it rose to 38.7°C later that day. Cough was productive of green sputum with brown flecks. Inspiratory rhonchi were present at the left base and both apexes, and crackles were heard at the apex. Bowel sounds were normal, and there was no abdominal pain, tenderness, or distention. Cultures of the blood and urine remained sterile, and the sputum was unchanged. The intravenous catheter was removed, and the catheter tip was cultured. Administration of vancomycin was begun.

On the eighth hospital day, the temperature rose to 39.1°C and nausea with vomiting developed. On examination, the blood pressure was 99/52 mm Hg, the pulse 117 beats per minute, the respiratory rate 18 breaths per minute, and the oxygen saturation 90% while the patient was breathing ambient air. The patient appeared comfortable. There were crackles in the upper lung fields, with occasional wheezes. Bowel sounds were normal; the right upper quadrant was tender, without distention or rebound. Results of laboratory tests are shown in Table 1. Ceftazidime was stopped and cefepime was begun.

On the ninth hospital day, vomiting increased in frequency, without anorexia or diarrhea. The systolic blood pressure was 70 to 80 mm Hg. Bowel sounds were decreased, and the abdomen was slightly distended, with diffuse tenderness and rebound tenderness. Tobramycin was discontinued, and metronidazole and intravenous fluids were administered. Oral intake was stopped. Laboratory-test results are shown in Table 1; results of other tests were pending. A chest radiograph was unchanged, and radiographs of the abdomen revealed nondilated loops of small and large

Table 1. Laboratory Data.*

Variable	Reference Range, Adults†	On Admission	8th Day	9th Day
Hematocrit (%)	41.0–53.0 (men)	40.2	39.3	52.0
Hemoglobin (g/dl)	13.5–17.5 (men)	13.6	13.7	17.9
White-cell count (per mm^3)	4,500–11,000	4,800	15,200	31,500
Differential count (%)				
Neutrophils	40–70	80	91	75
Band forms	0–10	0	0	15
Lymphocytes	22–44	16	6	5
Monocytes	4–11	3	3	5
Eosinophils	0–8	1	0	0
Platelet count (per mm^3)	150,000–350,000	142,000	173,000	269,000
Sodium (mmol/liter)	135–145	137	129	127
Potassium (mmol/liter)	3.4–4.8	4.8	4.4	5.1
Chloride (mmol/liter)	100–108	100	90	91
Carbon dioxide (mmol/liter)	23.0–31.9	28.6	26.5	18.1
Urea nitrogen (mg/dl)	8–25	14	24	55
Creatinine (mg/dl)	0.6–1.5	0.9	1.1	2.3
Glucose (mg/dl)	70–110	210	157	301
Phosphorus (mg/dl)	2.6–4.5	3.5	4.0	8.1
Calcium (mg/dl)	8.5–10.5	8.5	8.1	6.3
Alkaline phosphatase (U/liter)	45–115	260	207	168
Aspartate aminotransferase (U/liter)	10–40	57	30	34
Alanine aminotransferase (U/liter)	10–55	59	40	31
Lipase (U/dl)	1.3–6.0	0.8	1.0	0.7
Lactate (mmol/liter)	0.5–2.2			2.8

* To convert the values for urea nitrogen to millimoles per liter, multiply by 0.357. To convert the values for creatinine to micromoles per liter, multiply by 88.4. To convert the values for glucose to millimoles per liter, multiply by 0.05551. To convert the values for phosphorus to millimoles per liter, multiply by 0.3229. To convert the values for calcium to millimoles per liter, multiply by 0.250.

† Reference values are affected by many variables, including the patient population and the laboratory methods used. The ranges used at Massachusetts General Hospital are for adults who are not pregnant and do not have medical conditions that could affect the results. They may therefore not be appropriate for all patients.

bowel, without free air or obstruction. Computed tomography (CT) of the chest showed mild bronchiectatic changes in both lung bases, and tree-in-bud opacities in the right lung base were thought to represent bronchiolitis. CT of the abdomen after the administration of oral contrast material revealed marked thickening of the wall of the entire colon that extended into the distal small bowel; material within the small bowel was suggestive of fecal contents. Prominent mesenteric stranding and moderate ascites were present, without pneumatosis or free air. The liver had a nodular contour consistent with cirrhosis, and there was fatty replacement of the pancreas; the ureters and bladder were normal. During the next 12 hours after the CT scanning, the patient's discomfort increased and the abdomen became massively distended. On the 10th hospital day, a procedure was performed, and additional test results were received.

DIFFERENTIAL DIAGNOSIS

Dr. Steven D. Freedman: May we review the radiology images?

Dr. Raul N. Uppot: Frontal and lateral radiographs performed on admission showed hyperexpanded lungs with diffuse bronchiectasis and architectural distortion bilaterally, features that were unchanged from previous chest radiographs and consistent

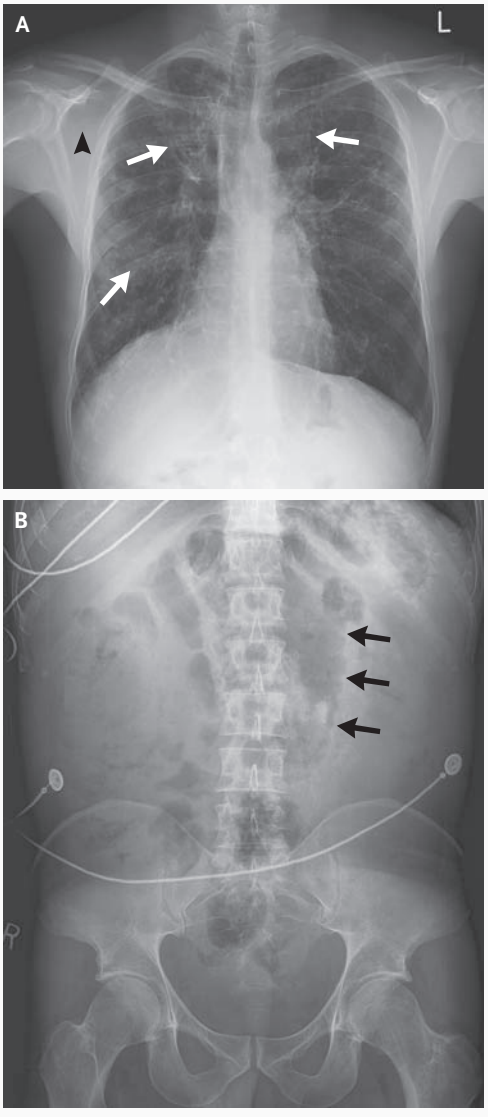

Figure 1. Chest and Abdominal Radiographs.

A frontal chest radiograph obtained on the day of admission shows hyperexpanded lungs (Panel A). There is diffuse bronchiectasis and architectural distortion bilaterally (arrows). The tip of a percutaneous central venous catheter overlies the right scapula (arrowhead). A radiograph of the abdomen obtained 8 days after admission (Panel B) shows mild mucosal thickening involving midabdominal loops of bowel (arrows). There is no dilatation to suggest obstruction. There is no free intraperitoneal air.

with the patient's known history of cystic fibrosis (Fig. 1A). No focal air-space opacity to suggest a pneumonia or pleural effusion was visualized.

Abdominal radiographs obtained 8 days after admission, with the patient in the supine and upright positions, suggested mild mucosal edema involving midabdominal loops of bowel (Fig. 1B). There was no evidence of free intraperitoneal air. There was no dilatation to suggest an obstruction. CT of the abdomen and pelvis after the administration of oral contrast material revealed marked circumferential bowel-wall thickening from the rectum to the cecum (Fig. 2A), with extensive mesenteric stranding (Fig. 2B) and moderate ascites (Fig. 2C). Mucosal thickening produced alternating edematous haustral folds separated by transverse mucosal ridges, called the "accordion sign" because of its resemblance to the musical instrument[1] (Fig. 2C). The findings are consistent with colitis involving the entire length of the colon. The differential diagnosis includes pseudomembranous colitis, ulcerative colitis, and ischemic colitis. The appearance of heterogeneous fecal material within the terminal ileum suggests the presence of intestinal stasis, probably related to the patient's cystic fibrosis. No evidence of small-bowel obstruction was seen. The entire pancreas was replaced with fat, a finding consistent with the patient's known history of cystic fibrosis. The liver had a nodular contour, a finding consistent with cirrhosis or fibrosis.

Dr. Freedman: This 34-year-old man with cystic fibrosis presented with an exacerbation of his pulmonary disease, for which he was treated with multiple antibiotics. By the ninth day, the patient had vomited and was hypotensive, with diffuse abdominal tenderness. The white-cell count was elevated. The hematocrit and creatinine level increased, features consistent with intravascular depletion. Lactic acidosis developed, and metronidazole was added. The CT scans revealed findings consistent with pancolitis; within 12 hours, the abdomen became massively distended, with increased pain.

There are two questions. First, what is causing this patient's acute illness, and second, given his rapid deterioration, is there loss of intestinal viability that would require emergency surgery? I will first address the differential diagnosis and then comment on the features that indicate prompt surgical exploration. The differential diagnosis can be grouped into four areas: vascular compromise, mechanical obstruction, inflammation, and infection.

VASCULAR EVENTS

Acute vascular events such as occlusive or nonocclusive thrombosis rarely lead to total colonic in-

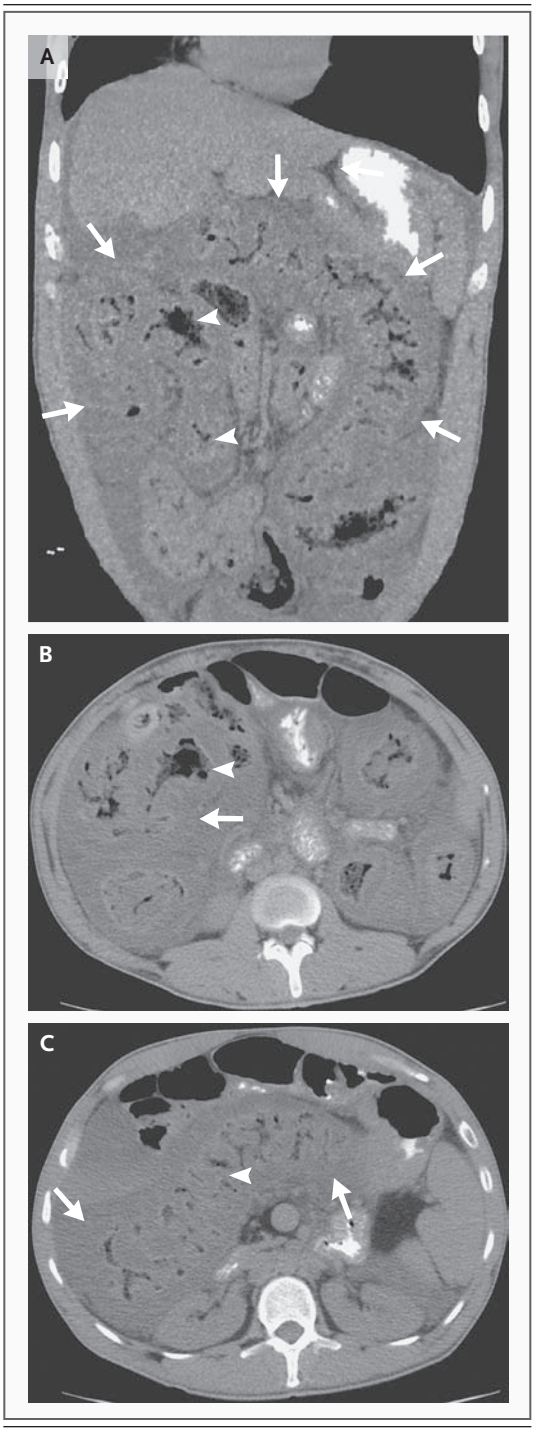

Figure 2. CT Scan of the Abdomen Obtained after the Administration of Oral Contrast Material on Hospital Day 8.

A coronal image of the abdomen (Panel A) shows colonic-wall thickening, from the rectum to the cecum (arrows) and also involving the distal small bowel. Heterogeneous fecal material within the lumen of the terminal ileum (arrowheads) is consistent with a "small-bowel feces" sign, a finding suggestive of intestinal stasis. An axial image at the level of the terminal ileum (Panel B) shows diffuse circumferential wall thickening (arrow) and the small-bowel feces sign (arrowhead). An axial image at the level of the transverse colon shows diffuse circumferential wall thickening (Panel C, arrows). The mucosal thickening is consistent with an "accordion sign" (arrowhead).

volvement, because of the redundant vascular supply to the colon. Portal-vein or mesenteric-vein thrombosis is unlikely in this case and, if present, would have demonstrated overt small-bowel involvement. Although the CT scan was obtained without contrast material, no density consistent with a clot was seen in the vasculature. However, in ischemic colitis, a true arterial clot is rarely seen, even on angiography.

OBSTRUCTION

This patient has a history of the distal intestinal obstruction syndrome, a complication that occurs in 10 to 20% of patients with cystic fibrosis. The pathophysiology is similar to that of meconium ileus (lack of passage of meconium from the colon within 48 hours after birth), which is the earliest clinical manifestation of cystic fibrosis and is seen in up to 15% of newborns with the disease. Mutations in the *CFTR* gene (encoding for an epithelial chloride channel in the apical plasma membrane)[2] lead to thick, tenacious secretions in organs that engage in luminal secretion (lungs, intestine, pancreatic and bile ducts, and male reproductive tract) and an excessive host inflammatory response that result in impaired passage of fecal material in the intestine. Patients with the distal intestinal obstruction syndrome have recurrent bouts of abdominal pain (typically in the right lower quadrant) and constipation.[3] The syndrome may also involve the left colon and rectum, resulting in chronic constipation and acquired megacolon. Although this patient had this syndrome in the past, the rapid onset, diffuse thickening of the colon, and toxic presentation would not be consistent with this diagnosis. Poor motility in the stomach and intestine is not unusual in persons with cystic fibrosis and may lead to bacterial overgrowth that results in abdominal pain and distention. However, this is also a chronic, indolent problem, in contrast to the acute presentation seen here, and would not explain the abnormal imaging findings.

Intermittent abdominal pain in patients with cystic fibrosis can be the result of intussusception

in the ileocecal region, in which inspissated fecal material acts as the "lead point."[4] However, this patient did not have the classic doughnut or target sign of edematous bowel and intermixed fat on CT imaging.

Rectal prolapse is seen in approximately 20% of patients with cystic fibrosis as a result of bulky stools and poor muscle tone. However, this condition is rare in adults and was not seen on examination of this patient. Also, the risk of cancer in patients with cystic fibrosis is seven times as great as the risk in persons without cystic fibrosis. The cancers are mostly confined to the gastrointestinal tract[5] and include adenocarcinomas of the esophagus, small intestine, and biliary tract, and most commonly adenocarcinomas of the colon and rectum, which are seen as early as age 13. CT scans showed no evidence of a tumor or a single point of obstruction in this case.

INFLAMMATION

In asymptomatic adults with cystic fibrosis, imaging studies of the colon frequently show variable degrees of thickening of the colonic wall. Pneumatosis intestinalis, which is confined to the colon, is seen in approximately 5% of patients and is most likely secondary to obstructive lung disease. Thus, abnormal colonic findings by CT imaging may not be indicative of an acute event, and careful clinical correlation is always required to determine the significance of these findings. In this case, the imaging abnormalities correlated with the patient's worsening clinical condition and suggest the diagnosis of severe colitis.

Appendicitis is unusual in patients with cystic fibrosis, despite the fact that the appendix is chronically distended. The prevalence of Crohn's disease — but not ulcerative colitis — may be higher in these patients than in the general population.[6] Fibrosing colonopathy, a complication of high-dose pancreatic-enzyme supplementation, can present with thickening or stricturing, typically of the right colon, due to submucosal fibrosis.[7,8] Patients may report obstructive symptoms, bloody diarrhea, or both. Cross-sectional imaging studies show thickening of the colonic wall with narrowing of the intestine, generally most prominent in the ascending colon. With the exception of ulcerative colitis, which can cause toxic megacolon, none of these diagnoses are likely in this case.

INFECTION

Could this patient have an infectious colitis? Cytomegalovirus (CMV) colitis is unlikely, since this patient was not immunocompromised and did not have the features of primary CMV infection, which includes a mononucleosis syndrome with skin lesions, abnormal aminotransferase levels, and atypical lymphocytosis.

Bacterial infections of the intestine should be considered, including salmonella, shigella, and campylobacter, but these infrequently lead to toxic megacolon. However, the patient has been treated with multiple antibiotics within the hospital setting, a combination that increases the risk of the development of *Clostridium difficile* colitis. *C. difficile* colitis is rare in patients with cystic fibrosis, although asymptomatic carriage has been reported in 22 to 50% of such patients.[9,10] The rarity of overt colitis may relate to resistance of the colonic epithelial cells to toxins such as cholera.[11] Although the literature shows only a few case reports of *C. difficile* colitis in patients with cystic fibrosis,[12-14] each of them highlights the fact that the course is characterized by fulminant disease, with progressive abdominal distention and pain, and absence of diarrhea. Low-grade fevers and leukocytosis are common. CT reveals pancolitis and pericolic stranding and, in one reported case, severe ascites and the accordion sign.[15] Although the accordion sign can be seen in any form of severe colitis, in a series of five patients with cystic fibrosis and *C. difficile* colitis, three had trapping of gas between thickened folds, leading to the "gas accordion sign"[1] designation; the gas accordion sign was seen in this patient. The mortality rate in reported cases was approximately 50%. Most patients in whom an exploratory laparotomy with subtotal colectomy could be performed survived.

C. difficile infection with fulminant colitis and toxic megacolon is highly likely in this patient. Use of broad-spectrum antibiotics including clindamycin, fluoroquinolones, and cephalosporins are linked to the development of *C. difficile* colitis. Similar to the cystic fibrosis case reports in the literature, this patient presented with fulminant colitis, lack of diarrhea, and rapid progression to toxic megacolon. The diagnosis can be made by sending a stool sample for analysis of the toxin. Although most assays that detect *C. difficile* toxin have a specificity of 99%, the sensitivity is approximately 60%.[16] Endoscopic examination with

the finding of pseudomembranes can be used to aid in the diagnosis when the patient has severe disease and either the stool sample is negative or there is a lack of response to therapy. The occasional sparing of the rectosigmoid colon may require a colonoscopy rather than a sigmoidoscopy. However, in patients with severe colitis, the introduction of air into the bowel can cause perforation and is thus contraindicated.

MANAGEMENT OF *C. DIFFICILE* COLITIS

In this case, several features suggest severe colonic ischemia or necrosis and should prompt consideration of emergency surgery. No signs of peritoneal irritation on physical examination were mentioned, but there was massive distention of the abdomen, which causes concern about the presence of necrosis. Another indicator of loss of viability of the colon is evidence of extravasation of fluids, which would indicate ischemic or necrotic bowel. When this occurs, a decrease in the intravascular volume is seen that is accompanied by a substantial increase in the hematocrit and, if severe enough, increases in the creatinine and urea nitrogen levels. The intravascular deficit can be roughly calculated as follows: subtract the baseline hematocrit from the current hematocrit and divide the result by the baseline hematocrit; then multiply the result by one third of the body weight in kilograms.

This patient weighed approximately 55 kg; his hematocrit was 40 on admission and rose to 52, reflecting a volume deficit of 5.5 liters. This explains the development of hypotension and renal failure and indicates that rapid resuscitation with volume expansion is required. Adequate repletion of intravascular volume may help spare ischemic regions of the intestine from necrosis due to hypoperfusion.

SUMMARY

In this patient, pancolitis developed in the context of the administration of multiple antibiotics. His clinical course and imaging studies are consistent with fulminant *C. difficile* infection. The rapid deterioration, including shock, massive abdominal distention, and laboratory values consistent with severe loss of intravascular fluids, suggests loss of colonic viability. Although stool analysis for *C. difficile* toxin may be helpful, neither a positive nor a negative result would be diagnostic because of the high carrier rate in patients with cystic fibrosis and the low sensitivity of the assay. Flexible sigmoidoscopy would most likely show pseudomembranes, confirming the diagnosis. However, in view of his rapid deterioration in the context of toxic megacolon, an emergency subtotal colectomy is warranted in order to save his life. Although appropriate antibiotics are curative in the majority of cases of acute infection, 1 day of intravenous metronidazole therapy had already been administered in this patient, and the damage to the colon was too advanced to respond to antibiotics.

CLINICAL DIAGNOSIS

Fulminant *Clostridium difficile* colitis.

DR. STEVEN D. FREEDMAN'S DIAGNOSIS

Fulminant *Clostridium difficile* colitis with toxic megacolon.

PATHOLOGICAL DISCUSSION

Dr. Mari Mino-Kenudson: A specimen of stool obtained on the ninth hospital day was positive for *C. difficile* toxin. The next day, an ileocolectomy was performed. The specimen consisted of a 171-cm segment of colon and a 5-cm segment of terminal ileum. The colon was distended and the wall was thickened (Fig. 3A). The mucosal surface along the entire length of the colon and terminal ileum was covered by tan-yellow-green material that was easily peeled off, a finding that was consistent with a pseudomembrane (Fig. 3A, inset).

On microscopical examination, the thickening of the colonic wall was mostly due to edema and congestion of the submucosa (Fig. 3B). There was a fibrinopurulent exudate on the mucosal surface, which in areas could be seen extruding from the mucosal crypts, with a volcanic-like appearance, consistent with the pseudomembrane seen on gross examination. The surface crypts were distended by mucin and inflammatory cells (Fig. 3C). There was necrosis and desquamated epithelial cells intermingled with fibrin and neutrophils (Fig. 3D). The pathological diagnosis is pseudomembranous colitis and enteritis, which is consistent with *C. difficile* enterocolitis.

Dr. Eric S. Rosenberg (Pathology and Medicine):

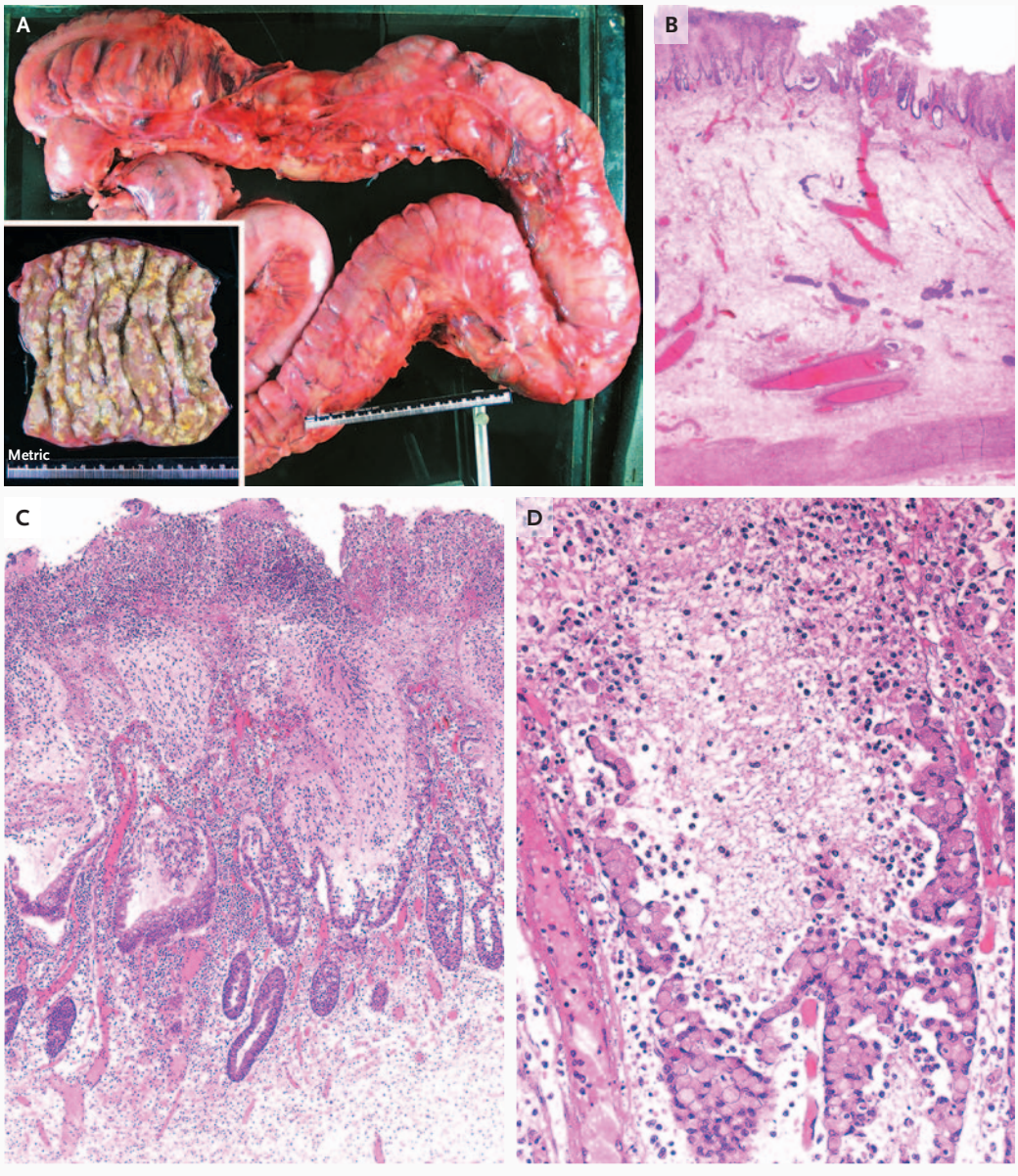

Figure 3. Specimen of Intestine Obtained at the Time of Surgery.

A gross photograph of the resected colon shows massive dilatation (Panel A); the mucosal surface of the entire length of the colon and terminal ileum was covered by tan-yellow-green fibrinoid material that was easily peeled off, in a manner consistent with a pseudomembrane (inset). A low-power view of the colonic wall (Panel B, hematoxylin and eosin) shows marked thickening, caused mostly by edematous expansion of the submucosa with congestion; the muscularis propria is attenuated because of necrosis. The mucosal layer shows edematous lamina propria with inflammatory-cell infiltration, as well as surface crypts distended by mucin and inflammatory cells, covered by a pseudomembrane (Panel C, hematoxylin and eosin). A high-power magnification shows desquamation of epithelial cells and ghostlike structures that are intermingled with fibrin and neutrophils (Panel D, hematoxylin and eosin).

Dr. Dudzinski, could you tell us what happened to this patient?

Dr. Dudzinski: In the first 24 hours after the operation, the patient's condition improved, with a decline in the white-cell count and correction of the acidosis. However, on the 11th hospital day, after extubation of the trachea, dyspnea, hypotension, and acidosis developed, requiring reintubation and vasopressor support. In the next 24 hours, refractory hypotension and lactic acidosis devel-

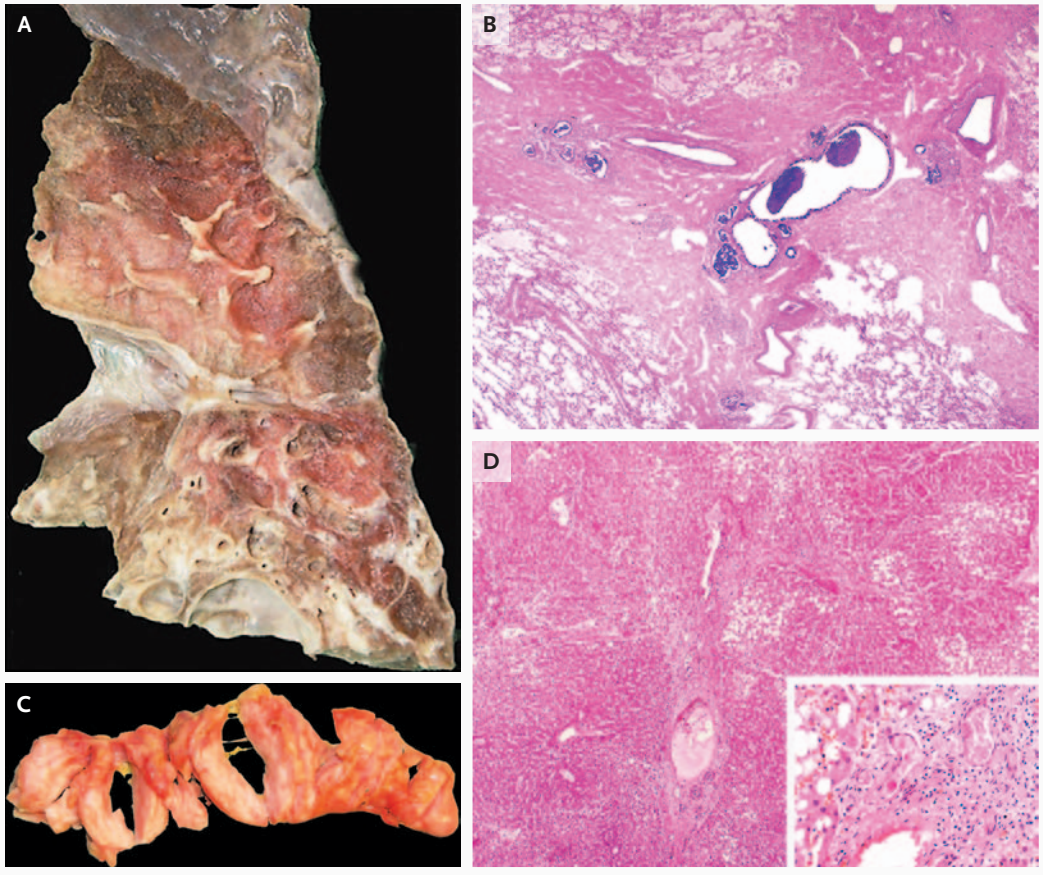

Figure 4. Autopsy Findings.

A gross photograph of the lung shows numerous dilated air spaces with thickened walls and several large cystic lesions resulting from old abscesses (Panel A). Ill-defined areas of consolidation are also evident in the lower lobes. The air spaces from terminal bronchioles to respiratory bronchioles are extensively dilated (bronchiolectasis), with viscid mucin in the lumen (Panel B, hematoxylin and eosin); peribronchiolar fibrosis is also present. The pancreas is almost entirely replaced by fat (Panel C). There is bridging fibrosis of the liver (Panel D, hematoxylin and eosin), with proliferation of bile ducts that contain thick secretions characteristic of cystic fibrosis (inset).

oped, the white-cell count rose to 90,200 per cubic millimeter with 28% band forms, aminotransferase levels rose, and disseminated intravascular coagulopathy and acute anuric renal failure developed. A bradycardic arrest occurred on the 12th hospital day, and attempted resuscitation was unsuccessful. An autopsy was performed.

Dr. Mino-Kenudson: At autopsy, only a short segment of colon remained, which was anastomosed to the ileum. The remaining ileum was distended, with serosal adhesions. Both the colonic and most of the ileal mucosa had pseudomembranes, and microscopical examination showed similar morphology to that seen in the ileocolectomy specimen, with more advanced degeneration of the crypt epithelium.

The lungs showed changes consistent with advanced cystic fibrosis (Fig. 4A), including cystic lesions representing pneumatoceles derived from old abscesses and bronchiectasis and bronchiolectasis with peribronchial and peribronchiolar fibrosis, extending from large bronchi to respiratory bronchioles, with viscid mucus in the dilated lumens (Fig. 4B). Fibrosis extended into the peribronchial and peribronchiolar lung parenchyma, leading to consolidation in some areas, but no active bronchopneumonia was seen.

The pancreas was atrophic, with replacement of the parenchyma by fat and fibrous tissue (Fig. 4C), as a result of inspissated secretions in the pancreatic ductal system, which cause inflammation and parenchymal atrophy. Damage to the liver

in cystic fibrosis is due to abnormally thick bile, which accumulates in the biliary tract, causing inflammation and subsequent loss of parenchyma. In this case, there were bridging hepatic fibrosis with mild steatosis (Fig. 4D), loss of the bile duct in some portal tracts, and proliferation of bile ductules that contained amorphous, eosinophilic secretions (Fig. 4D, inset), all of which are features characteristic of cystic fibrosis.

The cause of death in this case is pseudomembranous enterocolitis with septicemia in a patient with cystic fibrosis.

ANATOMICAL DIAGNOSES

Pseudomembranous colitis and enteritis, features consistent with *Clostridium difficile* enterocolitis.

Cystic fibrosis, associated with cystic bronchiectasis of the lungs, hepatic fibrosis, and pancreatic atrophy.

Dr. Freedman reports receiving consulting fees from Altus Pharmaceuticals and holding a patent for docosahexaenoic acid in the treatment of conditions related to cystic fibrosis, not currently licensed. No other potential conflict of interest relevant to this article was reported.

REFERENCES

1. Macari M, Balthazar EJ, Megibow AJ. The accordion sign at CT: a nonspecific finding in patients with colonic edema. Radiology 1999;211:743-6.
2. Accurso FJ. Update in cystic fibrosis 2007. Am J Respir Crit Care Med 2008; 177:1058-61.
3. Dray X, Bienvenu T, Desmazes-Dufeu N, Dusser D, Marteau P, Hubert D. Distal intestinal obstruction syndrome in adults with cystic fibrosis. Clin Gastroenterol Hepatol 2004;2:498-503.
4. Robertson MB, Choe KA, Joseph PM. Review of the abdominal manifestations of cystic fibrosis in the adult patient. Radiographics 2006;26:679-90.
5. Maisonneuve P, FitzSimmons SC, Neglia JP, Campbell PW III, Lowenfels AB. Cancer risk in nontransplanted and transplanted cystic fibrosis patients: a 10-year study. J Natl Cancer Inst 2003;95:381-7.
6. Lloyd-Still JD. Crohn's disease and cystic fibrosis. Dig Dis Sci 1994;39:880-5.
7. Schwarzenberg SJ, Wielinski CL, Shamieh I, et al. Cystic fibrosis-associated colitis and fibrosing colonopathy. J Pediatr 1995;127:565-70.
8. Smyth RL, Ashby D, O'Hea U, et al. Fibrosing colonopathy in cystic fibrosis: results of a case-control study. Lancet 1995;346:1247-51.
9. Peach SL, Borriello SP, Gaya H, Barclay FE, Welch AR. Asymptomatic carriage of Clostridium difficile in patients with cystic fibrosis. J Clin Pathol 1986; 39:1013-8.
10. Welkon CJ, Long SS, Thompson CM Jr, Gilligan PH. Clostridium difficile in patients with cystic fibrosis. Am J Dis Child 1985;139:805-8.
11. Gabriel SE, Brigman KN, Koller BH, Boucher RC, Stutts MJ. Cystic fibrosis heterozygote resistance to cholera toxin in the cystic fibrosis mouse model. Science 1994;266:107-9.
12. Binkovitz LA, Allen E, Bloom D, et al. Atypical presentation of Clostridium difficile colitis in patients with cystic fibrosis. AJR Am J Roentgenol 1999;172:517-21.
13. Rivlin J, Lerner A, Augarten A, Wilschanski M, Kerem E, Ephros MA. Severe Clostridium difficile-associated colitis in young patients with cystic fibrosis. J Pediatr 1998;132:177-9.
14. Yates B, Murphy DM, Fisher AJ, et al. Pseudomembranous colitis in four patients with cystic fibrosis following lung transplantation. Thorax 2007;62:554-6.
15. Kawamoto S, Horton KM, Fishman EK. Pseudomembranous colitis: spectrum of imaging findings with clinical and pathologic correlation. Radiographics 1999;19:887-97.
16. Blossom DB, McDonald LC. The challenges posed by reemerging Clostridium difficile infection. Clin Infect Dis 2007; 45:222-7.