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Fulminant pseudomembranous colitis of the left colon successfully treated by surgical resection

Sol kolonun fulminan psödomembranöz kolitinde cerrahi rezeksiyon ile başarılı tedavi

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Pseudomembranous colitis is the classical and most dramatic manifestation of Clostridium difficile infection. Surgery is required for patients with perforation and for those who fail to respond to medical treatment. This is a report of a patient with severe pseudomembranous inflammation confined to the left colon, which was successfully treated by surgical resection.

Key words: Pseudomembranous colitis, clostridium difficile, surgical excision

Psödomembranöz kolit clostridium difficile enfeksiyonunun klasik ve en dramatik tablosudur. Medikal tedaviye yanıt alınamayan ve perforasyon gelişen olgularda cerrahi girişim gereklidir. Bu yazıda, cerrahi rezeksiyon ile başarılı olarak tedavi edilen, sol kolon ile sınırlı şiddetli psödomembranöz enflamasyon olgusu sunulmaktadır.

Anahtar kelimeler: Psödomembranöz kolit, clostridium difficile, cerrahi eksizyon

INTRODUCTION

Accumulated evidence has established antibiotic use as the primary risk factor for pseudomembranous colitis and opportunistic Clostridium difficile infection as the cause of antibiotic–associated colitis, regardless of pseudomembrane formation (1, 2). The use of antibiotics can disrupt the normal bowel ecosystem and colonize the empty bowel. Although most antibiotics have been associated with predisposition to *C. difficile* infection, the most commonly implicated have been clindamycin, cephalosporins and ampicillin (3).

Five toxic factors of *C. difficile* have been described, but only two of these, toxins A and B, have been studied in any detail with good evidence of involvement in disease. The other three factors were described as a second, unstable, enterotoxic protein (4).

Disease may be associated with a spectrum of severity, ranging from mild diarrhea, through moderately severe disease, to life–threatening and sometimes fatal pseudomembranous colitis (PMC). This may be accompanied by toxic megacolon, electrolyte imbalance and occasional bowel perforation. PMC is a progressive, systemic inflammatory state that may develop in patients with *C. difficile* colitis unresponsive to medical therapy (5).

Characteristically, only the colon is involved and endoscopy reveals irregular ulcerations covered with pathognomonic fibrinous pseudomembranes and mucosal edema. There is formation of a pseudomembrane, comprising mucin, fibrin, leukocytes and cellular debris (6).

Sigmoidoscopy reveals the classic adherent yellow plaques that range in diameter from 2 to 10 mm. Intervening mucosa may look normal or plaques may become confluent. The left colon is most commonly affected, but there is rectosigmoid sparing in up to two-thirds of cases, and in 10% of cases, the disease is confined to the right colon. Although *C. difficile* infection has been thought of as a pure colitis, it is now clear that the small bowel is also vulnerable and may even form pseudomembranes (7).

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Endoscopy is an unreliable method of confirming or refuting the diagnosis of *C. difficile* infection (8). PMC arises when the normal colonic bacterial flora is disrupted such that *C. difficile* can colonize the bowel and produce enterotoxin. Therapy with broad-spectrum antibiotics is the key event allowing this to happen in most cases (9). Management of PMC with oral metronidazole and/or vancomycin is usually sufficient. However, progression to fulminant colitis with systemic toxin effects and acute abdominal symptoms is seen with increasing frequency, especially in the elderly and immunosuppressed populations (10, 11).

This case report presents a patient with severe pseudomembranous inflammation confined to the left colon, which was successfully treated by surgical resection.

CASE REPORT

Our patient was a 60-year-old female who was transferred to our surgical intensive care unit from a medical care unit. Her medical history revealed that she was given prophylactic treatment of 480 mg of trimethoprim-sulfamethoxazole bid per oral due to chronic renal insufficiency for two years. Chief complaints on admission to our clinic included diffuse abdominal pain, nausea, vomiting and a very small amount diarrhea. On examination her temperature was increased (39°C) and pulse rate was 110/minute. There was excessive tenderness and guarding in the left upper and lower quadrants. The abdomen was slightly distended but no masses. Digital and rectosigmoidoscopic examination of the rectum was normal. Laboratory tests included a white blood cell count of 17,000 cells/mm^3 and a positive *C. difficile* toxin assay. Stool culture showed *C. difficile*.

Plain abdominal radiographs showed hydroaerobic levels in bowels without pneumoperitoneum. An abdominal ultrasonography demonstrated moderate diffuse bowel wall thickening. Repeated white blood count was 18,000 cells/mm^3. The patient had been treated in the first day of illness with intravenous vancomycin and electrolyte replacement in the medical care unit before being transferred to our surgical unit because of peritoneal irritation and acute abdomen.

At the same time, emergency laparotomy was performed. At operation, left colon demonstrated diffuse wall thickening and inflammation; the remainder of the colon and rectum was normal. A left hemicolectomy and end to end anastomosis were performed. Vancomycin was given intravenously during four days in the postoperative stage.

She was afebrile and had no abdominal pain. Postoperative convalescence was uneventful. The stool culture was negative at the postoperative sixth day for *C. difficile*. The operative specimen showed multiple irregular ulcers with overlying pseudomembranes through the entire colon. Mucosa between the ulcers exhibited edema and congestion. The lesions stopped abruptly at the splenic flexure and distal sigmoid colon (Figure 1).

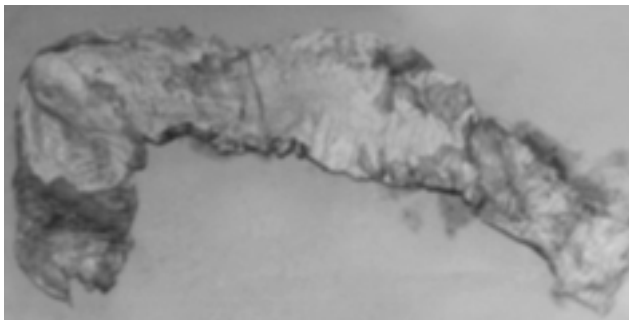

Figure 1. The lesion extending the splenic flexure and distal sigmoid colon

Histology showed generalized inflammation throughout all coats, with foci of superficial necrosis of the mucosa covered by fibrin and mucus in which no protozoan fungi could be demonstrated. A spore forming anaerobic Gram-positive bacillus (*C. difficile*) was demonstrated (Figures 2-3). There was no intramural hemorrhage and the lymph no-

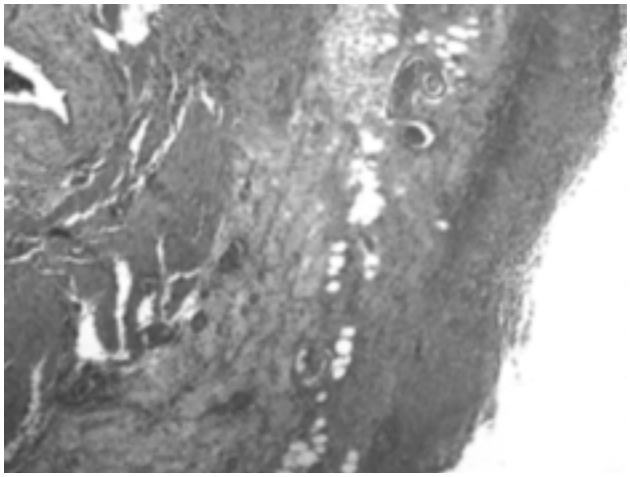

Figure 2. This is a representative section demonstrating pseudomembrane covered with mucosal surface (HE x 50)

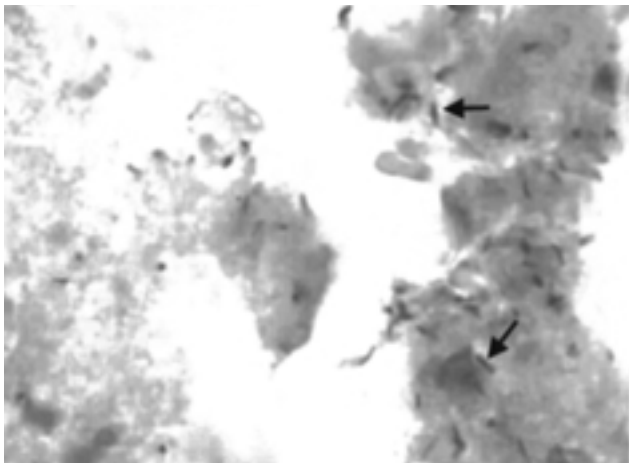

Figure 3. Histopathologic examination showed Gram-positive bacillus in luminal surface of the large bowel (Gram x 1000)

des were unremarkable. The blood vessels were normal and no malignancy was present. The diagnosis was antibiotic-associated pseudomembranous colitis and it was successfully treated by surgical excision.

DISCUSSION

C. difficile is a spore-forming Gram-positive bacterium that was first identified as the cause of antibiotic-associated diarrhea and colitis in the late 1970s. It produces two major toxins referred to as toxins A and B. These are thought to be primarily responsible for the virulence of the bacterium and the major contributors to the pathogenesis of antibiotic-associated gastrointestinal disease (5).

In a hamster model, Borriello et al. clearly demonstrated the differences in virulence between strains of *C. difficile* and showed that the more virulent strains produced more toxin A in vivo than less virulent strains (12).

The administration of antibiotics is the most significant and most frequently reported predisposing factor for *C. difficile*-associated disease. Antibiotics might influence the risk of disease by affecting colonic adhesion, toxin production and the microflora of the large bowel. The broad-spectrum penicillins and cephalosporins are most often culpable, although nearly all antibiotics used orally, parenterally or topically have been implicated. Although parenterally administered aminoglycosides have never been associated with *C. difficile* infection, prolonged courses of combination antimicrobial therapy are particularly prone to cause PMC (3). In our case, the patient was given oral prophylactic antibiotic treatment due to long-standing chronic renal insufficiency.

PMC was first recognized as a clinical entity in the 1950s. The advent of broad spectrum antibiotics in the 1960s and 1970s led to a marked rise in the numbers of patients developing PMC, an increase that has continued to the present day.

The first presentation of *C. difficile* infection might be a surgical emergency with complications more commonly associated with fulminant ulcerative colitis, namely toxic dilatation and perforation (12-14). Volvulus has also been reported in association with PMC and *C. difficile* infection (15). Patients may undergo emergency laparotomy before the true diagnosis is established, particularly in the case of suspected bowel obstruction with marked systemic upset and a distended tender abdomen with or without peritonitis. Plain abdominal radiographs may show dilated small and/or large bowel (16).

In our case, the patient had diffuse peritoneal irritation, particularly in left upper and lower quadrants, and a very little diarrhea output. Patient's plain abdominal radiographs showed dilated small bowel and partially proximal colon.

These appearances cannot be distinguished reliably from those of obstruction or ischemia. Colonoscopy has been recommended as a diagnostic procedure and as a means of decompression but this may induce perforation. Water-soluble contrast enema examination may help to exclude mechanical obstruction, but it is not without risk (1, 17).

Computed tomography (CT) may show the "clover leaf "in less than 20% of PMC cases. Bowel wall thickening, pericolic streaking and ascites are noted in over half of the patients. The severity of disease does not correlate reliably with appearance on CT (18). In our patient, abdominal CT was not performed but ultrasonography showed bowel wall thickening and dilated small and large bowel without free fluid in the peritoneal cavity.

The first approach in the treatment of *C. difficile* infection must be to stop the precipitating antibiotic whenever possible. Studies have indicated that approximately 15–25% of patients respond to this approach alone. Specific treatment is indicated if the patient has systemic symptoms, particularly if there is evidence of severe colonic inflammation or pseudomembrane formation (3). Emergency surgery is required for patients with perfo-

ration and for those who fail to respond to medical treatment (19). The disease is often fatal and in many cases the diagnosis is made only at necropsy. Some seriously ill patients who have fulminant or intractable symptoms may require colectomy or partial colectomy, as in our case.

REFERENCES

1. Bradbury AW, Barrett S. Surgical aspects of Clostridium difficile colitis. Br J Surg 1997: 150-9.
2. Kreisel D, Savel TG, Silver AL, et al. Surgical antibiotic prophylaxis and Clostridium difficile toxin positivity. Arch Surg 1995: 989-93.
3. Spencer RC. The role of antimicrobial agents in the aetiology of Clostridium difficile-associated disease. J Antimicrob Chemother 1998: 21-7.
4. Borriello SP, Davies HA, Kamiya S, et al. Virulence factors of Clostridium difficile. Rev Infect Dis 1990; 12: S185-91.
5. Borriello SP. Pathogenesis of Clostridium difficile infection. J Antimicrob Chemother 1998: 13-9.
6. Schnitt SJ, Antonioli DA, Goldman H. Massive mural edema in severe pseudomembranous colitis. Arch Pathol Lab Med 1983: 211-3.
7. Tsutaoka B, Hansen J, Johnson D, et al. Antibiotic-associated pseudomembranous enteritis due to Clostridium difficile. Clin Infect Dis 1994: 982-4.
8. Bergstein JM, Kramer A, Wittman DH, et al. Pseudomembranous colitis: how useful is endoscopy? Surg Endosc 1990: 217-9.
9. Privitera G, Scarpellini P, Ortisi G, et al. Prospective study of Clostridium difficile intestinal colonization and disease following single-dose antibiotic prophylaxis in surgery. Antimicrob Agents Chemother 1991: 208-10.
10. Bartlett JG. Clostridium difficile-associated enteric disease. Curr Infect Dis Rep 2002: 477-83.
11. Kralovich KA, Sacksner J, Karmy-Jones RA, et al. Pseudomembranous colitis with associated fulminant ileitis in the defunctionalized limb of a jejunal-ileal bypass. Report of a case. Dis Colon Rectum 1997: 622-4.
12. Borriello SP, Ketley JM, Mitchell TJ, et al. Clostridium difficile--a spectrum of virulence and analysis of putative virulence determinants in the hamster model of antibiotic-associated colitis. J Med Microbiol 1987: 53-64.
13. Rexroth G. [Toxic megacolon in pseudomembranous colitis. Complicated course of antibiotic-induced Clostridium difficile colitis]. Fortschr Med 1993: 219-23.
14. Triadafilopoulos G, Hallstone AE. Acute abdomen as the first presentation of pseudomembranous colitis. Gastroenterology 1991: 685-91.
15. Yaseen ZH, Watson RE, Dean HA, et al. Case report: transverse colon volvulus in a patient with Clostridium difficile pseudomembranous colitis. Am J Med Sci 1994: 247-50.
16. Kuntz DP, Shortsleeve MJ, Kantrowitz PA, et al. Clostridium difficile enteritis. A cause of intramural gas. Dig Dis Sci 1993: 1942-4.
17. Strada M, Meregaglia D, Donzelli R. Double-contrast enema in antibiotic-related pseudomembranous colitis. Gastrointest Radiol 1983: 67-9.
18. Boland GW, Lee MJ, Cats AM, et al. Clostridium difficile colitis: correlation of CT findings with severity of clinical disease. Clin Radiol 1995: 153-6.
19. Wilcox MH. Treatment of Clostridium difficile infection. J Antimicrob Chemother 1998: 41-6.