

A 41-YEAR-OLD WOMAN WITH DIARRRHEA AFTER ANTIBIOTIC USE

Christen Harris, MD, Catherine T. Hudson, MD, MPH, Bradley Spieler, MD, Fred A. Lopez, MD, MACP

INTRODUCTION

The association between diarrhea and colitis due to antibiotic mediated disruption of gut microbiota is well established. The causative organism of antibiotic-associated diarrhea and colitis in most cases is *Clostridium difficile* with clindamycin as the antibiotic largely responsible for the earliest cases of infection.^{1,2} A strain of *C. difficile* designated as NAP1/BI/027 is associated with increased virulence compared to other strains and has led recently to more frequent, severe, and refractory infection.¹ Relapse following *C. difficile* treatment with vancomycin or metronidazole is common with 10-25% of patients affected.³ Relapse prevention and treatment are being targeted with new antibiotic regimen guidelines in addition to fecal microbiota transplantation.

CASE REPORT

We present a case of a 41 year-old obese woman with a past medical history of hidradenitis suppurativa who presented to the Emergency Department complaining of mild, crampy abdominal pain and diarrhea for two weeks. The diarrhea was described as non-bloody, watery stool containing mucus. She reported approximately twelve occurrences of diarrhea daily without fever, chills, nausea, or vomiting. The patient admitted to a history of recent left axillary abscess that had been treated in the outpatient setting with a 14 day course of clindamycin about ten days prior to onset of diarrhea and abdominal pain. Her vital signs were stable on arrival. Her physical exam was significant for mild right upper quadrant tenderness without

rebound, guarding, or evidence of a Murphy's sign. Initial labs were significant for leukocytosis of $14.3 \times 10^3/\mu\text{L}$ ($4.5\text{-}11.0 \times 10^3/\mu\text{L}$), mild hypokalemia measured as 3.4mmol/L ($3.6\text{-}5.2\text{mmol/L}$), and normal Cr 0.59mg/dL ($0.7\text{-}1.4\text{mg/dL}$). A CT scan of the abdomen and pelvis with IV contrast revealed pancolitis worse in the pericecal region (Figures 1, 2).⁴ The patient initially

received intravenous ciprofloxacin and metronidazole in the Emergency Department. Stool testing results one day later confirmed the diagnosis of *Clostridium difficile* infection. The patient was discharged to complete a ten day course of oral vancomycin.

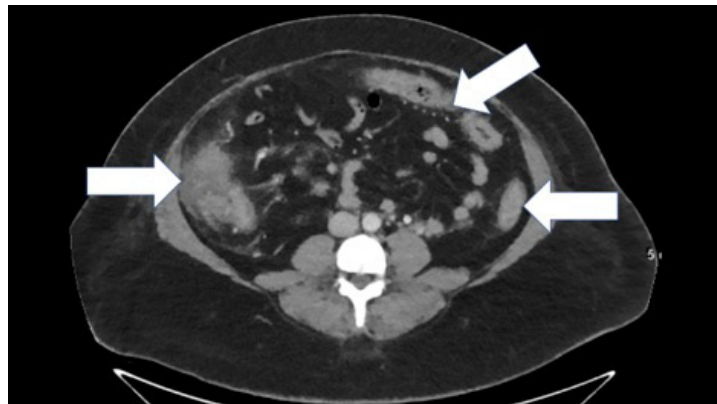


Figure 1. Axial images from a CT of the abdomen and pelvis with intravenous contrast show diffuse colonic mural thickening and pericolic fat stranding (segments of ascending, transverse, and descending colon depicted by the white arrows) that is most pronounced about the ascending colon where there is also nonoccluded fluid which insinuates into the right paracolic gutter.

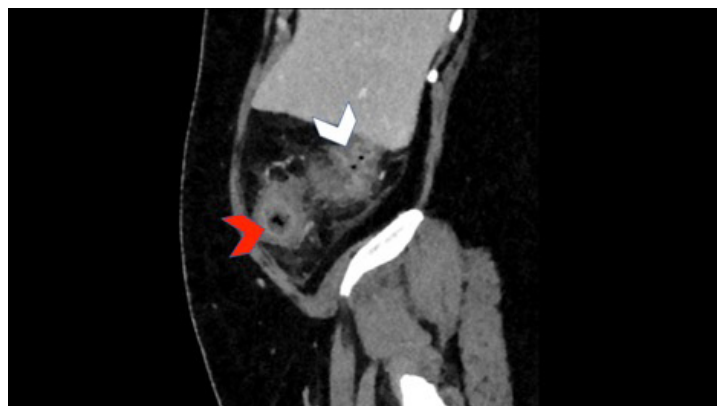


Figure 2. Sagittal reformatted CT images of the hepatic flexure demonstrate mural thickening with mucosal hyperenhancement (red arrowhead) along thickened low attenuation submucosal folds (white arrowhead). This is compatible with an accordion sign, a nonspecific finding often linked to pseudomembranous colitis.

DISCUSSION

Human gut microbiota consists of more than 1,014 bacteria consisting of about 1,000 various species located predominately in the colon.⁵ In addition to influencing the development of the immune system through interactions with gut epithelium, the host microbiota promotes competitive exclusion of gut pathogens.⁶ This role is impaired when species of bacteria are eliminated with antibiotic use which can lead to subsequent enteral infections such as those caused by *C. difficile*.⁷ For this reason, it is important to discontinue use of the inciting antibiotic if possible.⁸ Clindamycin, fluoroquinolones, carbapenems, and cephalosporins are frequently associated with *C. difficile*-associated infections. Source control through use of contact precautions and proper hand hygiene should also be implemented.

C. difficile infection should be considered in patients with new, unexplained diarrhea (≥ 3 loose stools/24 hours) in the setting of recent or ongoing antibiotic use. Stool can be tested with enzyme immunoassay (EIA) for *C. difficile* toxin presence in addition to glutamate dehydrogenase (essential enzyme found in *C. difficile* isolates). Nucleic acid amplification testing (NAAT) for detection of *C. difficile* toxin genes may be used alone or in addition to EIA tests for the diagnosis of *C. difficile*.

The approach to management of *C. difficile* infections is based on disease severity. Proposed criteria from the Infectious Diseases Society of America and Society for Healthcare Epidemiology of America include defining nonsevere infections as those with white blood cell counts $\leq 15,000$ cells/mL and serum creatinine < 1.5 mg/dL.⁸ These infections should be treated with oral vancomycin, 125 mg orally four times daily, or fidaxomicin, 200 mg orally twice daily, for ten days. If these agents are unavailable, oral metronidazole, 500 mg orally three times daily, can be used alternatively for the same duration. Severe infections are defined as those with white counts $\geq 15,000$ cells/mL or a serum creatinine > 1.5 mg/dL. These infections should also

be treated with oral vancomycin, 125 mg orally four times daily, or fidaxomicin, 200 mg orally twice daily, for ten days.⁸ Fulminant colitis refers to cases where hypotension or shock, megacolon, or ileus is present. These cases should be managed with enteric vancomycin, 500 mg four times daily, and intravenous metronidazole, 500mg every 8 hours, in addition to surgical evaluation.⁹

Recurrences of *C. difficile* infection are defined as reappearance of symptoms within 2-8 weeks after treatment cessation.⁸ Fidaxomicin is bactericidal and associated with lower recurrence rate of infections when compared to bacteriostatic vancomycin and metronidazole.¹ First recurrence treatment consists of standard ten day course of oral vancomycin if treated with fidaxomicin or metronidazole initially. A prolonged pulsed-tapered vancomycin regimen should be administered if vancomycin or fidaxomicin was used for initial episode. In second or subsequent *C. difficile* recurrences, options include a prolonged pulse-tapered oral vancomycin regimen, oral fidaxomicin (200 mg orally twice daily for 10 days), oral vancomycin (125 mg orally four times daily for 10 days) followed by rifaximin (400 mg 3 times daily for 20 days); fecal microbiota transplantation should be considered after 2 recurrences.

Fecal microbiota transplantation from healthy individuals to those with severe and recurrent *C. difficile* infection has been utilized in those who have failed standard therapy multiple times.¹⁰ Prepared stool can be delivered via several routes with colonoscopic or nasogastric route occurring most commonly. Cure rates with fecal microbiota transplantation ranges from 81-94 percent in patients with recurrent disease.¹¹ According to one systematic review, the incidence rate of adverse effects associated with fecal microbiota transplantation is 28.5%; the most common is abdominal discomfort.¹² Additionally, standard risks associated with route of transplantation (colonoscopy or NGT placement) should be considered. In summary, after diagnosis of *C. difficile* infection, management should be guided by severity of infection as well as whether the presentation is an initial or recurrent

episode.

CONCLUSION

Clostridium difficile infections are commonly precipitated by antibiotic use. New guidelines for treatment of these infections have recently been introduced. Our patient had a first, non-severe case of *C. difficile* colitis which was ultimately treated with oral vancomycin. For many who are treated for *C. difficile* infection, recurrence becomes problematic.

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