Pseudomembranous Colitis: Do we Need a Screening?

ASHISH GAUTAM*, PRABHAT AGRAWAL*, ABHISHEK RAJ*, ASHWINI K NIGAM*, SUBHASH CHANDRA*, MANISH K BANSAL†

ABSTRACT

In the last few decades, increasing use of antibiotics has dramatically increased the incidence of antibiotic-associated diarrhea. An unopposed homing of *Clostridium difficile* in intensive care unit (ICU) and wards puts forward new challenges for physicians. Development of diarrhea during or just after hospital stay, especially in old patients, is a typical clinical presentation of *C. difficile* diarrhea. Cytotoxin assay from tissue culture is a gold standard diagnostic test but its poor availability, high cost, time bound results and rapid development of life-threatening complications made us to think of a screening test. Demonstration of pathognomonic summit lesions and pseudomembrane with colonoscopy or sigmoidoscopy is relatively inexpensive, easily available and diagnosis is prompt. Our experience in few patients with colonoscopy makes us recommend it as a screening test for all clinically suspected patients. It is refuted as first-line investigation because of good number of false negative results but demonstration of pathognomonic lesions even in few patients saves the life with minimal expenditure and least time wastage before initiation of definitive treatment.

Keywords: Pseudomembranous colitis, summit lesion, antibiotic-associated diarrhea

Clostridium difficile is a Gram-positive, anaerobic, spore-forming bacillus with toxicogenic property. Its presence in intensive care units (ICUs), wards and now even in outpatients has put forward new challenges for treating physicians. Moreover, the cost of treatment and hospital stay increases only because of inadvertent antibiotic use and failure to follow aseptic precautions.

CLINICAL FEATURES

Infection from *C. difficile* has a wide-spectrum of presentation i.e., from asymptomatic carriage to fulminant colitis. Pseudomembranous colitis (PC) is one of the rare but catastrophic presentations of *C. difficile* infection. Other uncommon presentations are non-PC and a milder form of *C. difficile* diarrhea. Collectively, these presentations are called *C. difficile*-associated diarrhea (CDAD). Besides being associated with *C. difficile*, PC can occur in less than 25% of other bacterial, viral and toxic causes of diarrhea, gastroenteritis and anorectal fistulas.

A patient of PC is typically an old age patient with history of antibiotic use during hospitalization, who develops recurrent diarrhea with or without blood in stools. Rarely, patient can present with hypoproteinemia and electrolyte imbalance, hypotension, toxic megacolon, severe sepsis or bowel perforation. Besides age and antibiotic use, other risk factors for PC are use of proton pump inhibitors, nonsteroidal anti-inflammatory drugs (NSAIDs), chronic kidney disease (CKD) and methicillin-resistant *Staphylococcus aureus* (MRSA) co-infection. Rarely, abdominal and pelvic surgeries, Shigella infection, Crohn's disease, neonatal necrotizing enterocolitis, intestinal obstruction, Hirschsprung's disease and colonic carcinoma are associated with development of PC.

DIAGNOSIS

The gold standard for diagnosis of *C. difficile* infection is cytotoxin assay that uses tissue culture. It takes 24-72 hours for reporting and also is not easily available even at tertiary healthcare centers. An alternative enzyme immunoassay (EIA) of toxin A and B of *C. difficile* is less sensitive with 10-20% false negative rate but is relatively easily available and gives result within 24 hours. Diagnostic colonoscopy or sigmoidoscopy is less sensitive with high false positive rates for asymptomatic and nonpseudomembranous type of CDAD. Presence of pathognomonic feature summit

*Assistant Professor
†Associate Professor
Dept. of Medicine, SN Medical College, Agra, Uttar Pradesh
Address for correspondence
Dr Ashish Gautam
Assistant Professor
Dept. of Medicine
SN Medical College, Agra, Uttar Pradesh
E-mail: dr_ashishgautam@yahoo.co.in

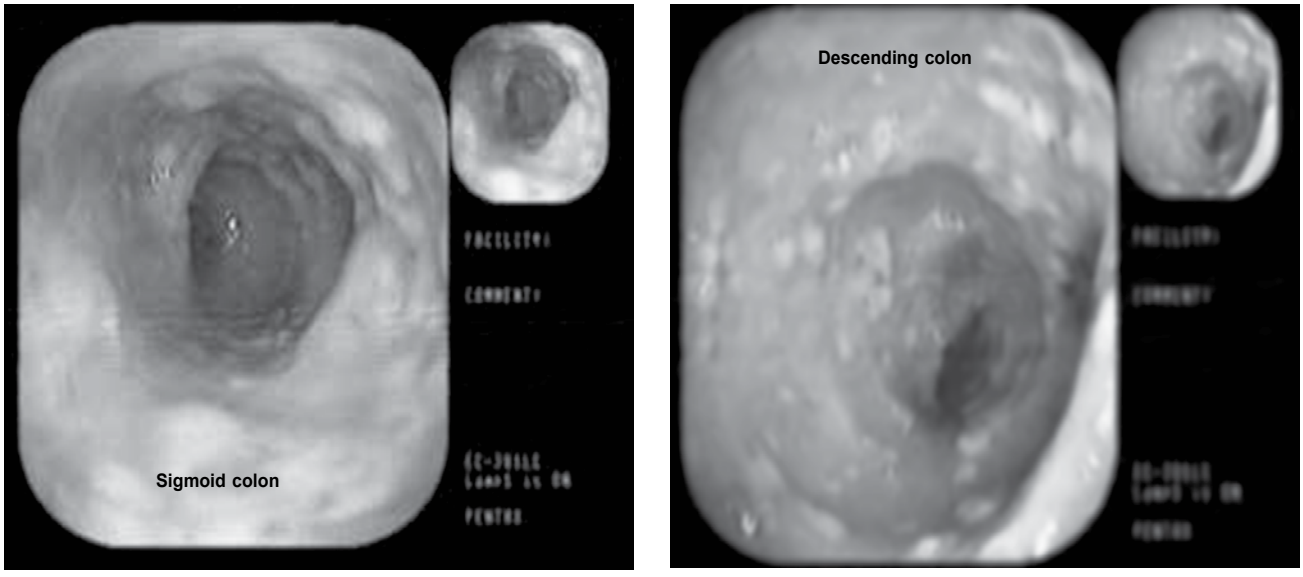

Figure 1. Colonoscopy demonstrates multiple yellow white spots in descending and sigmoid colon.

lesions and pseudomembrane on colonoscopy promptly make diagnosis of PC and usually do not require tissue culture or EIA. PC is sometimes a fatal condition and requires urgent initiation of treatment. Johal et al, in a study of 136 patients, suggest routine sigmoidoscopy in all clinically suspected patients where stool cytotoxin is negative for *C. difficile*. Although CDAD can present with normal appearing colonic mucosa, still a screening colonoscopy of patient with typical clinical presentation can easily clinch the diagnosis of PC and early institution of definitive treatment. Also, colonoscopy is available easily at small cities in India, where the facility of tissue culture and EIA for toxin A and B is not available. Colonoscopy is relatively inexpensive, allows assessment of disease severity and facilitates subsequent management. Ulcerative colitis, Crohn's disease, infectious colitis and other similar conditions can be easily differentiated after colonoscopy. We present here two cases in which an early colonoscopy helped us make out an early diagnosis and institute specific therapy that saved the lives of patients.

CASE 1

A 64-year-old female patient was shifted from orthopedic recovery ward to medicine ward for complaint of severe diarrhea since 5 days. She had been operated for hip fracture 20 days back and was in recovery phase. Most of her antibiotics had been stopped 3 days back when she developed first diarrheal episode. A presumptive diagnosis of antibiotic-associated diarrhea was made and she was put on probiotics. Her general condition continued to worsen so her stool was sent for culture and intravenous ciprofloxacin and metronidazole were started. Ultrasonography of abdomen was normal. Her colonoscopy was planned till report of culture was awaited. Her colonoscopy demonstrated multiple yellow white spots in transverse, descending and sigmoid colon (Fig. 1) with continuous membrane in rectum and anal canal. Her general condition rapidly started improving and she became asymptomatic after 10 days of intravenous and 4 days of oral metronidazole therapy. Retrospective evaluation of antibiotic use disclosed that she was given cephalosporins and aminoglycosides after surgery. Stool culture report later confirmed presence of Clostridium species.

CASE 2

A 72-year-old female was admitted for bleeding per rectum, loose stools since past 3 weeks, pedal edema and altered senses since past 1 week. She was operated and given intravenous clindamycin for gangrene of right middle finger 2 weeks prior to development of loose stools. Her vitals were stable and except for presence of pallor and anasarca, general examination was normal. She was drowsy but no neurological deficit was observed. Abdomen was soft and nontender and there was no apparent organomegaly. Her hemoglobin was 3.5 gm%; serum albumin was 2.13 gm%, serum creatinine 0.75 mg%, and alanine aminotransferase/aspartate aminotransferase (ALT/AST) were 34/24 U/l. *Escherichia coli* × 10^6 was grown on stool culture with sensitivity for all third- and

Table 1. Differences Between Antibiotic-associated Diarrhea from *C. difficile* Infection and from Other Causes

Characteristic	AAD from *C. difficile* infection	AAD from other causes
Most commonly implicated antibiotics	Clindamycin, cephalosporins, penicillins, fluoroquinolones	Clindamycin, cephalosporins, ampicillin or co-amoxiclav
History	Usually no history of antibiotic intolerance	History of diarrhea with antibiotic therapy is common
Clinical features		
Diarrhea	May be florid; evidence of colitis with cramps, fever and fecal leukocytes is common	Usually moderate in severity (nuisance diarrhea) without evidence of colitis
Findings on CT or colonoscopy	Evidence of colitis is common; pseudomembranes often are present	Usually normal
Complications	Hypoalbuminemia, anasarca, toxic megacolon; relapse can occur after treatment with metronidazole or vancomycin	Usually none except occasional cases of volume depletion
Results of assay for *C. difficile* toxin	Positive	Negative
Epidemiologic pattern	May be epidemic or endemic in hospitals or long-term care facilities	Sporadic
Treatment		
Withdrawal of implicated antibiotic	Condition can resolve but often persists or progresses	Condition usually resolves
Antiperistaltic agents	Contraindicated	Often useful
Oral metronidazole or vancomycin	Prompt response	Not indicated

fourth- generation cephalosporins. She was given ceftriaxone 1 g b.i.d. and metronidazole 100 mL t.d.s. Total 6 units of blood transfusion was done and 100 mL of intravenous albumin was given for 6 days. Her general condition improved but except for diarrhea all symptoms subsided. Ultrasonography of abdomen showed an ill-defined mass of 2.6 × 3.2 cm in right iliac fossa with bilateral minimal pleural effusion. Her sigmoidoscopy demonstrated yellow white membranous layer on colonic mucosa with intermittent bleeding ulcer. In descending colon, the membrane scattered into spots and normal appearing intermittent mucosa. These lesions were summit lesions, which were pathognomonic of PC. She was started with vancomycin after which she improved dramatically in 48 hours and complete recovery occured in next 14 days.

Many more cases present to us but most of them respond very well to oral metronidazole therapy. So, based on above experience, we propose to use sigmoidoscopy as screening test for patients who are suspected to have antibiotic-associated diarrhea on clinical grounds. A keen observer can easily make diagnosis of PC on colonoscopy if typical lesions are present. The prime concern is to differentiate between antibiotic-associated diarrhea from *C. difficile* and antibiotic-associated diarrhea due to other causes. Table 1 differentiates between the clinical features and treatment of above two.

DISCUSSION

Pseudomembranous colitis is a rare but frequently fatal presentation of CDAD. Although gold standard for diagnosis of *C. difficile* infection is cytotoxin assay that uses tissue culture, still colonoscopy in an unprepared bowel, which is considered inappropriate for diagnosis, can be sometimes rewarding. Demonstration of pathognomonic summit lesions on colonoscopy makes prompt diagnosis and enables rapid institution of specific treatment and is thus lifesaving. We hereby recommend a diagnostic colonoscopy as screening test in all clinically suspected patients of antibiotic-associated diarrhea. It is easily available, makes prompt diagnosis and helps to differentiate from other similar conditions, is relatively less expensive, needs only a keen observer at cost of high false negative rate.

SUGGESTED READING

1. McFarland LV. Epidemiology of infectious and iatrogenic nosocomial diarrhea in a cohort of general medicine patients. Am J Infect Control. 1995;23(5):295-305.
2. Lai KK, Melvin ZS, Menard MJ, Kotilainen HR, Baker S. *Clostridium difficile*-associated diarrhea: epidemiology, risk factors, and infection control. Infect Control Hosp Epidemiol. 1997;18(9):628-32.
3. Samore MH, DeGirolami PC, Tlucko A, Lichtenberg DA, Melvin ZA, Karchmer AW. *Clostridium difficile* colonization and diarrhea at a tertiary care hospital. Clin Infect Dis. 1994;18(2):181-7.
4. McFarland LV, Mulligan ME, Kwok RY, Stamm WE. Nosocomial acquisition of *Clostridium difficile* infection. N Engl J Med. 1989;320(4):204-10.
5. Dial S, Delaney JA, Barkun AN, Suissa S. Use of gastric acid-suppressive agents and the risk of community-acquired *Clostridium difficile*-associated disease. JAMA. 2005;294(23):2989-95.
6. Wakefield RD, Sommers SC. Fatal membranous staphylococcal enteritis in surgical patients. Ann Surg. 1953;138(2):249-52.
7. Merz CS, Kramer C, Forman M, Gluck L, Mills K, Senft K, et al. Comparison of four commercially available rapid enzyme immunoassays with cytotoxin assay for detection of *Clostridium difficile* toxin(s) from stool specimens. J Clin Microbiol. 1994;32(5):1142-7.
8. Kelly CP, LaMont JT. *Clostridium difficile* - more difficult than ever. N Engl J Med. 2008;359(18):1932-40.
9. Kelly CP, Pothoulakis C, LaMont JT. *Clostridium difficile* colitis. N Engl J Med. 1994;330(4):257-62.
10. Kwon JH, Kelly CP. *Clostridium difficile* and antibiotic-associated diarrhea. In: Bayless RM, Diehl AM (Eds.). Advanced Therapy in Gastroenterology and Liver Disease. 5th Edition, BC Decker: Hamilton, Ontario; 2005. p. 302.
11. Johal SS, Hammond J, Solomon K, James PD, Mahida YR. *Clostridium difficile* associated diarrhoea in hospitalised patients: onset in the community and hospital and role of flexible sigmoidoscopy. Gut. 2004;53(5):673-7.
12. Adams SD, Mercer DW. Fulminant *Clostridium difficile* colitis. Curr Opin Crit Care. 2007;13(4):450-5.
13. Mylonakis E, Ryan ET, Calderwood SB. *Clostridium difficile* - Associated diarrhea: A review. Arch Intern Med. 2001;161(4):525-33.

■■■■

Living Near Convenience Stores could Increase Risk of Atherosclerosis

A new study published in the *Journal of the American Heart Association* has shown a 34% increase in the likelihood of developing atherosclerosis with each 10% increase in nearby convenience stores. In the study, researchers examined 10-year data from the Coronary Artery Risk Development in Young Adults study and compared changes in CAC results over that time to changes in the percentage of convenience stores and fast food restaurants within about 2 miles of the participant's house.

Panic Button Becomes Available to Women with Launch of ERSS and Pan-India Emergency Number 112

The Union Home Minister Shri Rajnath Singh and Minister for Women and Child Development, Smt. Maneka Sanjay Gandhi jointly launched the Women Safety Initiative of Emergency Response Support System (ERSS) in 16 States/UTs and Mumbai city. People in these states and UTs can now call a single pan-India number 112 for any emergency. In addition, Investigation Tracking System for Sexual Offences (ITSSO) and Safe City Implementation Monitoring Portal were also launched. Speaking on the occasion, Shri Rajnath Singh said launch of ERSS is a "milestone in women safety in the country." (*PIB, Ministry of Women and Child Development, February 19, 2019*)

Greater Reduction in Body Fat Percentage with Interval Training

A systematic review and meta-analysis comparing moderate-intensity continuous training with high-intensity interval training concluded that both interval training and moderate-intensity continuous training reduce body fat percentage (%). But, interval training provided 28.5% greater reductions in total absolute fat mass (kg) than moderate-intensity continuous training. These findings are published online February 14, 2019 in the *British Journal of Sports Medicine*.