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Clostridium difficile infection presenting as hematochezia: A case report

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Abstract

Introduction: Clostridium difficile infection (CDI) caused by *Clostridioides difficile*, an organism capable of producing toxins, is the leading cause of antibiotic-associated diarrhea worldwide. It usually presents as watery diarrhea with mucus or occult blood and lower abdominal pain. Severe hematochezia is rarely seen with CDI.

Clinical Presentation: We discuss a case of an elderly female who initially presented with symptomatic anemia, and then severe hematochezia. Colonoscopy revealed varisized ulcers, and edematous and friable intervening mucosa. Histology revealed severe active inflammation, fibrinopurulent exudate, granulation tissue and reactive epithelial cell. The patient also tested positive for C. difficile toxin and antigen. The patient was then managed as CDI with vancomycin and mesalamine for 10 days, and clinically improved.

Conclusion: Although rare, CDI may present as hematochezia. Oral vancomycin is the drug of choice for treating CDI and mesalamine suppository may be given to improve colitis caused by CDI.

Keywords: Clostridium difficile infection, Clostridioides difficile, Hematochezia

Introduction

Clostridium difficile infection (CDI) is the leading cause of nosocomial intestinal infection in the United States and antibiotic associated diarrhea worldwide.[1,2] It is caused by *Clostridioides difficile,* a gram-positive, spore-forming bacterium, and obligate anaerobic bacillus capable of producing toxins.[3] Symptoms vary from being asymptomatic to severe diarrhea and life-threatening colitis, but it usually presents as watery diarrhea with mucus or occult blood, anorexia, nausea, vomiting , low-grade fever, and lower abdominal pain.[4] Clinically, diarrhea frequently occurs, but severe hematochezia is rarely seen with CDI.[5] A systematic review by Borren et al. in 2017, about the emergence of CDI in Asia, demonstrated a pool prevalence of 14.8% among all patients tested and 16.4% among hospitalized patients with diarrhea.[6] CDI is also associated with elevated all-cause and cause-specific mortality, despite possible confounding ill health.[7]

Clinical Presentation

The patient was an 89-year-old female, hypertensive, diabetic, coming in for abdominal pain. She was diagnosed to have an obstructing choledocholithiasis at risk for cholangitis, thus intravenous ciprofloxacin and metronidazole were started. She underwent endoscopic retrograde cholangiopancreatography with sphincterotomy and stone extraction. The patient subsequently underwent laparoscopic cholecystectomy which was converted to open cholecystectomy due to an adherent gallbladder. Post-operatively, she was transferred to the intensive care unit (ICU) due to delayed recovery from anesthesia and extubation. She was maintained on mechanical ventilator, put on nothing per orem (NPO) and started on total parenteral nutrition (TPN). Antibiotics were shifted to piperacillin tazobactam. On the 4th post-operative day, there was improvement of sensorium; weaning from the ventilator was tolerated, and the patient was extubated. TPN was consumed and shifted to enteral feeding. She had no fever, tolerated feeding and with bowel movement. However, she was noted to have leukocytosis and elevation of procalcitonin. She was referred to infectious disease service. Piperacillin tazobactam was shifted to meropenem, given 1 dose of vancomycin, and started on fluconazole. On the 5th post-operative day, she was noted to have decreased sensorium. On work up, there was anemia (hemoglobin 5.3 g/dL) with stable vital signs and no overt GI bleeding. Blood transfusion was done with improvement on sensorium. Fecal immunochemical test (FIT) was positive. Plain CT scan of the whole abdomen was done and was unremarkable. She underwent esophagogastroduodenoscopy (EGD) which revealed blood oozing from the sphincterotomy site. Injection sclerotherapy and application of hemoclips controlled the bleeding. On day 2 post EGD, she had episodes of hematochezia, but vital signs remained stable. Serial CBC showed decreasing hemoglobin trends despite blood transfusion. Physical examination of the abdomen showed normoactive bowel sounds with soft and non-tender abdomen. Digital rectal examination showed lax sphincter tone, no palpable mass with black tarry stool on examining finger. A second look EGD was done and revealed no active bleeding in the ampulla with hemoclips in place. She then underwent colonoscopy. Standard bowel preparation with polyethylene glycol and bisacodyl was given. The examination reached only up to 60cm level due to persistent looping. On withdrawal, at 35 cm level up to the rectum, there were varisized ulcers, some coalescing with dirty looking exudates with edematous and friable intervening mucosa (Figure 1). Biopsies were taken and sent for histopathology. The rest of the visualized colonic mucosa was pale with significant amount of hematin-stained fecal material. No polyps or other mass lesions were noted in the visualized colonic mucosa. Histopathology revealed colonic mucosa with severe active inflammation, fibrinopurulent exudate, granulation tissue, reactive epithelial change (Figure 2). Stool C. difficile toxin and antigen were positive. Mesalamine 1g/suppository twice daily and vancomycin 125mg/5ml to give 5ml per nasogastric tube every 6 hours were administered. Lower gastrointestinal bleeding was resolved on day 2 of mesalamine and vancomycin use, and was completed for 10 days. The rest of her hospital stay was uneventful. She was, thus, eventually discharged on the 32nd hospital stay. A repeat colonoscopy as outpatient was contemplated to complete the examination and assess resolution of previously noted colonic ulcers, but the patient was lost to follow up.

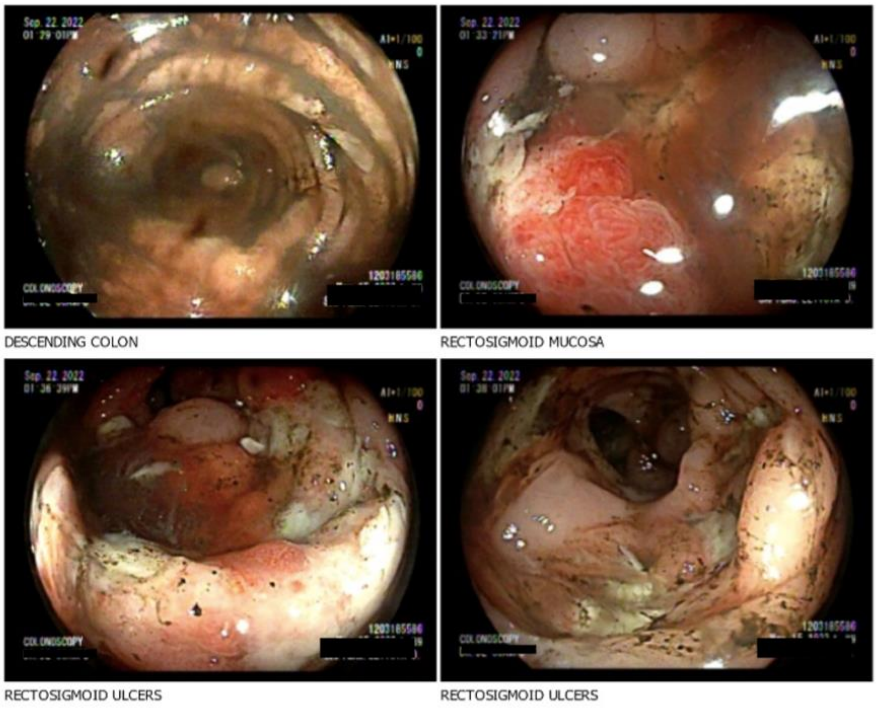

Figure1. Mucosa was edematous and friable with several varisized ulcers, some coalescing with dirty looking exudates from 35 cm level to the rectum.

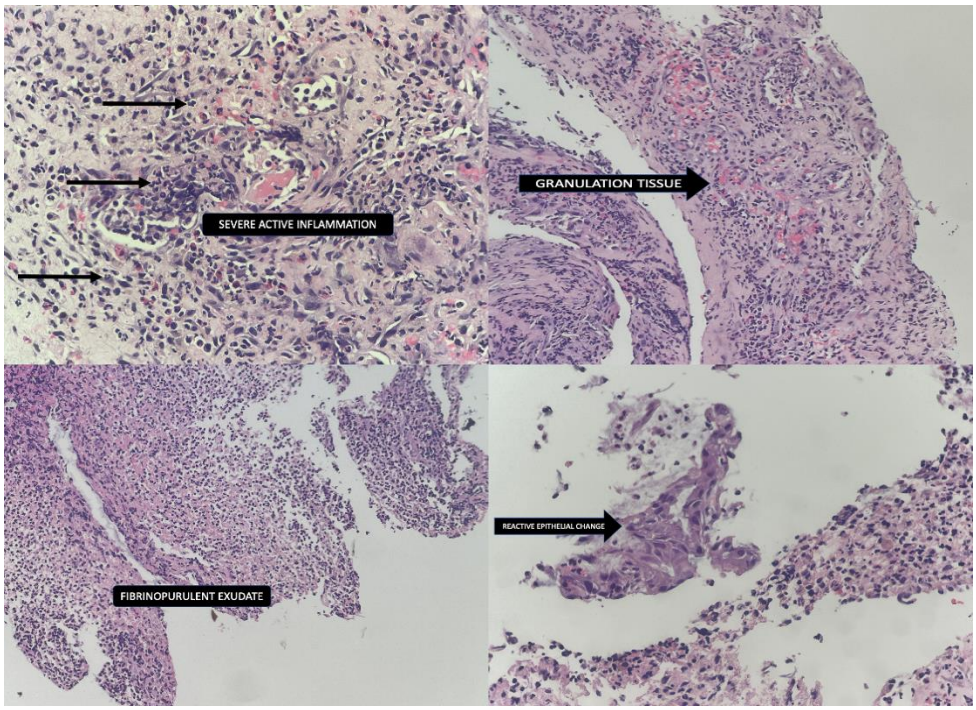

Figure 2. Colonic mucosa with severe active inflammation, fibrinopurulent exudate, granulation tissue, reactive epithelial change; no granuloma or dysplasia seen.

Discussion

The gut microbiome is responsible for maintaining homeostasis in the host, including immune function and gut barrier protection.[8] The pathophysiology of CDI is related to loss of normal gut microbial structure and function, with the disruption of normal gut flora. Risk factors include hospitalization, use of antibiotic therapy, old age, severe illness, enteral feeding, obesity, chemotherapy, gastric acid suppression, and hematopoietic stem cell transplant.[9,10]

Differentials for colitis include infectious colitis, inflammatory bowel disease, ischemic colitis and colorectal cancer. Diagnosis for C. difficile colitis and the decision to treat were based on high clinical suspicion. With endoscopic findings of mucosal edema and multiple varisized rectosigmoid ulcers, histologic findings of severe active inflammation and fibrinopurulent exudate on colonic mucosa coupled with a positive C. difficile test, the patient was managed as a case of C. difficile infection.

Prior antibiotic exposure is the most important risk factor for the development of CDI.[11] Most common antibiotics related to CDI were piperacillin/tazobactam, meropenem, vancomycin, ciprofloxacin, ceftriaxone, and levofloxacin.[12] Our patient underwent open cholecystectomy and was treated with multiple antibiotics for biliary infection which might have predisposed her to develop CDI. Clinical manifestation of CDI may vary but it most commonly manifests as diarrhea.[13] Notably, our patient presented with hematochezia causing anemia. Occurrence of melena or hematochezia in CDI is rare.[14] Exact incidence was not reported, but case reports had described clinical manifestation of hematochezia secondary to CDI.[5] Morimoto et al. concluded that CDI with hematochezia is closely associated with ulcer formation[15] which coincides with the colonoscopic finding in our patient of varisized ulcers in the rectosigmoid. Histopathology revealed colonic mucosa with severe active inflammation, fibrinopurulent exudate, granulation tissue, reactive epithelial change. The Infectious Disease Society of America (IDSA) guidelines recommend oral vancomycin 125 mg, four times daily for 10 to 14 days for both non-severe and severe CDI.[16] C. difficile treatment has also evolved; shifting from the previous standard metronidazole or vancomycin to now vancomycin or fidaxomicin as first-line treatments.[14] Mesalamine suppository has been shown to control the hematochezia and improved the colitis caused by CDI.[17] Our patient was treated with mesalamine 1g/suppository twice daily and vancomycin 125mg/5ml to give 5ml per nasogastric tube every 6 hours for 10 days with clinical response.

Conclusion

Although rare, CDI may present as hematochezia. Oral vancomycin is the drug of choice for treating CDI and mesalamine suppository may be given to improve colitis caused by CDI.

Patient Consent Statement

Upon inquiry, the patient had already expired. Extensive efforts were done to reach out to the relatives who gave their consent through text messages, but failed to sign formal written consent. The patient's privacy and confidentiality were ensured, and remained anonymous. This case report complied with the ethical guidelines set forth by the policies of this journal.

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