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Unusual Presentation of Clostridium Difficile Infection in a Patient with Inflammatory Bowel Disease

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ABSTRACT

Clostridium difficile infection (CDI) is commonly associated with nosocomial diarrhea; however, certain atypical presentations can challenge its diagnosis. We report a case of CDI in a 25-year-old male with inflammatory bowel disease (IBD), presenting with unusual clinical features, including abdominal distension, lower extremity edema, and persistent non-bloody diarrhea. Diagnostic uncertainty arose due to the patient's prior IBD diagnosis and atypical symptoms. Nevertheless, CDI was confirmed through stool toxin assay and colonoscopy findings of pseudomembranes. Treatment with oral vancomycin resulted in complete symptom resolution, underscoring the importance of considering CDI in cases with atypical symptoms. Prompt diagnosis is essential for effective management and prevention of complications.

Introduction

Clostridioides difficile infection (CDI) is a common nosocomial infection caused by a spore-forming, gram-positive anaerobic bacterium that produces enterotoxin A and cytotoxin B. These toxins disrupt the intestinal epithelial barrier, leading to inflammation and diarrhea [1, 2]. CDI is a leading cause of healthcare-associated diarrhea, with clinical manifestations ranging from mild diarrhea to severe complications, such as pseudomembranous colitis, toxic megacolon, and sepsis. Risk factors include antibiotic use, proton pump inhibitor (PPI) use, prolonged hospitalization, advanced age, and immunosuppression [3]. While CDI typically presents with watery diarrhea and abdominal pain, rare atypical symptoms, such as ascites and peripheral edema, may complicate the diagnostic process [4, 5]. These uncommon features, often linked to conditions like hypoalbuminemia, can obscure the diagnosis, particularly in patients with underlying gastrointestinal diseases. Diagnostic confirmation is achieved through stool toxin assays, enzyme immunoassays, polymerase chain reaction (PCR) for toxin genes, or direct visualization of pseudomembranous colitis during colonoscopy [6].

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Patients with inflammatory bowel disease (IBD) are at heightened risk for Clostridioides difficile infection (CDI) due to frequent antibiotic use, altered gut microbiota, and impaired mucosal immunity [7]. CDI in IBD patients is associated with more severe disease manifestations, prolonged hospitalizations, and higher mortality rates. The diagnostic challenge lies in distinguishing a CDI flare from an IBD flare, as overlapping symptoms, such as diarrhea and abdominal pain, are common to both conditions [8, 9]. This report presents an unusual case of CDI in a young male patient with ulcerative colitis who exhibited uncommon clinical features, including ascites, peripheral edema, and hypoalbuminemia, alongside persistent watery diarrhea. The case underscores the importance of considering CDI in patients with uncommon clinical features, particularly those with predisposing conditions such as IBD, to ensure timely diagnosis and treatment.

Case presentation

A 25-year-old male presented to our facility with a 20-day history of abdominal distension and bilateral lower extremity edema. His medical history was notable for ulcerative colitis (UC), diagnosed eight months earlier, for which he was receiving mesalamine. The patient reported a three-month history of persistent, non-bloody watery diarrhea (approximately three episodes per day), accompanied by nausea, vomiting, and mild hypogastric abdominal pain. He denied fever, weight loss, or alcohol consumption.

On admission, the patient was alert and hemodynamically stable, with a blood pressure of 110/70 mmHg, heart rate of 90 beats/min, respiratory rate of 15 breaths/min, and oral temperature of 37.2°C. Physical examination revealed abdominal distension, 2+ pitting edema of the lower extremities, and pale conjunctiva. Laboratory tests showed a white blood cell count of 9,800/mm³ (74.4% neutrophils, 16.4% lymphocytes), hemoglobin level of 11 g/dL, hematocrit of 36.4%, mean corpuscular volume (MCV) of 85.25 fL, red blood cell (RBC) count of 4.27 million/mm³, platelet count of 528,000/mm³, and serum albumin level of 1.8 g/dL. Inflammatory markers (ESR) and coagulation profiles were within normal limits

Ascitic fluid analysis revealed a high serum-ascites albumin gradient (SAAG) and low protein concentration, consistent with ascites due to portal hypertension. The fluid contained a glucose level of 105 mg/dL, protein concentration of 0.3 g/dL, albumin level of 0.1 g/dL, amylase level of 7 U/L, RBC count of 3,100/mm³, and WBC count of 500/mm³ (45% lymphocytes). Gram stain, tuberculosis (TB) smear, and cultures were negative, and a repeat analysis confirmed these findings.

The etiology of the ascites was investigated. According to Starling's law, a high SAAG reflects increased oncotic pressure counterbalancing portal pressure. High-SAAG ascites with low protein concentration typically results from conditions such as cirrhosis, Budd-Chiari syndrome, or veno-occlusive disease. Liver function tests, platelet counts, and imaging (ultrasound and Doppler sonography) showed no evidence of liver pathology. Endoscopy ruled out esophageal varices, and a CT scan revealed no splenomegaly or hepatomegaly. Other potential causes were excluded: thyroid function tests were normal; tumor markers (CEA and CA19-9) and serological tests for Hepatitis B, Hepatitis C, and HIV were negative. Echocardiography and ECG ruled out cardiac etiologies, and a 24-hour urine analysis excluded renal protein loss. Given the patient's chronic diarrhea and IBD history, stool testing for Clostridioides difficile toxins (via enzyme immunoassay) was performed, yielding positive results for toxins A and B. Colonoscopy revealed diffuse pseudomembranes, polyps, and fibrotic bands. Histopathological examination confirmed pseudomembranous colitis, consistent with CDI. Cytomegalovirus (CMV) infection was ruled out using immunohistochemistry (IHC).

The patient was treated with oral vancomycin (250 mg QID for 14 days). Supportive measures, including fluid and electrolyte management, were provided. His symptoms improved significantly within one week, with complete resolution of diarrhea, ascites, and edema by the end of treatment. At one- and three-month follow-up visits, he remained symptom-free. It is noteworthy that, due to the unavailability of intravenous albumin, the patient did not receive albumin therapy.

Discussion

CDI is typically associated with symptoms such as non-bloody diarrhea and abdominal pain (2); however, the presence of ascites and peripheral edema in this case posed a diagnostic challenge. The ascites and lower extremity edema, which resolved with antibiotic therapy, could be attributed to several mechanisms. CDI triggers a strong inflammatory response in the gastrointestinal tract, leading to increased vascular permeability and fluid shifts. This systemic inflammation can result in hypoalbuminemia, which reduces oncotic pressure within blood vessels and promotes fluid leakage into interstitial spaces, causing both ascites and peripheral edema [5]. CDI can also damage the intestinal mucosa, leading to protein-

losing enteropathy (PLE), where proteins like albumin are lost through the gut wall. As CDI resolves with antibiotic treatment, the intestinal mucosa heals, protein loss decreases, and edema and ascites may subsequently resolve [4].

Bacterial toxins also play a role in this process. The disruption of tight junction proteins by C. difficile toxins compromises the integrity of the intestinal barrier, increasing permeability and enabling the potential translocation of bacteria and toxins into the bloodstream [1, 10]. The inflammatory response triggered by C. difficile toxins involves the release of proinflammatory cytokines, which can exacerbate tissue damage and fluid accumulation [11]. In the presence of inflammatory bowel disease (IBD), the patient's baseline inflammatory state may have been aggravated by a superimposed infection such as CDI [8].

Conclusion

In summary, the resolution of ascites and edema following antibiotic therapy for CDI in this patient is likely attributable to a combination of reduced systemic inflammation, improved protein levels, and healing of the intestinal mucosa. Prompt recognition and diagnosis, using stool assays and colonoscopy, are crucial in atypical presentations to prevent delays in treatment.

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Ethical Considerations

Ethical approval

This research is confirmed by Zanjan University of Medical Sciences and an informed consent is obtained for this manuscript publication.

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Conflict of Interests

The authors declare that they have no conflicts of interest.

Authors' contribution

Sattar Jafari: Conceptualization; methodology; supervision; writing – review and editing. Shalaleh Aghaei: Methodology; writing – review and editing. Behnam Sajedi: Conceptualization; methodology; writing—original draft preparation. Samira Akbarieh: Conceptualization; methodology; writing—original draft preparation.

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