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Case Report

Clostridium difficile Bacteremia as a Rare Presentation of Polymicrobial Pyogenic Liver Abscesses and Its Management Challenges

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Keywords
Clostridium difficile · Liver abscess · Pylephlebitis · Polymicrobial infection

Abstract
Extracolonic manifestations of *Clostridium difficile* have been rarely reported. We herein report a case of a 60-year-old immunocompetent man presenting with fever, nausea, abdominal pain, and loose stools for 2 weeks. Triple-phase liver computed tomography demonstrated pyogenic liver abscesses and portal pylephlebitis. Blood cultures grew *C. difficile* and *Bacteroides fragilis*, and liver abscess cultures grew *Proteus mirabilis*, *Escherichia coli*, and the viridans group *Streptococci*. Antibiotics coverage was selected to direct at all identified organisms. This demonstrates an unusual case of *C. difficile* bacteremia in a patient with polymicrobial pyogenic liver abscesses and pylephlebitis.

Binu V. John and Lorena Cuebas-Rosado jointly supervised this work.

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Introduction

Clostridium difficile (CD) is a Gram-positive toxin-generating bacterium that commonly causes pseudomembranous colitis in patients with history of antimicrobial use [1]. Risk factors for CD colitis include older age, previous hospitalization, use of proton pump inhibitors, use of chemotherapy, and immunocompromised state [1, 2]. CD colitis presents with watery diarrhea and is often accompanied by fever, abdominal pain, and leukocytosis [1]. The varied symptoms and severity of the illness largely stem from the CD infection (CDI) of the colon.

CD has been rarely reported to cause extracolonic infections, such as bacteremia and hepatic abscess [1, 3, 4]. Most cases of extracolonic CDI have been associated with gastrointestinal pathology [1, 3], which may be related to gut barrier disruption and bacterial translocation. Here, we present a rare case of an immunocompetent patient with polymicrobial pyogenic liver abscesses involving CD, *Bacteroides fragilis, Proteus mirabilis, Escherichia coli*, and the viridans group *Streptococci*.

Case Presentation

A 60-year-old African American man with a history of chronic obstructive pulmonary disease was admitted with fever (39.4°C), nausea, abdominal pain, and loose stools for 2 weeks. He denied history of antimicrobial use within the past 6 months, multiple hospital visits, or sick contacts. Physical examination was significant for mild tenderness to palpation of the right upper quadrant abdomen. Initial laboratory results were notable for abnormal liver enzymes: aspartate aminotransferase = 134 IU/L, alanine aminotransferase = 143 IU/L, alkaline phosphatase = 125 IU/L, total bilirubin = 0.7 mg/dL, international normalized ratio = 1:3, and albumin = 3.4 g/dL. His white blood cell count was 9,200 cells/cmm, hemoglobin was 10.8 g/dL, and platelet count was 485 × 10^9/L. Hepatitis A antibody, hepatitis B surface antibody/core antibody/surface antigen, hepatitis C antibody, and human immunodeficiency virus screening test were negative. Blood cultures and stool studies (bacterial culture and ova and parasite exam) were sent. Due to formed stool consistency, *Clostridium* toxins were unable to be obtained. Empiric piperacillin-tazobactam was started.

Triple-phase liver computed tomography (CT) demonstrated the presence of variably sized rim-enhancing, centrally low-attenuating "cluster of grapes"-like structures, pathognomonic of pyogenic hepatic abscesses (Fig. 1). Additionally, triple-phase CT demonstrated portal vein thrombosis, visualized as a well-demarcated filling defect straddling right anterior and left portal veins (Fig. 2), seen in the arterial (Fig. 2b) and venous phase (Fig. 2b). The thrombus did not definitively enhance and was unchanging in its low attenuation appearance, suggesting bland venous thrombus as opposed to tumor thrombosis. Overall, this likely reflected ascending septic thrombophlebitis. Notably, the CT also depicted mild sigmoid colon thickening, possible source of hepatic abscesses [5–10].

On empiric piperacillin-tazobactam, patient showed clinical improvement, with resolution of symptoms and improving liver enzymes. Microbiological analyses revealed blood cultures positive for *B. fragilis* and CD, liver abscess cultures positive for *P. mirabilis*, *E. coli*, and the viridans group *Streptococci*, and negative stool studies. Antibiotics were transitioned to intravenous ceftriaxone and metronidazole based on culture speciation and sensitivities. Oral vancomycin was added due to the possibility of CD colonization and risk of developing CD colitis while on intravenous antibiotics. Anticoagulation was started for portal thrombophlebitis. Patient was discharged home to complete 6 weeks of antibiotics and 6 months of anticoagulation. The repeat CT scan at 6 weeks showed near complete resolution of liver abscesses. Outpatient colonoscopy revealed no evidence of malignancy.

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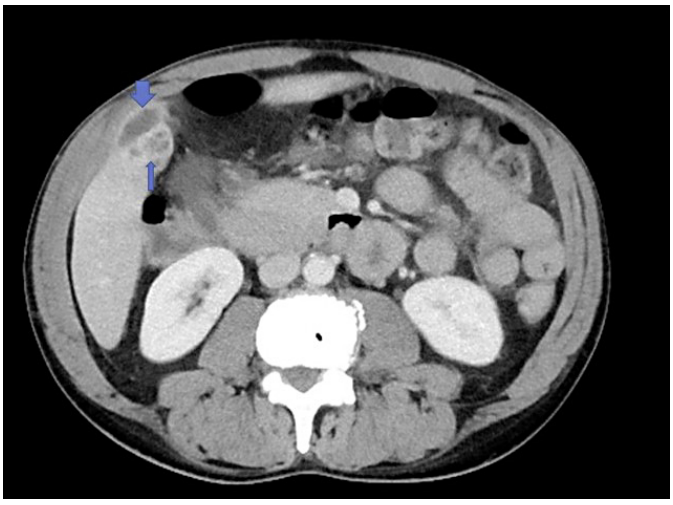

Fig. 1. Triple-phase liver CT (portal venous phase, axial) demonstrates an aggregation of variably sized rim-enhancing, centrally low-attenuating rounded structures, to form a larger, 3 cm abscess cavity within segment V at a subcapsular location (arrows).

Discussion

Extracolonic manifestations of CD are infrequently reported with limited epidemiologic studies and case reports [3, 4]. In a retrospective review of 164,304 hospitalizations in a USA rural hospital from 1990 to 1997, 74 patients had positive blood cultures for *Clostridium* species (incidence of 0.03% among hospitalized patients), and only 1 patient had CD bacteremia [3]. ≥50% of patients with *Clostridium* bacteremia had a gastrointestinal source [3]. The bacterial translocation from the gut can occur in processes that disrupt the gut barrier, such as infections that disrupt the gut epithelia integrity [11]. As intestinal blood supplies convene at the liver, an infectious agent may cross the gut-blood barrier and cause pyogenic liver abscesses [1, 12]. CD toxins are known to cause the disruption of the colonic intestinal epithelial barrier, increase the level of vascular endothelial growth factor A (VEGF-A), and increase the vascular permeability [13]. Extracolonic infections of CD are rare but when they occur, the majority are associated with polymicrobial infection given the pathogenesis involving the altered gut permeability [1]. Our patient likely had gut barrier disruption in colitis leading to bacterial translocation.

Limited literature exists on patients with CD bacteremia and liver abscesses. Morioka et al. [14] (PMID: 28858131) described a 74-year-old man with primary biliary cirrhosis and hepatocellular carcinoma who underwent transarterial chemoembolization and subsequently developed fever and watery diarrhea. The patient was found to have CD in blood and liver abscess cultures [14]. Of note, the patient had a recent antibiotics exposure and rabeprazole use [14]. In contrast, our patient did not have hepatobiliary disease or known CD risk factors. CD and *B. fragilis* were isolated in blood cultures but not in liver abscess cultures. As few hepatic abscesses were not drained due to their size and location, abscess samples may not have fully captured microbes present in blood cultures. The likely source of liver abscesses was colitis, evidenced by the patient's symptoms (nausea, abdominal pain, and loose stools) and CT findings of sigmoid colon thickening and mesenteric retroperitoneal lymphadenopathy. Although our patient's stool samples for testing were inadequate to be processed (formed stools), there is a wide spectrum in the presentation of CDI and colitis and we suspect that our patient had a transient colonic epithelial injury due to CDI that led to bacterial translocation that subsequently led to polymicrobial bacteremia and pyogenic liver abscesses.

Numerous pathogens identified and the isolation of CD had important management implications in our patient. We selected antibiotics to target all identified organisms and also target possible CD colonization to prevent complications related to CDI. In setting of

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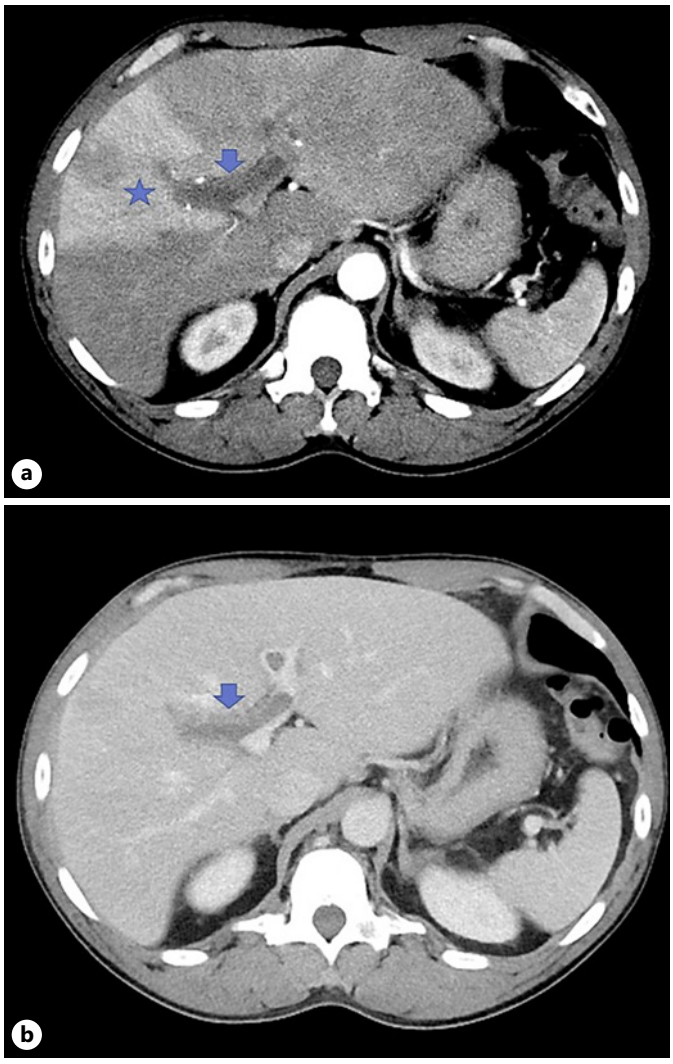

Fig. 2. a Triple-phase liver CT (arterial phase, axial) demonstrates a well-demarcated filling defect (arrow) straddling right and left portal veins (right more occlusive than left). Secondary to the hepatic dual vascular supply, there is a large, sectorial wedge-shaped region of right anterior (segment V/VIII) parenchymal hyperenhancement (star), or transient hepatic attenuation difference. **b** On the portal venous phase, this area becomes relatively isodense to liver parenchyma. The venous filling defect (arrow) does not change in its low attenuation appearance.

pylephlebitis, we reinforced the importance of anticoagulation and treated the infection as an intravascular infection with intravenous antimicrobials for 6 weeks. Interestingly, *B. fragilis* has been described in the literature to worsen the hypercoagulable state [15] and may be associated with the thrombus formation in our patient. Our case highlights the complexity of managing patients with polymicrobial/CD bacteremia in the context of septic thrombophlebitis and liver abscesses in immunocompetent individuals. The CARE Checklist has been completed by the authors for this case report, attached as online supplementary material (for all online suppl. material, see https://doi.org/10.1159/000531892).

Statement of Ethics

Written informed consent was obtained from the patient for publication of the case report and the accompanying images. Ethical approval is not required for this study in accordance with local or national guidelines.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

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Author Contributions

Junghyun Lim, Catherine Zaw, and Simon Abramson wrote and revised the manuscript for intellectual content and approved the final manuscript. Paola N. Lichtenberger, Binu V. John, and Lorena Cuebas-Rosado revised the manuscript for intellectual content and approved the final manuscript. Lorena Cuebas-Rosado is the article guarantor.

Data Availability Statement

All data generated or analyzed during this study are included in this article and its online supplementary material files. Further inquiries can be directed to the corresponding author.

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