Clostridium hastiforme Sepsis in a Patient with Gastrointestinal Malignant Disease

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Abstract

Background: Different Clostridial organisms, commensal in gut flora, can cause blood stream infections, especially in underlying malignant disease. Here, we are presenting first case report of *Clostridium hastiforme* sepsis in a patient with rectal malignant disease.

Methods: Case report and review of pertinent English-language literature.

Result: A 49-y-old female with known rectal malignant disease was admitted for sepsis with sudden onset sharp rectal pain, fever, leukocytosis, and lactic acidosis. The patient was undergoing palliative chemotherapy. Computed tomography (CT) revealed large rectal carcinoma with central necrosis and distant metastasis. She was started empirically with intravenous vancomycin and piperacillin-tazobactam. Blood culture grew gram-variable rods only in anaerobic bottles, which was subsequently identified as *C. hastiforme*. Antimicrobials were changed to metronidazole. The patient improved clinically and was discharged subsequently.

Conclusions: The report emphasizes the importance of rare Clostridial organisms to cause sepsis in patients with underlying gastrointestinal malignant disease. Patients with this condition are usually gravely ill and the infection can be easily missed if anaerobic culture is not routinely ordered.

SEPSIS IN COLORECTAL CANCER is mostly caused by certain bacteria, especially *Streptococcus bovis* and Clostridial species. Both of them are normal flora in the gastrointestinal tract [1]. Among the Clostridial organisms, several studies reported *Clostridium septicum* as the causative agent for septic arthritis [2], liver abscess [3], aortitis [4], and sepsis in colorectal cancer [5–8]. Here, we present a case of sepsis caused by *Clostridium hastiforme* in a patient with anorectal malignant disease to substantiate the importance of other rare Clostridial organisms to cause blood stream infection.

Case

A 49-y-old Hispanic female, recently diagnosed with metastatic rectal carcinoma, presented to the emergency department with complaints of sudden onset of severe colicky and sharp rectal pain that woke her from sleep in the middle of the night. The pain radiated anteriorly to the lower part of the abdomen and was associated with fever, chills, and palpitations. She also had a few episodes of non-bilious, non-bloody vomiting. She tolerated food and her last bowel

movement had been the previous day. She denied any dysuria, diarrhea, constipation, abdominal distension, chest pain, or shortness of breath. She had been admitted to the hospital three months ago and had been diagnosed to have poorly differentiated squamous cell carcinoma of the rectum and anus with metastasis to the liver and adrenal glands. The patient was deemed non-operative and palliative chemotherapy with 5-fluorouracil and cisplatin was begun.

On physical examination the patient was alert and in mild distress for pain. Vital signs were significant for sinus tachycardia and low-grade fever (Tmax 100.2°F). The abdomen was soft and mildly distended with mild tenderness in the lower abdomen and pelvis; bowel sounds were present. Rectal examination was significant for severe tense mass and a small streak of blood. The examination was incomplete due to severe pain. Laboratory workup showed leukocytosis of 21,040 per microliter with left shift and lactate of 3.3 mmol/L. Computed tomography (CT) scan of the abdomen and pelvis revealed large rectal carcinoma with central necrosis anteriorly with hepatic and adrenal metastasis and probable communication into the vagina, likely a rectovaginal fistula.

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Computed tomography also showed the presence of an intra-uterine contraceptive device (IUCD) in situ. Blood cultures were sent and the patient was started on intravenous vancomycin and piperacillin-tazobactam and was admitted to intensive care unit for sepsis. Blood cultures were provisionally positive for gram-variable bacilli only in anerobic bottle. Vancomycin was discontinued. Lactate trended down with aggressive intravenous fluid resuscitation. Tachycardia and leukocytosis were resolved. The organism was finally identified as *Clostridium hastiforme*. Piperacillin-tazobactam was changed to metronidazole. The patient underwent explorative laparotomy followed by palliative diverting loop colostomy. The IUCD was also removed to reduce the risk of further infection. Subsequently the patient improved clinically and was discharged with metronidazole to complete total 14 days of antibiotics.

Discussion

The genus *Clostridium* encompasses more than 60 species that may be commensals of the gut microflora or may cause a variety of infections including blood stream infections in human beings. Molecular epidemiologic studies of anaerobic bacteremia have identified *C. perfringens* and *C. tertium* as the two most frequently isolated species; these organisms cause up to 79% and 5%, respectively, of Clostridial bacteremias [9]. *Clostridium septicum* is also commonly associated with bacteremia, especially with some gastrointestinal anomaly (e.g., diverticular disease), underlying colorectal malignant disease, diabetes mellitus, and severe atherosclerotic cardiovascular disease. Other Clostridial species, e.g., *C. clostridioforme*, *C. hathewayi*, *C. bifermentans*, *C. sordellii*, *C. bolteae*, etc. have also been reported rarely to cause bacteremia [9]. To the best of our knowledge, this is the first reported case of *C. hastiforme* causing sepsis in human beings. There are two previous reports of *C. hastiforme* causing eyelid gas gangrene [10] and brain abscess [11]. It has also been reported as colonizer in a four-year-old male with severe combined immune deficiency [12]. *Clostridium hastiforme* is a slender, rod-shaped obligate anaerobic organism with rounded ends, 0.3–0.6 µm in size. The current taxonomy of this organism is *Tissierella praeacuta* [13]. DNA-DNA hybridization and 16S rRNA gene sequences showed that they seem to be members of same genomic species [14]. They are also indistinguishable based on their biochemical characteristics [13]. Although Clostridia stain gram-positive in the early stages of growth, they may appear to be gram-negative or gram-variable later in the growth cycle or in infected tissue specimens leading to the difficulties in choosing the appropriate antibiotics [9]. In the present case also *C. hastiforme* was provisionally reported as a gram-variable rod. There are few instances in which other bacteria, e.g., *Helcococcus kunzii*, have been misidentified as *C. hastiforme* [15]. The clinical importance of recognizing Clostridial bacteremia and starting appropriate treatment immediately cannot be overemphasized. The bacteremia most commonly occurs after hematogenous dissemination usually from ulceration or necrosis in gastrointestinal mucosa. The possible explanation for this association is that the anaerobic glycolysis of the tumor may provide a hypoxic and acidic environment that favors germination of Clostridial spores [16]. These areas of tissue necrosis may explain why gastrointestinal malignant growths have also been reported with Clostridial sepsis. The presence of flagella and the production of various enzymes including fi-

brinolysin, hyaluronidase, deoxyribonuclease, and hemolysins also help the Clostridial organisms to invade and spread through the tissue [2]. Thus, patients with this condition usually are gravely ill and infection may metastasize to distant anatomic sites, resulting in spontaneous myonecrosis [9]. Alternative methods to identify these strains, such as polymerase chain reaction (PCR) or other rapid diagnostic tests, are not currently available. The infection can be easily missed if anaerobic culture is not routinely ordered. Anaerobic blood cultures and gram stain interpretation remain the best diagnostic tests at this point. As Clostridial sepsis is an uncommon diagnosis, early identification, administration of appropriate antibiotics, and surgery if possible will improve the outcome.

Author Disclosure Statement

No competing financial interests exist.

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Abbreviations Used

CT = computed tomography
IUCD = intrauterine contraceptive device
DNA = deoxyribonucleic acid
rRNA = ribosomal ribonucleic acid
PCR = polymerase chain reaction

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