

Case Report

Diffuse Large B-cell Lymphoma of the Abdomen Presenting as *Clostridium Septicum* Sepsis

Siegel EJ^{1*}, Joseph S², Cook J³, Goldman J⁴, Liu Y⁴ and Cheriya P²

¹Drexel University College of Medicine, USA

²Department of Internal Medicine, Pinnacle Health Harrisburg Hospital, USA

³Department of Surgery, Pinnacle Health Harrisburg Hospital, USA

⁴Department of Infectious Diseases, Pinnacle Health Harrisburg Hospital, USA

*Corresponding author: Elana J. Siegel, Drexel University College of Medicine, c/o 1727 South 9th Street, 2F Philadelphia, PA 19148, USA

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Abstract

Background: The association between *Clostridium septicum* and gastrointestinal malignancy has been well documented in the literature. Additionally, the presence of *Clostridium septicum* infection has been described in immunocompromised patients, such as those with lymphoma undergoing active treatment. We present a here a novel case in which diffuse large B-cell lymphoma initially presented as *clostridial* sepsis, in an otherwise immunocompetent host.

Case Presentation: An 81 year-old female presented with a chief complaint of abdominal pain. CT scan demonstrated extensive lymphadenopathy. Blood cultures were positive for *Clostridium septicum*. Colonoscopy visualized friable ulcers within the right colon. Free air noted in post procedure xray prompted urgent surgical intervention, where the surgeons found submucosal mass in the cecum. The patient underwent right hemicolectomy with formation of an end ileostomy. Pathology analysis definitively established the diagnosis of diffuse large B-cell lymphoma.

Conclusions: *C. septicum* sepsis may ensue in immunocompetent patients, and, once discovered, should prompt an investigation to exclude malignancy. In our case, we present a unique finding of diffuse large B-cell lymphoma.

Keywords: *Clostridium septicum*; B-cell lymphoma

Introduction

Clostridium septicum (*C. septicum*) infection is rare, and is often characterized as having an insidious nature and high mortality rate [1]. The association between malignancy and *C. septicum* has been documented in the scientific literature for over 40 years [2], where the discovery of the malignancy often follows initial identification of *C. septicum*. While diagnosis and management of primary colon cancer presenting as *Clostridium septicum* infection is considerably represented in the literature, the equivalent recommendations for lymphoma are tenuous. Whereas the majority of cases are colon adenocarcinoma, we present a unique case of diffuse large B-cell lymphoma.

Case Presentation

The patient is an 81 year-old female with past medical history significant for atrial fibrillation, hypertension and acid reflux who presented to the emergency department with severe abdominal pain. Her condition rapidly worsened, and she was intubated for airway protection. She was started on broad-spectrum antibiotics after blood cultures, which grew *C. septicum*, were drawn. The patient was transferred to our institution for advanced level care.

On arrival, the patient was found to be in septic shock. She was treated with aggressive fluid resuscitation, vasopressors, and stress dose steroids. Her antibiotic coverage was broadened in advance of culture sensitivity data. A CT scan of the chest/abdomen/pelvis with contrast showed mediastinal, retroperitoneal, pelvic, and inguinal adenopathy, with a small to moderate amount of ascites

and inflammatory changes around the cecum. On hospital day 3, she became anemic and underwent colonoscopy, at which time deep, friable ulcers were found in the right colon. Due to poor preparation of the bowel, the cecum was not visualized. The post-procedure imaging noted intra-abdominal free air and the patient was taken emergently to the operating room for perforated viscus. At laparotomy, the cecum was noted to be necrotic and palpation suggested the presence of a mass. The patient underwent right hemicolectomy with formation of an end ileostomy. On gross pathology, the resected bowel revealed a submucosal mass of the distal ileum; microscopically, sheets of large malignant cells containing numerous mitoses were present. Further immunophenotype studies ultimately established the diagnosis of diffuse large B-cell lymphoma. A subsequent bone marrow biopsy additionally showed distal invasion, with infiltration of malignant diffuse large B-cell lymphoma. The patient recovered uneventfully from surgery and continued to improve with tailored antibiotics. She completed a 3-week course of meropenem and was discharged to a rehab facility after a 24-day hospital course.

Four days later, the patient was re-admitted to the intensive care unit due to hemodynamic instability.

On physical exam, she was edematous with diffuse abdominal tenderness, guarding, and signs of peritonitis. A CT scan revealed free intraperitoneal air. Exploratory laparotomy yielded pneumoperitoneum and copious ascites, but no specific source of perforation could be identified. The patient continued to decline postoperatively, with rising lactic acid levels and increasing pressor requirements. Consequently, the patient's family elected for comfort

care, and the patient expired shortly thereafter.

Discussion

In 1969, Alpern and Dowel first described the association between *C. septicum* infection and occult malignancy. They reported the coincidental finding of malignancy in 23 of 27 patients with *C. septicum* infection; 14 of the malignancies were leukemia and 6 were colon cancer [3]. Over the past 40 years there have been isolated case reports describing the relationship of *C. septicum* sepsis and malignancy, more specifically adenocarcinoma of the colon [4].

The prevalence of colonic malignancy has led many to speculate that unique environmental factors in the cecum predispose to mucosal invasion by *C. septicum* [5,6]. In fact, 28 autopsy cases of *C. septicum* sepsis found tumors of the cecum and distal ileum to be the most probable portals of entry in 65% of cases [7]. Koransky, et al. hypothesized that pH, electrolyte and osmotic characteristics of the distal ileum and cecum favor the growth of *C. septicum* in comparison to other areas of the gastrointestinal tract, further bolstering the opportunity to breach the compromised mucosal barrier. Chew, et al. hypothesized that *Clostridium* infections thrive in patients with malignancy because the tumor provides a hypoxic and acidic milieu that promotes spore germination [8]. Our patient's initial colonoscopy did not visualize the cecum; however, the exploratory laparotomy found a necrotic appearing mass at the level of the cecum. This is consistent with previously described literature of a port of entry for bacterial invasion.

Other cases of *C. septicum* bacteremia have been reported in association with chemotherapy or stem cell transplant for leukemia or lymphoma, with ensuing neutropenia enhancing immunosuppression [5,9-12]. Indeed, this represents the majority of reported cases of *clostridial* bacteremia: immunocompromised hosts, with a known diagnosis of underlying malignancy, neutropenia or even diabetes mellitus [13]. Our case illustrates the importance of compromised ileal mucosa as a risk factor for bacterial invasion, even without obvious signs of an immunocompromised or neutropenic state. In a review by Barie, et al. chronicling *Clostridial* bacteremia in patients undergoing surgery over an 8-year span, the authors demonstrated that these patients already had an underlying diagnosis of malignancy prior to being admitted for sepsis. Interestingly, no patients had received chemotherapy or radiation therapy at the time of sepsis diagnosis [14]. This leads to the question: in patients with no known diagnosis of cancer, who present with *clostridial* sepsis, should clinicians pursue a search for occult malignancy?.

A recent review of 4 cases of *C. septicum* and colon cancer concluded that all patients with blood cultures positive for *C. septicum* should undergo colonoscopy, even without the clinical suspicion for malignancy [15]. No analogous recommendations exist for the workup of lymphoma. We believe it is reasonable to extend the same recommendations to include radiological imaging to look for lymphadenopathy and evaluate occult lymphoma as a differential diagnosis. This recommendation could extend to patients whose

gram stains are consistent with *clostridial* species, where the index of suspicion is high for *C. septicum* sepsis.

In 2008, Hermsen, et al. termed *C. septicum* "a surgeon's infectious disease," after concluding that infected patients who underwent surgery for their malignancy had significantly better survival outcomes (57% versus 26%; $P < 0.0001$). They concluded that a more liberal surgical approach should be adopted when evaluating patients with *C. septicum* sepsis [16]. As seen with our patient, surgical intervention ultimately helped make prove the presence of occult lymphoma; despite this diagnosis, the virulent nature of *Clostridial* species ultimately predicted the fatal clinical course.

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