CASE REPORT

Clostridium perfringens bacteremia caused by choledocholithiasis in the absence of gallbladder stones

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INTRODUCTION

Clostridium species are the second most common causes of anaerobic bacteremia, with Clostridium perfringens the most frequently isolated. Malignancies, gastrointestinal disorders and other chronic illnesses have been associated with Clostridium perfringens bacteremia. Clostridium perfringens can cause food poisoning, gas gangrene, necrotizing enterocolitis, tuboovarian abscess, emphysematous cholecystitis, discitis, and liver abscesses. Choledocholithiasis has rarely been reported as a source of Clostridium perfringens bacteremia. We describe a case of Clostridium perfringens bacteremia caused by choledocholithiasis in the absence of gallbladder stones and with normal common bile duct (CBD) diameter and discuss management and review of the literature of this interesting but rare entity.

CASE REPORT

A 67-years-old male presented with periumbilical abdominal pain, fever and jaundice. His anaerobic blood culture was positive for Clostridium perfringens. Computer tomogram scan of the abdomen and abdominal ultrasound showed normal gallbladder and common bile duct (CBD). Subsequently magnetic resonance cholangiopancreatogram showed choledocholithiasis. Endoscopic retrograde cholangiopancreatogram with sphincterotomy and CBD stone extraction was performed. The patient progressively improved with antibiotic therapy. Choledocholithiasis should be considered as a source of Clostridium perfringens bacteremia especially in the setting of elevated liver enzymes with cholestatic pattern.

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two years prior and showed sigmoid diverticulosis and colon polyps. On physical examination his heart rate was 103 and he had scleral icterus. The remainder of physical examination including abdominal examination was normal. Initial laboratory data showed white cell count of 8.2 (4.8-10.5), total bilirubin: 3 (0.2-1.0 mg/dL), direct bilirubin: 0.4 (0.0-0.2 mg/dL), aspartate transaminase: 131 (15-46 U/L), alanine transaminase: 86 (7-56 U/L) and alkaline phosphatase: 254 (38-126 U/L). His liver enzymes were normal one year earlier. Computed tomography (CT) scan of the abdomen and pelvis showed normal gallbladder, normal CBD diameter and colonic diverticulosis without diverticulitis. Ultrasound (US) of the abdomen revealed no stone in the gallbladder and the CBD diameter was 4.5 mm. Anaerobic blood culture was positive for clostridium perfringens. Patient was treated with vancomycin, aztreonam and metronidazole. He was allergic to penicillin. Urine culture was negative. Magnetic resonance cholangiopancreatography (MRCP) showed revealed a 6 mm ovoid filling defect and additional smaller filling defects within the distal common bile duct (Figure 1). Subsequently, endoscopic retrograde cholangiopancreatography confirmed the diagnosis of choledocholithiasis for which sphincterotomy and stone extraction was performed (Figure 2). Following the procedure, liver enzymes improved. He was discharged home on ertapenem and he had colonoscopy on outpatient basis that showed sigmoid diverticulosis.

**DISCUSSION**

*Clostridium* bacteremia is a rare occurrence that can lead to a devastating outcome. Early recognition and treatment of *clostridium* bacteremia can be life saving. The aim of this report is to present a rare case of *Clostridium perfringens* bacteremia caused by choledocholithiasis. There are few epidemiological studies documenting the incidence of *clostridium* bacteremia. A retrospective population-based surveillance for clostridial bacteremia among all residents of the Calgary Health Region (population 1.2 million) during 2000-2006 showed that the incidence of clostridium bacteremia was 1.8/100 000 per year. *Clostridium perfringens* was the most common isolate accounting for 42% of cases followed by *Clostridium Septicum*, *Clostridium ramosum*, *Clostridium clostridiiforme*, and *Clostridium difficile*. Another review of blood cultures drawn in a rural hospital in Wisconsin, United States from 1990-1997 yielded *clostridium* infection in 0.12% of drawn cultures with *Clostridium perfringens* being the most common (21.7%). A review of blood cultures in a Japanese tertiary center during 2001-2009 showed that only 18 patients had *clostridium perfringens* bacteremia. *Clostridium perfringens* is an anaerobic gram positive rod that can produce a wide spectrum of diseases related to toxin production. *Clostridium perfringens* produce four principal toxins including alpha, beta, epsilon, and iota toxins. Alpha toxin can produce gas gangrene while beta toxin can produce necrotic enteritis. *Clostridium perfringens* has also been reported to cause tuboovarian abscess, necrotizing enterocolitis, emphysematous cholecystitis, discitis, and liver abscess. *Clostridium perfringens* bacteremia has been reported to occur following colonoscopy and gynecological procedures. Advanced age and co-morbidities such as hemodialysis, cancer, heart disease, diabetes, Crohn’s disease, COPD, stroke and asthma increase the risk for clostridial infections. Advanced age increases the risk independent of co-morbidities which could be explained by age-related increase of clostridial species in the normal intestinal flora. *Clostridium perfringens* bacteremia has been associated with intravascular hemolysis and death. Alpha toxin...
produced by *Clostridium perfringens* can cause hemolysis, platelet destruction and widespread capillary damage. Intravascular hemolysis can be fatal unless treatment is instituted early. Sudden severe hemolytic anaemia, very low MCV, hemolyzed blood samples and negative Coombs test in a patient with fever should prompt the clinician to consider *clostridium perfringens* infection. The morphological findings seen on blood cell examination are spherocytes, microspherocytes, and neutrophils with vacuoles or Dohle bodies. Fortunately, our patient did not manifest these abnormalities. In our patient it is difficult to determine if the predominance of indirect hyperbilirubinemia is caused by intravascular hemolysis that was limited by early antibiotics use or by choledochohliasis. Therefore we would encourage clinicians to obtain peripheral blood smear in patients with *clostridium perfringens* bacteremia with any evidence suggestive of intravascular hemolysis.

When the clinician encounters *clostridium perfringens* bacteremia, discovery of the source is very important. Sources of *Clostridium perfringens* bacteremia include colon, biliary tree, lungs, tuboovarian, endometrium and decubitus ulcer. Unlikely sources include urinary tract, pancreas, small bowel, esophagus and brain abscess or unknown source. *Clostridium perfringens* bacteremia has been rarely reported as a cause of *Clostridium perfringens* bacteremia. We report an unusual case of *Clostridium perfringens* bacteremia caused by choledochohliasis in the absence of gallbladder stones and with normal CBD diameter. This case demonstrates the importance of pursuing an extensive differential diagnosis because the identification of the underlying source may be necessary to prevent a fatal outcome. Our patient presented with *clostridium perfringens* bacteremia along with newly elevated liver function tests leading to consideration of biliary source for his bacteremia. This led to further imaging for evaluation of the biliary tract despite normal gallbladder and common bile duct seen on abdominal US and CT scan of the abdomen.

*Clostridium perfringens* bacteremia is a rare occurrence. We would like to emphasize the importance of discovery of the source of bacteremia and the early administration of antibiotics. It is important to recognize the occurrence of intravascular hemolysis with *Clostridium perfringens* bacteremia. Imaging of the biliary system by MRCP or endoscopic US is needed despite normal ultrasound and CT scan of the abdomen when biliary source of *Clostridium perfringens* bacteremia is suspected.

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