World Journal of Gastroenterology

Online Submissions: http://www.wjgnet.com/esps/
wjg@wjgnet.com
doi:10.3748/wjg.v18.i39.5632

World J Gastroenterol 2012 October 21; 18(39): 5632-5634
ISSN 1007-9327 (print) ISSN 2219-2840 (online)

CASE REPORT

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

Antwan Atia, Tejas Raiyani, Pranav Patel, Robert Patton, Mark Young

Antwan Atia, Robert Patton, Mark Young, Departments of Gastroenterology, James H Quillen VA Medical Center, Johnson, Mountain Home, TN 37615, United States
Tejas Raiyani, Pranav Patel, General Internal Medicine, Quillen College of Medicine, East Tennessee State University, Johnson, Mountain Home, TN 37615, United States
Author contributions: Atia A managed patient while being hospitalized and he wrote the discussion section; Raiyani T and Patel P wrote the abstract, introduction and case part; Patton R managed the case and did revision of the manuscript; and Young M did final critical revision of the papers.
Correspondence to: Antwan Atia, MD, Departments of Gastroenterology, James H Quillen VA Medical Center, Johnson, Mountain Home, TN 37615,
United States. antwan.atia@yahoo.com
Telephone: +1-423-7477774 Fax: +1-423-7477774
Received: August 30, 2011 Revised: April 20, 2012
Accepted: April 22, 2012
Published online: October 21, 2012

Abstract

A 67-years-old male presented with periumbilical abdominal pain, fever and jaundice. His anaerobic blood culture was positive for *clostridium perfringens*. Computed tomogram scan of the abdomen and abdominal ultrasound showed normal gallbladder and common bile duct (CBD). Subsequently magnetic resonance cholangiopancreaticogram showed choledocholithiasis. Endoscopic retrograde cholangiopancreaticogram-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.

Key words: Choledocholithiasis; Clostridium perfringens; Bacteremia

Peer reviewer: Taketo Yamaguchi, MD, PhD, Vice Director, Department of Gastroenterology, Chiba Cancer Center, 666-2 Nitona-cho, Chuo-ku, Chiba 260-8717, Japan

Atia A, Raiyani T, Patel P, Patton R, Young M. Clostridium perfringens bacteremia caused by choledocholithiasis in the absence of gallbladder stones. *World J Gastroenterol* 2012; 18(39): 5632-5634 Available from: URL: http://www.wjgnet.com/1007-9327/full/v18/i39/5632.htm DOI: http://dx.doi.org/10.3748/wjg.v18.i39.5632

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 abscess. 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-year-old male with medical history of coronary artery disease, diabetes mellitus, hypertension, hypothyroidism, chronic obstructive pulmonary disease (COPD) and diverticulosis presented with abdominal pain and fever. Fever with chills started four days prior to admission. Abdominal pain was sharp, periumbilical, non-radiating, lasted for 4 h, unrelated to food and resolved on its own. He denied nausea, vomiting, blood in stools but had chronic constipation. His last colonoscopy was

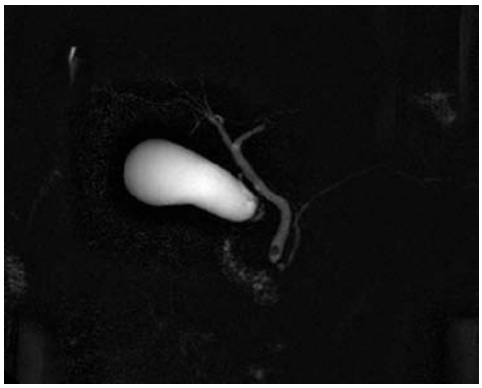

Figure 1 Magnetic resonance cholangiopancreatography shows filling defects within the distal common bile duct.

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.

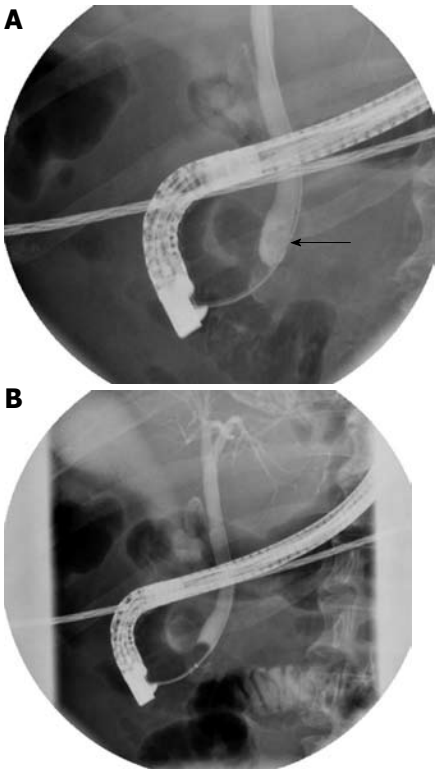

Figure 2 Endoscopic retrograde cholangiopancreatography. A: Filling defects within the distal common bile duct (arrow); B: Filling defects after sphincterotomy and ballon sweep.

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*[1]. 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%)[2]. A review of blood cultures in a Japanese tertiary center during 2001-2009 showed that only 18 patients had *clostridium perfringens* bacteremia[3]. *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[4]. Alpha toxin can produce gas gangrene[5] while beta toxin can produce necrotic enteritis[6]. *Clostridium perfringens* has also been reported to cause tuboovarian abscess[7], necrotizing enterocolitis[8], emphysematous cholecystitis[9], discitis[10], and liver abscess[11]. *Clostridium perfringens* bacteremia has been reported to occur following colonoscopy and gynecological procedures[12,13]. 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[1]. *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[14-16]. 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 choledocholithiasis. 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[2]. Choledocholithiasis has been rarely reported as a cause of *Clostridium perfringens* bacteremia[17]. We report an unusual case of *Clostridium perfringens* bacteremia caused by choledocholithiasis 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 emphasis 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.

REFERENCES

1 **Leal J**, Gregson DB, Ross T, Church DL, Laupland KB. Epidemiology of Clostridium species bacteremia in Calgary, Canada, 2000-2006. *J Infect* 2008; **57**: 198-203
2 **Rechner PM**, Agger WA, Mruz K, Cogbill TH. Clinical features of clostridial bacteremia: a review from a rural area. *Clin Infect Dis* 2001; **33**: 349-353
3 **Fujita H**, Nishimura S, Kurosawa S, Akiya I, Nakamura-Uchiyama F, Ohnishi K. Clinical and epidemiological features of Clostridium perfringens bacteremia: a review of 18 cases over 8 year-period in a tertiary care center in metropolitan Tokyo area in Japan. *Intern Med* 2010; **49**: 2433-2437
4 **Diaz GC**, Boyer T, Renz JF. Survival of Clostridium perfringens sepsis in a liver transplant recipient. *Liver Transpl* 2009; **15**: 1469-1472
5 **Sakurai J**, Nagahama M, Oda M. Clostridium perfringens alpha-toxin: characterization and mode of action. *J Biochem* 2004; **136**: 569-574
6 **Popoff MR**, Bouvet P. Clostridial toxins. *Future Microbiol* 2009; **4**: 1021-1064
7 **Wagner A**, Russell C, Ponterio JM, Pessolano JC. Ruptured tuboovarian abscess and septic shock with Clostridium perfringens in a postmenopausal woman: a case report. *J Reprod Med* 2009; **54**: 652-654
8 **Schlapbach LJ**, Ahrens O, Klimek P, Berger S, Kessler U. Clostridium perfringens and necrotizing enterocolitis. *J Pediatr* 2010; **157**: 175
9 **Gottignies P**, Hossey D, Lasser L, Cherifi S, Devriendt J, De Bels D. Upper gastrointestinal bleeding related to emphysematous cholecystitis due to Clostridium perfringens. *Int J Infect Dis* 2010; **14**: e257-e258
10 **Caudron A**, Grados F, Boubrit Y, Coullet JM, Merrien D, Domart Y. Discitis due to Clostridium perfringens. *Joint Bone Spine* 2008; **75**: 232-234
11 **Umgelter A**, Wagner K, Gaa J, Stock K, Huber W, Reindl W. Pneumobilia caused by a clostridial liver abscess: rapid diagnosis by bedside sonography in the intensive care unit. *J Ultrasound Med* 2007; **26**: 1267-1269
12 **Kunz AN**, Riera D, Hickey P. Case of Clostridium perfringens bacteremia after routine colonoscopy and polypectomy. *Anaerobe* 2009; **15**: 195-196
13 **Halawa S**, Kassab A, Fox R. Clostridium perfringens infection following endometrial ablation. *J Obstet Gynaecol* 2008; **28**: 360
14 **Rajendran G**, Bothma P, Brodbeck A. Intravascular haemolysis and septicaemia due to Clostridium perfringens liver abscess. *Anaesth Intensive Care* 2010; **38**: 942-945
15 **Merino A**, Pereira A, Castro P. Massive intravascular haemolysis during Clostridium perfrigens sepsis of hepatic origin. *Eur J Haematol* 2010; **84**: 278-279
16 **Boyd SD**, Mobley BC, Regula DP, Arber DA. Features of hemolysis due to Clostridium perfringens infection. *Int J Lab Hematol* 2009; **31**: 364-367
17 **Aukee S**, Alhava EM, Koskela E, Lahtinen J, Salmela J. Clostridium septicemia following biliary surgery in a gastrectomized patient. *Scand J Gastroenterol* 1975; **10**: 109-111

S- Editor Cheng JX **L- Editor** A **E- Editor** Li JY