**Clostridium perfringens** and **Escherichia coli** Bacteremia in a Patient with Acute Obstructive Suppurative Cholangitis: A Case Report and Review of the Literature

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Conflict of interest: None declared

**Patient:** Male, 74-year-old

**Final Diagnosis:** Acute obstructive suppurative cholangitis

**Symptoms:** Nausea and vomiting and chills

**Medication:** —

**Clinical Procedure:** —

**Specialty:** Infectious Diseases

**Objective:** Rare disease

**Background:** *Clostridium perfringens* (CP), one of several clostridial species gram-positive bacteria, is a major cause of animal necrosis enteritis and traumatic gangrene. In some reports, CP can cause acute emphysematous cholecystitis in patients with biliary tract infections. However, *C. perfringens* combined with other aerobic bacteria (eg, *E. coli*) in bloodstream co-infection is extremely rare and often fatal. Herein, we present a case of co-infection to underscore this unusual situation so that clinicians can adequately evaluate and treat patients in time.

**Case Report:** A 74-year-old man presented to the Emergency Department half a day after the onset of acute abdominal pain accompanied by nausea, vomiting, and chills. The patient was admitted, following development of jaundice, chills, high fever, confusion, and shock. Computed tomography (CT) revealed that the patient had cholangiectasis with acute obstructive suppurative cholangitis (AOSC). We subsequently performed percutaneous transhepatic gallbladder drainage surgery combined with antibiotics, including ceftriaxone, levofloxacin, and metronidazole. *C. perfringens* and *Escherichia coli* infections were identified by in vitro blood culture. Fortunately, the patient responded favorably to treatment in our hospital and was cured within 1 week.

**Conclusions:** We report a rare case of *C. perfringens* and *E. coli* bloodstream co-infection in a patient with AOSC. We suggest that anaerobic and aerobic co-infection should be considered in future clinical diagnoses. Effective antibiotic treatment combined with surgical drainage is crucial if mixed infection occurs.

**Keywords:** *Clostridium Infections* • Coinfection • Microbiology • Bacterial Infections • *Escherichia coli* Infections

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Background

*Clostridium perfringens* (CP) is a common anaerobic gram-positive bacterium that can be isolated from the soil and from the human gastrointestinal and urogenital tracts [1]. CP can cause septicemia through release of more than 20 different toxins, including α-toxin, which can induce hemolysis, and with poor prognosis [2]. Moreover, the released toxin is capable of causing toxinosis in the host, even if the bacteria are eliminated. For survival, control of potentially fatal hemolysis using appropriate antibiotics and surgery is necessary, and effective therapy should be started before getting the result of blood cultures.

Rare cases of CP in bloodstream infection have been described in the medical literature and the mortality rate is up to 59.7% (74/124) according to recent studies [3,4]. CP infections show broad clinical manifestations, including gangrene, massive intravascular hemolysis, and multi-organ failure from septic shock. Additionally, CP can occur as co-infection with other pathogens, which dramatically increases patient risk.

Herein, we present a case report of a patient with acute obstructive suppurative cholangitis with *C. perfringens* and *E. coli* co-infection. In addition, we provide an overview of all reported CP infections since 1990 in humans with gastrointestinal disease and co-infection of CP with other pathogens.

Case Report

On 30 Oct 2017, a 74-year-old man presented to the Emergency Department of Shanghai Pudong New Area Gongli Hospital after he had begun to experience abdominal pain for half a day. He was febrile (38.7°C) and had a pulse rate of 113 times/min, breathing rate of 20 times/min, and blood pressure of 112/69 mmHg. A repeat computed tomography (CT) scan of the abdomen was obtained, which showed a significant gallbladder distention and dilated common bile duct, indicating the possibility of bile duct calculus (Figure 1A, 1B). A blood test demonstrated a high count of WBC and neutrophils, as well as an abnormal liver function index (Table 1). Above all, the patient was diagnosed with a biliary tract infection and was taken to the Department of Gastroenterology. After clinical admission, the patient completed relevant examinations and fasting.

A total of 4 bilateral blood culture flasks (aerobic culture and anaerobic culture) were sent to the Clinical Bacteriology Department for examination. The treatment course was carefully determined and administered, which include the anti-infective drugs ceftazidime and levofloxacin. However, the symptoms worsened, including persistent abdominal pain, jaundice, chills, and confusion, the temperature rose to 40.4°C, heart rate of 100 beats/min, and blood pressure of 95/50 mmHg. Due to concern about septic shock and acute obstructive suppurative cholangitis, the patient was immediately transferred to the Department of Surgery at 8 PM. The antibiotic treatment regimen was adjusted to ceftriaxone and metronidazole sodium chloride injection. The patient underwent percutaneous transhepatic gallbladder drainage the next day, and his body temperature dropped to 36.5°C and remained normal for 72 h. On 1 Nov, the patient underwent magnetic resonance cholangiogram cryptography (MRCP), which showed the gallbladder was contracted and there were fewer common bile duct calculi (Figure 1C, 1D).

Both anaerobic and aerobic flasks cultivational tests were positive after 12 h of incubation. The specific identification steps were performed. Gas was detected in the anaerobic flask, and direct image microscopic examination found coarse gram-positive bacilli, implying the possibility of anaerobic bacilli infection and the clinician was notified immediately (Figure 2A, 2B). Bacterial colonies with off-white, oblique, and hemolysis rings were detected on the plate after 24 h of anaerobic culture.

Staining of colony smears showed blunt-rounded gram-positive bacilli (Figure 2C). The colonies were selected and subsequently identified as *Clostridium perfringens* by MALDI TOF MS (Figure 3). Various off-white, smooth, and moist colonies could be seen on the aerobic plate after 24-h culture, suggesting a gram-negative bacillus, which was subsequently identified as *Escherichia coli* using the same automatic microbial identification, and the antimicrobial susceptibility was analyzed using the VITEK Compact-2 automatic system.

On 4 Nov, the patient continued to improve and was discharged from the hospital. A review CT after 1 week showed improved outcomes (Figure 1E, 1F). Three months later, the patient underwent the surgical combined treatment of cholecystectomy and choledochotomy by T-tube drainage.

We searched the literature for all cases of *C. perfringens* bloodstream infection in humans with gastrointestinal symptoms disease since 1990 and the papers we found are listed in Table 2. We also searched cases caused by *C. perfringens* following co-infection with other pathogens and found only 7 reported cases in humans or other species (Table 3). Among these 7 cases, only 1 patient, who was infected with *C. perfringens* following *E. coli*, has been reported in 1993, whose death occurred as a result of a subsequent urea-instillation abortion [9]. For other species (eg, pigs, goats, and dogs), all of them died due to co-infection. To the best of our knowledge, this is the first reported case of *C. perfringens* and *E. coli* mixed infection in a patient with acute obstructive suppurative cholangitis who survived after gallbladder drainage surgical treatment.
Figure 1. Computed tomography and magnetic resonance images in the treatment course. CT images at the initial diagnosis (A, B), MRI images of the patient who received treatment (C, D), and CT images of the patient at follow-up examination (E, F). White boxes and arrows indicate the size and location of the lesion.
Discussion

*C. perfringens* sepsis is rare, with only a few cases described in the literature, but it is usually associated with serious hemo-
lysis and high mortality [5]. The α-toxin is produced by *C. per-
fringens*, which mainly causes severe intravascular hemolysis and deficiency of blood, associated with its role of degrada-
tion of phospholipids in the red blood cell membrane and the destruction of platelets, massive tissue necrosis, gas genera-
tion, and gangrene [6]. Based on previous reports, the median time from admission to death is only 8 h during CP blood infection [7]. However, early diagnosis of infection is usually difficult due to the high morbidity and short survival time. Therefore, it is necessary to establish effective guidelines for the treatment of *C. perfringens* infection.

The biliary tract infections, including cholecystitis and chol-
angitis, are usually secondary to predisposing factors leading to bacteremia or sepsis. In clinical practice, some biliary tract microbial agents are gram-negative bacteria, as well as fungi. A previous study showed that 60.9% of patients have bacte-
rial infections, of which *E. coli* infection accounted for 44.4%, followed by *K. pneumoniae*, which accounted for 27.3% [8]. Mixed anaerobic-aerobic infections occur in a variety of lo-
cations, including the abdomen, pelvis, and soft tissues [9]. However, bacteremia caused by *C. perfringens* and *E. coli* is rare

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**Table 1. Summary of the laboratory data.**

|                  | 10.30 (AM) | 10.30 (PM) | 10.31 | 11.1  | 11.2  | 11.10 |
|------------------|------------|------------|-------|-------|-------|-------|
| **WBC (×10⁹/L)** | 9.82†      | 9.97†      | 19.11†| 14.61†| 12.7† | 8.55  |
| **NEU (%)**      | 96†        | 96†        | 95†   | 94†   | 89.7† | 72.8  |
| **HGB (g/L)**    | 156        | 135        | 138   | 133   | 133   | 153   |
| **PLT (×10⁹/L)** | 117↓       | 89↓        | 77↓   | 75↓   | 86↓   | 268   |
| **h-CRP (mg/L)** | 11↑        | 17↑        | 100↑  | 50↑   | 60.2↑ | 2     |
| **K+ (mmol/L)**  | 3.82       | 4.2        | 4.5   | 4.26  | 4.5   | 3.75  |
| **Na+ (mmol/L)** | 137        | 135        | 134   | 130   | 134   | 136   |
| **Cl+ (mmol/L)** | 97.7       | 98.4       | 98.3  | 101   | 109   | 98.2  |
| **CREA (μmol/L)**| 76         | 89         | 81    | 70    | 64    | 62    |
| **UREA (mmol/L)**| 7.69†      | 8.56†      | 8.68† | 9.71† | 8.77† | 6.23  |
| **TBIL (μmol/L)**| 79.4†      | 93.2†      | 110.1†| 34.2† | 19    | 23.4  |
| **ALT (U/L)**    | 178.6      | 195.7†     | 127†  | 84†   | 44    | 50    |
| **AST (U/L)**    | 617†       | 734†       | 216†  | 81†   | 30    | 47    |
| **GGT (U/L)**    | 328†       | 387†       | 284.5†| 215†  | 160†  | 127†  |

† – increase; ↓ – decrease.

**Figure 2.** Bacterial colonies of anaerobic cultivation in vitro. Patient-derived blood sample smears (A) and staining (B) at initial diagnosis or after 24 hours of in vitro culture (C).
Figure 3. Identification of bacteria using mass spectrometry.

### Table 2. Cases of *C. perfringens* bloodstream infection in humans with gastrointestinal disease.

| Ref. No. | Year | Age | Sex | Pathologic diagnosis         | Outcome     | Country |
|----------|------|-----|-----|-------------------------------|-------------|---------|
| 12       | 2013 | 48  | Female | Cholecystitis                  | Survival    | USA     |
| 13       | 2020 | 80  | Female | Gastrointestinal symptoms     | Death       | Japan   |
| 14       | 2010 | 75  | Female | Cholecystitis                  | Death       | USA     |
| 15       | 1989 | 69  | Male  | Gallbladder empyema            | Survival    | Japan   |
| 16       | 2010 | 74  | Male  | Gallbladder stones             | Survival    | USA     |
| 17       | 1996 | 67  | Male  | Gallbladder stones             | Survival    | USA     |
| 18       | 2018 | 81  | Male  | Gastrointestinal stromal tumor | Death       | Germany |
| 19       | 2016 | 46  | Male  | Cholecystitis                  | Survival    | Netherlands |
| 20       | 2019 | 47  | Male  | Ulcerative colitis            | Survival    | Iran    |
| 21       | 2020 | 40  | Female | Enterocolitis                  | Survival    | Australian |
| 22       | 2016 | 76  | Female | Emphysematous gastritis       | Death       | Hungary |
| 23       | 2012 | 21  | Male  | Necrotizing duodenitis         | Survival    | Japan    |
| 24       | 2011 | 60  | Male  | Cholecystitis                  | Death       | USA     |
| 25       | 2015 | 81  | Female | Gastroenteritis                | Death       | Australia |
| 26       | 2020 | 63  | Male  | Gastroenteritis                | Death       | Switzerland |
| 27       | 2007 | 73  | Male  | Cholecystitis                  | Death       | Japan    |
| 28       | 2013 | 77  | Male  | Cholecystitis                  | Death       | Finland |
| 29       | 2020 | 51  | Male  | Enteritis                      | Death       | France  |
| 30       | 2020 | 83  | Female | Cholecystitis                  | Survival    | Japan    |
Table 3. Cases of Clostridium perfringens co-infection pathogens.

| Ref. No. | Year | Co-infection pathogen | Species | Age | Outcome |
|----------|------|------------------------|---------|-----|---------|
| 10       | 1993 | *E. coli*               | Human   | 18  | Death   |
| 32       | 2018 | *C. sordellii*          | Human   | 80  | Survival|
| 33       | 2012 | *T. gandii*             | Human   | 19  | Survival|
| 34       | 2013 | *E. coli*               | Pig     | NA  | Death   |
| 35       | 2007 | *S. aureus & E. coli*   | Goat    | NA  | Death   |
| 36       | 2016 | *C. difficile*          | Dogs (2 cases) | NA | Survival|
| 37       | 2020 | *Klebsiella variicola*  | Human   | 68  | Survival|

and can induce a more serious and fatal disease [10]. In this circumstance, the necessity of treatment by surgical drainage and appropriate antibiotics has been adequately determined in clinical studies [11].

In the present case, the patient was diagnosed with acute obstructive suppurative cholangitis based on clinical symptoms and imaging. Subsequently, the patient received relevant assessment after admission and we adjusted treatment strategies according to the clinical report. Fortunately, the patient did not have serious clinical outcomes, although he also had clinical symptoms such as high fever and cognitive deficits. A positive clinical response often depends on timely and effective treatment. The bloodstream infectious source is most likely via a damaged biliary tract caused by inflammation. Although the causes and mechanisms of this bloodstream mixed infection are still unclear, a possible explanation is a decreased ratio of oxygen in the blood due to *E. coli* infection through a biological mechanism, and this reduced level of oxygen increases the risk of facultative anaerobic *C. perfringens* proliferation. In the case of emphysema cholecystitis caused by *C. perfringens*, a large amount of gas is generally seen in the gallbladder on abdominal CT. However, we did not find this symptom in our patient, which may be related to effective treatment that had a bacteriostatic effect. Moreover, after admission, the diagnosis of acute obstructive suppurative cholangitis was confirmed by a series of typical clinical symptoms and choledocholithiasis. Timely treatment such as early empirical use of metronidazole and levofloxacin and gallbladder drainage-controlled infection prevented further deterioration. The patient’s body temperature returned to normal and no fever recurred. Blood cultures were negative after antibiotics were administered, indicating a bacterial infection causing transient bacteremia.

Limitations of this case report include the absence of anaerobic culture of gallbladder drainage fluid, leading to the inability to identify the source of bloodstream infection, and insufficient evidence of *C. perfringens* and *E. coli* co-infection. Imaging did not show abdominal gas, which was inconsistent with emphysema cholecystitis. However, we obtained and identified *C. perfringens* in both sides of anaerobic blood culture bottles to confirm our conclusion, which highlights the need to collect blood without contamination, and the collection should occur before antibiotics treatment.

**Conclusions**

We presented a rare case suggesting that bloodstream infection by *C. perfringens* following *E. coli* should be considered during acute inflammation. When this mixed anaerobic and aerobic infection is suspected, rapid recognition and effective antibiotic treatment combined with surgery are critical to improving clinical outcomes. More attention to determination and reporting of *C. perfringens* toxins will provide new insights and could reveal new targets for intervention.

**Declaration of Figures’ Authenticity**

All figures submitted have been created by the authors who confirm that the images are original with no duplication and have not been previously published in whole or in part.

**References:**

1. Kiu R, Hall LJ. An update on the human and animal enteric pathogen *Clostridium perfringens*. Emerg Microbes Infect. 2018;7:1-15
2. Simon TG, Bradley J, Jones A, Carino G. Massive intravascular hemolysis from *Clostridium perfringens* septicemia: A review. J Intensive Care Med. 2014;29:327-33
3. McIlwaine K, Leach MTJ. *Clostridium perfringens* septicaemia. Br J Haematol. 2013;163:549
4. Kurasawa M, Nishikido T, Koike J, et al. Gas-forming liver abscess associated with rapid hemolysis in a diabetic patient. World J Diabetes. 2014;5:224-29
5. Castro R, Mendes J, Amaral L, et al. *Clostridium perfringens*'s necrotizing acute pancreatitis: A case of success. J Surg Case Rep. 2017;6:rjx116
6. Kiu R, Hall LJ. An update on the human and animal enteric pathogen *Clostridium perfringens*. Emerg Microbes Infect. 2018;7:141
7. Law S-T, Lee MK. A middle-aged lady with a pyogenic liver abscess caused by Clostridium perfringens. World J Hepatol. 2012;4:252-55

8. Ballal M, Shenoy PA, Gabriel SR, et al. Biliary tract infections and their microbiological spectrum – a study from coastal region of Southern India. Revista Infection. 2019; 23:253-58

9. Tally FP, Gorbach SL. Therapy of mixed anaerobic-aerobic infections. Am J Med Pathol. 1993;14:151-54

10. Koole SN, Lohman BG, van Unen JM. Emphysematous cholecystitis due to Clostridium perfringens. Rev Esp Anestesiol Reanim. 2011;58(2):129-31

11. Law S-T, Lee MK. A middle-aged lady with a pyogenic liver abscess caused by Clostridium perfringens. Scand J Infect Dis. 1989;21:467-71

12. Bush GW, Clements RH, Phillips M, Kent RB. Clostridium perfringens septicemia with massive intravascular hemolysis after laparoscopic cholecystectomy. A case report and review of the literature. Neth J Med. 2010;68:343-46

13. Bari K, Aslanian HR, Pollak J, et al. Emphysematous cholecystitis resulting in secondary biliary cirrhosis. A rare complication of endoscopic retrograde cholangiopancreatography. Acta Chir Belg. 2016;116(1):54-57

14. Zeng S, Tsia Hin Fong CJ, et al. Acute hemorrhagic necrotizing enteritis: A novel watery diarrhoea caused by the co-infection. Revista Infection. 2019; 23:253-58

15. Hagiya H, Naito H, Sugiyama J, et al. Necrotizing duodenitis caused by Clostridium perfringens type A in a Japanese young man. Intern Med. 2012;51(10):2973-76

16. Van Bunderen CC, Bomers MK, Wesdorp E, et al. A newly reported complication. Am J Surg Pathol. 1993;14:151-54

17. Bush GW, Clements RH, Phillips M, Kent RB. Clostridium perfringens septicemia with massive intravascular hemolysis after laparoscopic cholecystectomy. A case report and review of the literature. Neth J Med. 2010;68:343-46

18. Wild W, Bormann F, Sweiht H, et al. Clostridium perfringens septicaemia and a bleeding ulcer of a jejunal interposition: A case report and short review of the literature. Case Rep Med. 2018;2018:4279904

19. Xoole SN, Lohman BG, van Unen JM. Emphysematous cholecystitis due to Clostridium perfringens successfully treated by cholecystectomy. Acta Chir Belg. 2016;116(1):54-57

20. Azimirad M, Yadegar A, Asadzadheh Aghdaei H, Kelly CR. Enterotoxigenic Clostridium perfringens infection as an adverse event after faecal microbiota transplantation in two patients with ulcerative colitis and recurrent Clostridium difficile infection: A neglected agent in donor screening. J Crohns Colitis. 2019;13(7):960-61

21. Walker RN, Liew KC, Adams V, et al. Necrotising enterocolitis caused by Clostridium perfringens: A life-threatening manifestation of a common food borne infection. Med J Aust. 2020;213(3):114-15

22. Sarvari KP, Vasas B, Kiss I, et al. Fatal Clostridium perfringens sepsis due to emphysematous gastritis: A case report. J Med Case Rep. 2019;13:125

23. Hagiya H, Naito H, Sugiyama J, et al. Necrotizing duodenitis caused by Clostridium perfringens type A in a Japanese young man. Intern Med. 2012;51(10):2973-76

24. España Fuente L, Soto Mesa D, Fernández Diez A. Emphysematous cholecystitis due to Clostridium perfringens. Rev Esp Anestesiol Reanim. 2011;58(2):129-31

25. Eltawansy SA, Merchant C, Alluri P, Dwivedi S. Multi-organ failure secondary to Clostridium perfringens gaseous liver abscess following a self-limited episode of acute gastroenteritis. Am J Case Rep. 2015;16:182-86

26. De Zylva J, Padley J, Badbess R, Dedigama M. Multiorgan failure following gastroenteritis: A case report. J Med Case Rep. 2020;14(1):74

27. Kirchhoff P, Müller V, Petrovsky H, Clavien PA. Fatal emphysematous cholecystitis caused by Clostridium perfringens. Surgery. 2007;141(3):411-12

28. Miyahara H, Shida D, Matsunaga H, et al. Emphysematous cholecystitis with massive gas in the abdominal cavity. World J Gastroenterol. 2013;19(4):604-12

29. De Zylva J, Padley J, Badbess R, Dedigama M. Multiorgan failure following gastroenteritis: A case report. J Med Case Rep. 2020;14(1):74

30. Zeng S, Tsia Hin Fong CJ, et al. Acute hemorrhagic necrotizing enteritis: A case report and review of the literature. Ann Palliat Med. 2021;10(5):5853-61

31. Bouras G, Lunca S, Vix M, Marescaux J. A case of emphysematous cholecystitis managed by laparoscopic surgery. JSLS. 2005;9(4):478-80

32. Takemura K, Sekoguchi S, Yamane S, et al. A case of a gas-forming liver abscess caused by Clostridium perfringens after transcatheter arterial chemoembolization. Nihon Shokakibyo Gakkai Zasshi. 2018;115(6):554-62

33. Alsammani MA, Ahmed SR, Alsheeha MA, et al. Co-infection with Toxoplasma gondii and Clostridium perfringens in a postpartum woman with uterine gas gangrene: A case report. J Obstet Gynaecol Res. 2012;38:1024-27

34. Wang X, Ren W, Nie Y, et al. A novel watery diarrhoea caused by the co-infection of neonatal piglets with Clostridium perfringens type A and Escherichia coli (K88, 987P). Vet J. 2013;197:812-16

35. Ribeiro MG, Lara SD, Bicudo SD, et al. An unusual gangrenous goat mastitis caused by Clostridium perfringens. Arq Bras Med Vet. Zootec. 2007;59:129-31

36. Diniz AN, Silva ROS, Oliveira Junior CA, et al. Emphysematous cholecystitis caused by Clostridium perfringens. Intern Med. 2011;50(2):129-31

37. Dahl SS, Thorsteinsson M, Lambine TL, Penninga L. Clostridium perfringens severe sepsis caused by a gas-forming and liver abscess following total pancreatectomy. BMJ Case Rep. 2020;13:e238896