Fulminant Massive Gas Gangrene Caused by *Clostridium perfringens*

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**Abstract**

*Clostridium perfringens* (C.P) gas gangrene is one of the most fulminant infectious diseases. We encountered fulminant massive gas gangrene in a 56-year-old man with alcoholic liver cirrhosis. The patient died 14 hours after diagnosis of gas gangrene (54 hours after admission). Dramatic changes in abdominal CT imaging revealed development of a massive volume of gas in the intra-portal vein, retroperitoneum and abdominal subcutaneous tissue within 24 hours. We also proved C.P infection by immunohistological staining, leading to a diagnosis of C.P gas gangrene. (Internal Medicine 44: 499–502, 2005)

**Key words:** gas gangrene, *Clostridium perfringens*, anti-*Clostridium perfringens* enterotoxin A polyclonal antibody

**Introduction**

Gas gangrene has been classified into three major types: posttraumatic, postoperative, spontaneous. The spontaneous type has the highest associated mortality (1) and is mostly caused by clostridial infection. This may occur following delivery, surgery, or malignancy (2), and is often observed in patients compromised with diabetes or liver cirrhosis (3). There are some species of clostridia (*C. perfringens*, *C. novyi*, *C. septicum*, *C. histolyticum*, *C. bifermentans*, and *C. fallax*) that cause gas gangrene in humans (4). Of these, *Clostridium perfringens* is the most commonly encountered, followed by *C. novyi*, and then *C. septicum* (5). Here, we report a case of fulminant massive gas gangrene caused by *Clostridium perfringens*, and show that this bacterium can be stained immunohistologically on tissue using anti-enterotoxin antibody.

**Material**

- Culture bottle: Bact/ALERT FAN Anaerobic (Bio Merieux, Inc).
- Culture medium: 5% Seep Blood Agar, BTB Lactose Agar, Chocolate Agar, ABHK (Anaerobic Blood Hemin vitamin K) Agar, BBE (Bacteroides Bile Esculin) Agar, CW (Clostridium welchii) Agar.
- Detection kit: VITEK Anaerobic card ANI.
- Antibody: anti-*C. perfringens* enterotoxin A polyclonal antibody (BGS 2119-9950, produced by Biogenesis Ltd, Technology Road, Poole BH17 7DA England, UK. Hannbai by Tanner group, Osaka, Japan).

**Case Report**

A 56-year-old man was admitted to our hospital complaining of fatigue and delirium. He had a history of alcohol dependence, and recently he had been drinking heavily, with a daily intake of 800 ml of Japanese “sake” and 1,000 ml of beer. He had undergone a partial gastrectomy for a gastric ulcer twenty years previously. He had been admitted to our hospital five months earlier because of hematemesis, and was diagnosed with Mallory-Weiss syndrome and alcoholic liver cirrhosis, but he had not visited our hospital since then.

At the time of his current admission, his consciousness appeared confused, his body temperature was 35.8°C, his heart rate was 72/min, and his blood pressure was 114/62 mmHg. A physical examination showed no evidence of a distended or tender abdomen. Laboratory studies showed a white blood cell count of 5,300/mm³, with 70% neutrophils, and a platelet count of 149,000/mm³. Liver function tests showed alanine aminotransferase; 86 IU/l, aspartate aminotransferase; 48 IU/l, and γ-glutamyltranspeptidase; 213 IU/l. Abdominal X-ray and CT scans revealed no abnormal find-
The patient appeared well 24 hours after admission, and his consciousness was clear. He had diarrhea and low grade fever, but did not have abdominal pain. However, 40 hours after admission he suddenly fell into a critical condition. Marbled discoloration spread rapidly on his right sided flank wall (Fig. 1). Laboratory studies showed multiple organ failure, elevation of liver enzymes and renal enzymes, and progression of anemia and leukopenia (2,300/mm$^3$), but hemolysis was not proved. An abdominal CT scan revealed thickness of the rectum wall and gas in the intra-portal vein, retroperitoneum, and subcutaneous tissue of the abdominal wall (Fig. 2A–C). On colonoscopy, the rectum was erosive and bleeding was apparent near the anus, but the proximal rectum was pale and markedly edematous (Fig. 3A, B). We diagnosed gas gangrene and septic shock. Dopamine, dobutamine, methylprednisolone, clindamycin phosphate and biapenem were administered, but the patient died 14 hours later (54 hours after admission), after reaching a critical state. Subsequently, the presence of *Clostridium perfringens*...
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*(C.P)* was proved in a blood culture at 42 hours after admission, and *C.P* septicemia was diagnosed.

**Discussion**

*C.P* gas gangrene is one of the most fulminant gram-positive bacterial infections that occurs in humans. *C.P* was formerly referred to as *Clostridium welchii*, and is an anaerobic gram-positive rod-shaped bacterium that is the most common cause of gas gangrene. It is a normal inhabitant of the human bowel and genital tract. *C.P* is detected in 60% to 90% of cases of clostridial myonecrosis. There are five types of *C. perfringens*, A to E, that are distinguished according to their production of four major lethal toxins. *C.P* produces at least 12 antigenic protein toxins, with the alpha-type toxin being the most common cause of human gas gangrene. Alpha toxin (phospholipase C) is hemolytic, destroys platelets, rapidly reduces cardiac index, and causes shock and multiple organ failure (6, 7).

Generally, the presence of *C.P* toxins in blood or stools has been shown by ELISA, using a polyclonal antibody. Rabbit anti-*C.P* enterotoxin A IgG was used for Western blotting, erythroimmunoassay and flow cytometric analysis (8–10). *C. perfringens* usually appears as a short, plump, strongly gram-positive rod that possesses a central or subterminal spore. The organisms are uniform in appearance, 2 to 4 μm long and 1 to 1.5 μm wide. In the present case, gram-positive rods were found in the rectal tissue. Immunohistologically, they were stained by anti-*C. perfringens* enterotoxin A polyclonal antibody, with staining particularly occurring on and around the spores (Fig. 4A, B). The antibody used was an anti-human *Clostridium perfringens* goat polyclonal antibody (Biogenesis). To our knowledge, this is the first report of detection of *C.P* infection using an enterotoxin antibody, and we suggest that this technique might provide for the early diagnosis of *C.P* infection in tissue.

In the present case of a compromised patient with alcoholic liver cirrhosis, we suspect that *C.P* infected the rectal mucosa, rapidly grew in the intrarectal vessels and rectal submucosa because of the prevalent anaerobic conditions, entered the bloodstream via a damaged mucosal barrier, and rapidly produced a massive volume of gas in the intra-portal vein, retroperitoneal space and abdominal subcutaneous tissue. It is difficult to make a diagnosis of *C.P* infection because the onset of the disease is extremely acute. Clinical features include acute hemolysis, and gas gangrene, and diffuse spreading of cellulites occurs infrequently (11, 12).

Treatment of gas gangrene may follow three clearly defined therapeutic pathways: surgical debridement, antibiotic therapy and hyperbaric oxygen therapy. All necrotic or questionable material should be debrided immediately.

If Clostridium is identified, penicillin has traditionally been the drug of choice. However, in an experimental animal model of gas gangrene caused by *C. perfringens*, Stevens et al have demonstrated that clindamycin, metronidazole, rifampin, and tetracycline used singly were all superior to penicillin (13), and broad spectrum antibiotic coverage with...
concomitant administration of penicillin G, aminoglycoside, and clindamycin is now recommended. The differential diagnosis of gas gangrene must include necrotizing fasciitis, synergistic gangrene, and streptococcal gangrene. Group A streptococcal necrotizing fasciitis/myonecrosis and *Clostridium perfringens* gas gangrene are two of the most fulminant gram-positive infections in humans, but *C. P* infection occurs more rapidly and results in more gas production (14).

Here, we reported a patient with rapidly progressive *C. P* septicemia and massive gas gangrene of the portal vein, retroperitoneum and subcutaneous tissue. Furthermore, we have proved *C. P* infection in tissue by using an anti-*C. perfringens* enterotoxin A polyclonal antibody, and we anticipate that this antibody staining may find future use for the detection of *C. P* infection.

References


Figure 4. A: The bacterium were stained by gram-staining (×500). B: The bacterium were stained by anti-C. perfringens enterotoxin A polyclonal antibody (×500).