# Successful treatment of non-clostridial gas gangrene extending from retroperitoneum to thigh associated with occult cecal cancer: a case report

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**A running title:** Successful treatment of gas gangrene

## Introduction

Clostridial myonecrosis is a necrotising infection of the skeletal muscles that is an uncommon life-threatening condition with a high mortality rate. Classically, gas gangrene was mainly associated with trauma and was caused by clostridial infection.[1,2] However, it has also been reported to occur in the absence of trauma or surgery, and gas gangrene without associated injury is called non-traumatic gas gangrene.[3,4] Most cases of non-traumatic gas gangrene are associated with underlying diseases that cause immunodeficiency, such as malignancy,[3-11] hematological disease,[5,7,12] and diabetes mellitus.[3,4,6,8,9,13] Non-traumatic gas gangrene is a rare condition, but is often rapidly progressive, and requires emergency care. Early diagnosis of non-traumatic gas gangrene arising in the abdomen is often difficult. Here, we describe a rare case of non-clostridial gas gangrene associated with an occult cecal cancer, in which gas was detected in the soft tissues extending from the retroperitoneum to thigh by radiological examination.

**Case Report**

The patient was informed that data from the case would be submitted for publication and gave his consent. He was a 71-year-old man who presented to our hospital because of pain in the lower back and right thigh for about 2 weeks. He had a history of hypertension, but there was no trauma. At presentation, the patient had a temperature of 38-39℃, and his right thigh was markedly enlarged compared with the left thigh, but there was no obvious crepitation. He had difficulty with standing or walking due to severe pain that radiated from the lumbar region to the right thigh, but there was no pain in his lower abdomen. Laboratory tests showed a leukocyte count of 15,300/μl and a C-reactive protein level of >30 mg/dl, indicating a strong inflammatory reaction.

Plain radiography showed gas within the adductor muscles of the proximal thigh (Fig.1). Computed tomography (CT) detected a mass in the descending colon that was contiguous with the iliopsoas muscle (Fig.2a). Swelling and heterogeneous gas bubbles were also seen in several muscles, ranging from the iliopsoas muscle to the adductors of the right thigh (Fig.2b,c). Magnetic resonance imaging revealed a multilocular abscess that was hypointense on T1-weighted images and hyperintense on T2-weighted images, and extended from the iliopsoas to the adductor muscles (Figs.3). These findings indicated a diagnosis of gas gangrene, and emergency surgery was performed to drain the abscess and debride the infected tissues. Because he had diffuse subcutaneous inflammation of the thigh, 21 skin and fascial incisions were made to drain gas and pus (Fig.4a). The femoral muscles were grey-white, and serous exudate with a foul odor was discharged from the incisions (Fig 4b). After the gas had been released, cleansing with saline was

performed and all the wounds were left open. Next, the pelvic cavity was entered via an iliac approach, and a large amount of yellowish-white watery pus was discharged from the retroperitoneal space (Fig4c). During dissection of the retroperitoneum, a fist-sized tumor was palpated in the ileocecal region. An abdominal surgeon was immediately consulted, but in view of the probable diagnosis of ileocecal cancer and the presence of strong adhesions to the retroperitoneum, it was judged to be impossible to resect the tumor during this emergency procedure because of the risk of intestinal perforation into the retroperitoneum. Thus, we only placed a drain in the retroperitoneal space and finished the operation. *Klebsiella pneumoniae*, alpha-streptococi, and anaerobic Gram-negative rods were detected in the pus collected from the pelvic cavity during surgery, while alpha-streptococci and anaerobic Gram-negative rods were recovered from pus in the thigh. Histological examination of muscular tissue removed from the thigh showed abscesses, necrosis, and infiltration of numerous inflammatory cells among degenerated muscle fibers (Fig 5).

After surgery, septic shock progressed to disseminate intravascular coagulation and the patient was managed in the intensive care unit. Although his fever and inflammation were alleviated by treatment with antibiotics, the C-reactive protein level was still 5.69 mg/ml and discharge of pus from the retroperitoneal cavity was persistent at 6 weeks after surgery. Culture of the pus yielded normal intestinal flora, including *Enterococcus faecalis*, alpha-streptococci, *Acinetobacter baumannii*/ha, and anaerobic Gram-negative rods. Contrast-enhanced CT scanning could not completely exclude the existence of a communication between the ileocecal tumor and the

abscesses in the pelvic cavity and thigh, so right hemicolectomy was performed at the Department of Gastroenterological Surgery. The resected specimen showed thinning of the intestinal wall at the site of tumor invasion and strong adhesion to the retroperitoneum, although no obvious perforation of the bowel was observed macroscopically. During the initial operation, this region was noted as the site of strong adhesions that might have increased the risk of intestinal perforation at the time of dissection. After this operation, the inflammatory reaction subsided gradually, and returned to normal by 2 weeks postoperatively. Purulent discharge ceased and the wounds closed spontaneously. The patient was discharged from hospital walking with a cane at 164 days after his initial surgery (Fig.6). He was subsequently found to have liver metastases from his ileocecal cancer and underwent hepatectomy combined with chemotherapy. At 2 years after surgery, he is doing well and there has been no evidence of recurrent infection.

**Discussion**

Gas gangrene is a term which embraces a number of conditions characterized by acute infection with gas-forming organisms which are usually anaerobes, mainly clostridia, but other anaerobic as well as aerobic bacteria may be involved. Non-clostridial gas gangrene is often a mixed infection that involves both aerobic and anaerobic bacteria.[9,10] It usually has a poor prognosis unless treated appropriately, with a reported mortality rate of 4-36%.[11,12] Non-clostridial gas gangrene is considered to be an opportunistic infection associated with host factor, i.e., impaired defenses against infection, since it is common in patients with diseases such as malignant tumors, diabetes, and liver cirrhosis.[6] Alpern et al.[4] reported that 23 (85%) out of 27 patients with *Clostridium septicum* infections had malignant tumors, 14 had anemia, and six had colon cancer. Koransky et al.[5] studied 59 patients whose blood cultures yielded *Clostridium septicum* and found that 42 had malignant tumors, 16 had anemia, and 14 had rectal cancer. They considered that tumor-related breakdown of intestinal mucosal defenses against infection was involved in the development of this disease and that the gastrointestinal tract was the source of the bacteria causing atraumatic myonecrosis.

Gas gangrene is an infection that has a poor prognosis unless appropriate treatment is provided immediately. In many cases, however, the prior history and presenting symptoms have not clearly indicated an intra-abdominal origin, and this has often created serious diagnostic problems. When it is caused by gastrointestinal perforation and fistulous tract formation, or by direct spread of abscesses, the mortality rate is around 50%.[13-15] The anatomic site of iliac perforation is mostly

situated in the reptoperitoneal space. The diagnosis of abscess formation in the reptoperitoneal space may be delayed or missed because of the insidious onset of symptoms and the paucity of local signs due to the relative mild reaction of the reptoperitoneum on infection. The duration of symptoms prior to the diagnosis is often weeks or months.[16] For this reason the abscess may be very extensive and may contain a large number of gas-forming organisms. These are E.coli, Aerobactor aerogenes, Proteus, Klebsiella, anaerobic bacilli of the Bacteroides group, Clostridium species, Pseudomonas, neisseria mucosa, anaerobic streptococci, Actinomyces, and synergism between one of more species of gram-negative aerobic bacteria and an anaerobe.[11,17-19] The diagnosis of gas gangrene is based on the history, local findings (including crepitation), and detection of gas bubbles on plain radiographs or computerized tomography (CT). In the present patient, the prior history and presenting symptoms have not clearly indicated an intra-abdominal origin. CT also revealed that the adductor muscles contained gas bubbles and lesions that communicated with those in the iliopsoas muscle as well as with the ileocecal tumor. This enabled us to promptly start treatment for the intestinal tumor, emphasizing the importance of CT examination. Thus, CT is capable of displaying the detailed localization of gas, which is particularly important when determining the site of incision for debridement, and also allows early diagnosis with improvement of the survival rate.[7,8,20,] In the present patient, ileocecal cancer was present as an underlying disease. Because of cancer-related increased susceptibility to infection and immunodeficiency, and because the retroperitoneum was infiltrated by ileocecal cancer, this region provided the entry for gas gangrene to develop in the right thigh after infection tracked through the retroperitoneal cavity and the

femoral triangle. In patients with gas gangrene extending from the iliopsoas muscle to the lower limb that develops without any apparent cause, we should always keep in mind the possibility of intestinal perforation due to cancer, and should develop strategies for examination and treatment that consider possible diseases of the abdominal organs.

The management of anaerobic infection depends upon general resuscitative measures and specific therapy, namely antibiotics, rapid surgery and hyperbaric oxygen therapy. The value of antibiotics is considered separately, but surgery and hyperbaric oxygen therapy appear to be closely linked. Antibiotic therapy should start immediately after blood and appropriate clinical sites are cultured under aerobic and anaerobic conditions. Treatment should not be deferred until culture results are known. Koransky found that patients with *Clostridium septicum* infections who were not treated with appropriate antibiotics within 12 hours after the onset of sepsis all died within 48 hours after admission.[5] Non-clostridial infection can mimic clostridial infections. The antibiotic of choice is penicillin in high dosage daily intravenously.[21,22] Additional broad spectrum antibiotic cover, such as Cephalosporins and Kanamycin sulfate, is standard.[21,22]

Surgical treatment of areas of necrosis is essential for eradication of infection. Kaiser et al.[23] stated that it is important not to waste much time on the details of diagnosis, but to immediately initiate surgical procedures after the detection of a progressive necrotizing infection in order to improve the outcome. When a diagnosis of gas gangrene has been made, the wounds should be left open for aeration, followed by collection of tissue culture specimens as well as thorough debridement and cleansing. Wounds must be debrided and cleaned every day and administration of

broad-spectrum antibiotics is essential. When available, hyperbaric oxygen may help by inhibiting clostridial growth and toxin production, but there are no controlled studies of the clinical value of such treatment. Surgery when used alone, or with hyperbaric oxygen therapy but without antibiotics, led to 100% mortality in a study group of dogs with *Clostridium perfringens* infections.[24] The use of antibiotics with surgery in the same study resulted in a 70% survival rate. No randomized prospective studies have ever shown that hyperbaric oxygen therapy has reduced morbidity and mortality. Furthermore, in vitro studies suggest that *Clostridium septicum* may be more resistant to hyperbaric oxygen therapy than other clostridial species.[25] Nevertheless, for patients with localized disease for whom a hyperbaric facility is easily accessible, this adjunctive therapy may be useful. Some researchers have noted dramatic results with hyperbaric oxygen therapy.[26-28] In the present patient, however, we could not performed that our hospital had not the apparatus of hyperbaric oxygen therapy. Debridement and drainage in addition to systemic administration of antibiotics led to improvement of his general condition.

Since the onset of gas gangrene was sudden, we could not perform satisfactory investigation of his abdominal complications. In addition, it is doubtful whether it is possible to perform one-stage excision of a tumor and intestinal anastomosis in an undernourished patient when the surgical field is infected. However, treatment of his cecal cancer was also necessary to achieve a cure, so it was difficult to decide the timing of this additional surgery while waiting for his general condition to improve. Given the morbidity and mortality associated with a progressive necrotising infection, prevention is a prime concern. This is particularly true with high-risk clinical settings, as in patients

with cancer, diabetes, DIC, vascular insufficiency, pneumonia, renal or hepatic failure or who are under immunosupression. Although statistical data are lacking, it would seem that preventive measures should include: appropriate attention to hygiene; aggressive would debridement; antibiotics; assurance of an adequate blood supply and tissue oxygenation; adequate drainage and/or delayed wound closure; and application of the principles of nutritional support. And also, CT is even more sensitive than physical examination in detecting soft tissue gas and may be very helpful in demonstrating a reptoperitoneal and/or psoas abscess.

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**Legends:**

**Fig. 1.** Anteroposterior radiograph of the hip joint and thigh showing multiple gas shadows (arrows) in the soft tissues on the medial aspect of the thigh.

**Fig. 2.** Axial computed tomography. A. CT scan of the lower abdomen shows a cecal cancer (head arrow). B. CT scan of the pelvis shows multiple gas bubbles in the iliopsoas muscle (arrow). C. CT scan of the proximal right thigh shows multiple gas bubbles and swelling of the adductor muscles.

**Fig. 3.** Axial MR imaging of the pelvis (A,B) and the proximal thigh (C,D). A, C. T1-weighted images (TR/TE: 500/35) B,D. T2-weighted images (TR/TE: 2000/100). Inflammation extends from the iliopsoas muscle to the muscles around the hip and the medial aspect of the thigh, and abscess formation in these areas is also observed.

**Fig. 4.** A-C: Surgical findings. A: A total of 21 incisions were made due to diffuse inflammation of the thigh. B: Foul-smelling clear serous exudate was discharged from the femoral incisions. C: A large amount of whitish yellow pus was discharged from the retroperitoneal cavity.

**Fig. 5.** Photomicrograph of the affected adductor muscle. Numerous inflammatory cells are infiltrating among atrophic muscle fibers. H&E. x100

**Fig. 6.** Postoperative course. At presentation, the patient underwent immediate incision and drainage. Soon afterward, septic shock developed into disseminated intravascular coagulation (DIC) and pneumonia requiring management in intermittent care unit (ICU). His fever and c-reactive protein (CRP) decreased gradually. After excision of a cecal cancer, discharge of pus ceased and his wounds closed spontaneously.

ABPC = ampicillin, CPFX = ciprofloxacin, CTM = cefazolin, FLCZ = fluconazole, MCFG = micafungin, MINO = minocycline, PAPM/BP = panipenem / betamipron, PIPC = piperacillin