

**CASE REPORT****PATHOLOGY/BIOLOGY**

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## Fatal *Clostridium perfringens* Septicemia After Colonoscopic Polypectomy, Without Bowel Perforation

**ABSTRACT:** Since its introduction, colonoscopy has played an important role as a diagnostic, therapeutic, and screening tool. In general, colonoscopy is regarded as a safe procedure, but complications may occur. The most dreaded of these complications is colonic perforation. Bacteremia postprocedure may occur, and although it is not uncommon, it rarely results in clinically significant complications. Patients with IBD (inflammatory bowel disease) are a high-risk population for bacteremia, which may lead to bowel wall overstepping by the bacteria. With regard to that, we report a fatal case of gas gangrene complicating colonoscopy polypectomy without bowel perforation in a healthy adult. To the best of our knowledge, only two other cases of retroperitoneal gas gangrene associated with colonoscopy polypectomy without bowel perforation have been described in international literature, but none of which was completed by a molecular biology analysis.

**KEYWORDS:** forensic science, gas gangrene, myonecrosis, *Clostridium perfringens*, retroperitoneal, polypectomy, colonoscopy, autopsy

Colonoscopy has become a routine investigation in the diagnosis and treatment of colonic disease. In general, colonoscopy is a safe procedure but complications may occur.

Common colonoscopy-related complications include prolonged distension and pain, and rarely draw medical attention or lead to hospitalization.

The most dreaded of these complications is colonic perforation. The frequency of perforation after colonoscopy is estimated to be 0.03–0.8% for diagnostic colonoscopy and 0.15–3% for therapeutic colonoscopy (1).

Colonoscopy-related complications may be classified as immediate complication and delayed ones (2). The immediate complications can be related to the use of sedation and include hypotension, vasovagal fainting, and nausea/vomiting or can be related to the technical procedure and include extensive pain/discomfort, abdominal distension, perforation, and bleeding. The delayed complications, those defined as the adverse events happening from the day after the initial colonoscopy, include late bleeding and inflammation caused by polypectomy.

Infectious complications resulting from endoscopy rarely occur. This is probably due to the efficiency of the gastrointestinal immune system (3). Endoscopy-related infections can result

from a patient's own microbial flora (autologous), can be transmitted from patient to patient by way of the endoscope (exogenous), or can be transmitted between the patient and the healthcare provider.

The mean frequency of postprocedure bacteremia ranges from 0.5% for flexible sigmoidoscopy to 2.2% for colonoscopy, 4.2% for esophagogastroduodenoscopy, 8.9% for variceal ligation, 11% for endoscopic retrograde cholangiopancreatography, 15.4% for variceal sclerotherapy, and 22.8% for esophageal dilation. Although postprocedure bacteremia is not uncommon, it rarely results in clinically significant complications (4).

With regard to that, we present a peculiar autopsy case of gas gangrene diffused to retroperitoneum, right hemithorax, and right thigh, associated with colonoscopy polypectomy without bowel perforation.

### Case Report

A 60-year-old woman was admitted in a state of severe hypotension and with severe back pain radiating in the right thigh, 1 day after apparently uncomplicated colonoscopic polypectomy. Three polyps, respectively, at the distance of 77, 68, and 15 cm from the anus, were removed from the left and sigmoid colon.

With the exception of preexisting Crohn's disease in good clinical compensation, the patient had been previously in good clinical condition. At the admission, a CT scan was performed and showed intra-abdominal free gas, retroperitoneal gas, and emphysema extended in the bellies of the right psoas muscle and right quadriceps muscle and into right hemithorax (Figs 1 and 2).

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FIG. 1—CT scan image showing diffuse gas gangrene in retroperitoneum and quadriceps muscle.

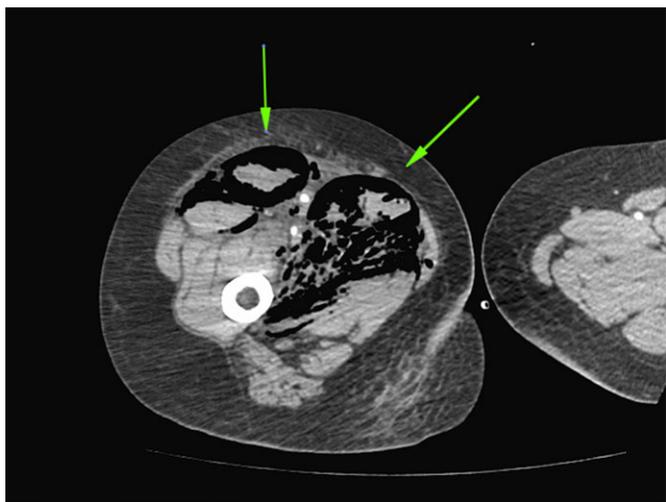


FIG. 2—CT scan image showing disruption of right quadriceps muscle due to clostridial myonecrosis.

Myoglobin in blood was 12000 ng/ml, and urine was dark brown as for myoglobinuria.

The patient developed renal and pulmonary failure and a severe septic shock, requiring high catecholamine doses.

Assuming a bowel perforation, the patient was brought on operating room to perform an exploratory laparotomy, but she suffered from a cardiac arrest and died, before the surgery started.

Medical liability was suspected, so the prosecutor ordered a medicolegal autopsy.

External examination of the body showed the following:

- diffuse red coloration of the skin;
- increased volume of the right thigh with cutaneous cellulitis (peau d'orange) with palpable crepitation;

- bullous lesions and blisters with red-dark liquid content on the skin of the right hemithorax and right thigh (probably from postmortem).

The subsequent internal examination of the body reported the following findings:

- massive gas gangrene of the right retroperitoneum with myonecrosis of the right iliopsoas muscle that showed brownish discoloration and soft consistency with palpable crepitation;
- thickening of the mesentery of the small intestine;
- gas gangrene of right thigh muscles with adjacent cellulitis and hemorrhagic-edematous appearance of the adipose tissues on cut surfaces (Fig. 3);
- pulmonary edema with foamy appearance of the lungs;
- right pleural effusion (550 cc).

No macroscopic perforation of small bowel either colon, or of the other organs, was detected at the autopsy.

The investigations have been completed with a histologic examination of the organs. Specimen was embedded in paraffin, and 4-micrometer-thick sections were cut and stained with hematoxylin-eosin (H&E staining). Preparation of samples confirmed the exclusion of perforations in polypectomy sites, with no signs of activity of Crohn's disease, revealed on the right thigh skin a papillary dermis expansion due to edema of the lymphatic vessels and showed lungs full of brownish granules filled macrophages, some accumulation of rod-shaped bacteria with no significant adjacent inflammatory reaction, along with pulmonary edema and emphysema; positive immunohistochemical staining for myoglobin was identified within renal tubules.

Postmortem microbiological analysis was performed. Blood samples were collected from aorta and inoculated in BACTEC Plus aerobic and anaerobic bottles (Becton-Dickinson, Erembodegem, Belgium). The anaerobic bottle flagged positive. After subculturing under anaerobic condition, colonies characterized by a double zone of beta-hemolysis were obtained on blood agar plates (Becton-Dickinson) (Fig. 4).

Gram staining of the colonies showed gram-positive bacilli that were identified by MALDI-TOF mass spectrometry (Bruker Daltonics, Bremen, Germany).



FIG. 3—Macroscopic view showing skin cellulitis and necrosis of the underlying subcutaneous fat in the right thigh.

The isolate was identified as *Clostridium perfringens* with a score >2.0, which is considered high-confidence (secure species) identification (Fig. 5).

In conclusion, the cause of death was a multiple organ failure due to a severe septic shock consequent to wide gas gangrene caused by *Clostridium perfringens*.

The postmortem investigations revealed no additional illness such as malignancy, diabetes, liver cirrhosis.

## Discussion

Gas gangrene, or clostridial myonecrosis, is one of the most serious infectious diseases. It is characterized by rapidly

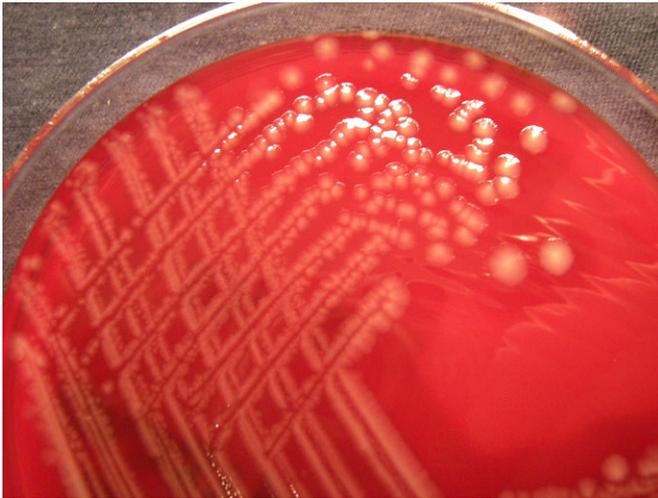


FIG. 4—*Clostridium perfringens* on blood agar, showing double zone of beta-hemolysis.

progressive destruction of soft tissues and production of gas (5) in total absence of an accompanying leukocyte infiltration (6). A diagnostic feature is gas dissecting into the muscle bellies, and CT scanning is especially useful for the diagnosis.

Gas gangrene is due to a *Clostridium spp.* infection and was frequent during wartime related to weapon injuries.

Although rare, gas gangrene is not a disease of the past: Nowadays, in forensic autopsy cases of fatal gas gangrene, tissue infiltration of *clostridia* is usually related to major or minor trauma occurred in civilian setting (7).

Gas gangrene, usually trauma-related, may also be spontaneous (6,10), especially when patients have conditions such as advanced malignancy (11), diabetes, liver cirrhosis (12), or immunosuppression (13).

*Clostridium spp.* infections have been increasing in frequency and severity in patients with inflammatory bowel disease (IBD) such as Crohn's disease, a chronic idiopathic inflammatory intestinal disorder (8,9).

Abdominal gas gangrene due to *Clostridium perfringens* infection is rare and is usually associated with bowel perforation (14). Traumatic rupture of the duodenum (15) and acute pancreatitis (16) have been also described as causes of retroperitoneal gas gangrene.

In our case, a macroscopic bowel perforation as a source for the infection was excluded by the autopsy and by the histologic examination.

In literature, only two other cases of retroperitoneal gas gangrene after colonoscopy polypectomy without bowel perforation have been described (17,18), but none of which was completed by a molecular biology analysis.

The etiology of clostridial myonecrosis in the present case remains unclear. In this regard, we may formulate the following hypothesis.

- A microperforation, due to mucosal defect in the polypectomy sites, was the exit point of autologous bacteria of microbial flora, from the colon lumen to the retroperitoneum.

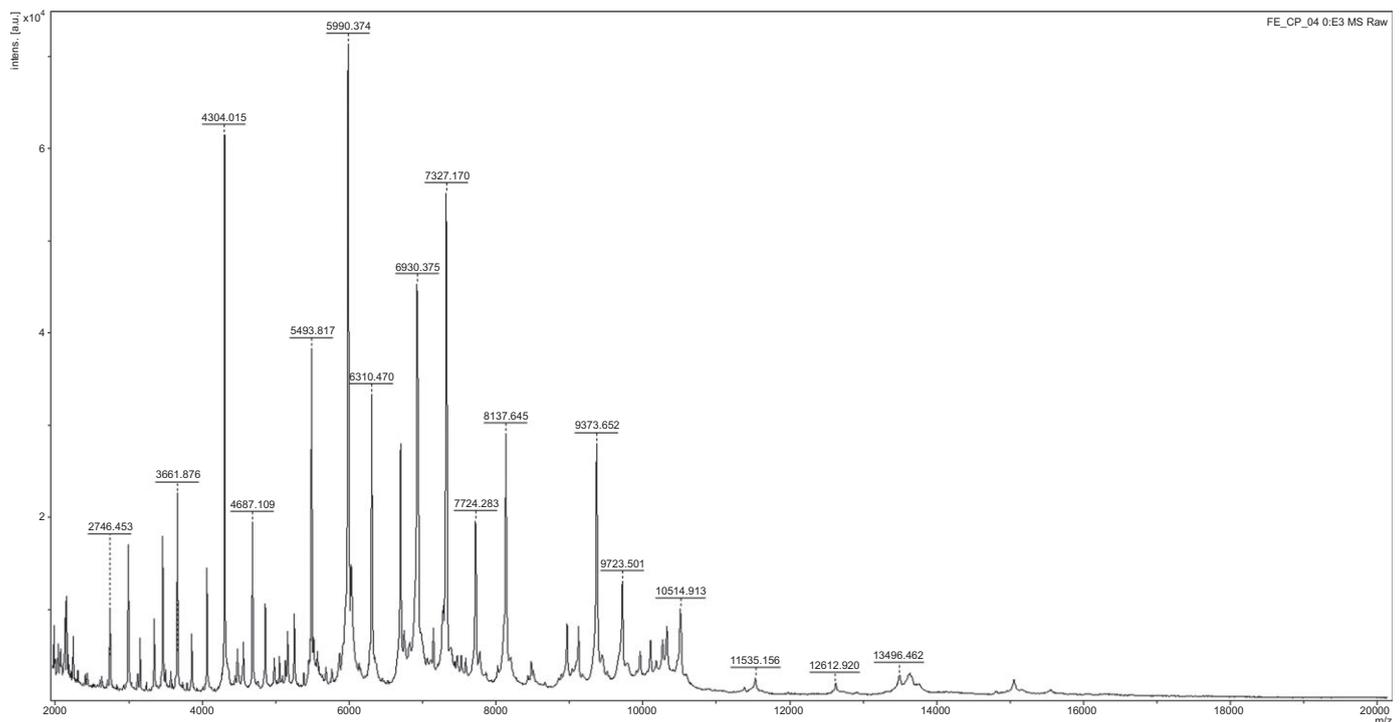


FIG. 5—MALDI-TOF mass spectrometry profile of *Clostridium perfringens* isolate.

- Hematogenous spread from the gastrointestinal tract with muscle seeding.
- The exit point of autologous bacteria was due to an increased permeability of the gastrointestinal mucosa due to Crohn's disease.

With regard to the last hypothesis, it is interesting to note that 2.2% of all patients undergoing colonoscopy displays uncomplicated bacteremia (4) and patients with IBD are a high-risk population for bacteremia (19), showing a possible mechanism for bacteria to overstep the bowel wall.

This may be due to an immunosuppression due to the chronic use of NSAIDs therapy (nonsteroidal anti-inflammatory drugs) or cocktails of immunosuppressive agents, or to the common invasive intervention on the gastro-intestinal tract; but this also may be due to a deranged mucosal architecture of the gut that in IBD shows an enhanced mucosal permeability.

In patients with IBD, several alterations of colonic mucosal glycoproteins have been observed: This may result in weakening the mucosal barrier (20). Moreover a recent study focuses on prolyl hydroxylase domain proteins (PHDs), which are involved in IBD and reports that especially PHD3 plays a critical role in maintaining intestinal epithelial barrier function. A deletion of PHD3 decreases the level of tight junction protein occludin, leading to a failure of intestinal epithelial barrier function. Human biopsy analysis showed that PHD3 is decreased in ulcerative colitis patients (1).

In conclusion, *Clostridium perfringens* is responsible for a number of clinical conditions ranging from relatively mild food poisoning to the potentially life-threatening gas gangrene. Gas gangrene, also known as clostridial myonecrosis, is one of the most serious infectious diseases, characterized by rapidly progressive destruction of soft tissues and production of gas.

Our case and two other cases described in literature show the possibility of retroperitoneal gas gangrene after colonoscopy polypectomy without bowel perforation.

With regard to that, even if retroperitoneal gas after colonoscopy is a major sign of bowel perforation, gas gangrene should also be supposed especially when gas involves the muscle bellies, to consider the possibility of a severe and life-threatening *Clostridium spp.* infection.

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