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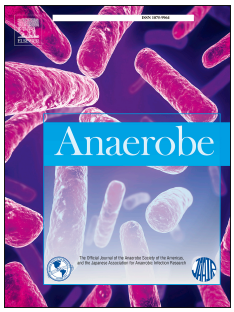

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Introduction

Spontaneous *Clostridium septicum* gas gangrene is a rare opportunistic infection with a high mortality rate and is often associated with underlying immunosuppression or malignancy [1-3]. It is a gram positive, anaerobic bacterium. Its main virulence factor is the ability to produce alpha-toxin, which is considered the main cause of *C. septicum* induced atraumatic myonecrosis [4]. It usually gains access into the bloodstream or tissues by penetrating the intestinal wall through a mucosal defect, most commonly the cecum or the colon ascendens [2]. We present a case of spontaneous *C. septicum* gas gangrene in a previously otherwise healthy individual with a history of robot assisted renal resection.

Description of the case

A 37 – year –old female was referred to the Helsinki University Hospital Emergency Department from a regional hospital with a suspected necrotizing soft tissue infection. The patient had undergone robot-assisted resection to her right kidney four years earlier for renal oncocytoma with no evidence of recurrence during follow-up. The patient had a normal body mass index and no other underlying diseases, regular medications or tobacco use. She signed a written consent to publish this case study.

The patient had presented to the regional hospital with complaints of general malaise and pain in the lower back and the right upper and lower extremities as well as vomiting the night before. During observation, the patient had developed increased pain, swelling and

crepitation in her right upper extremity and had been rapidly referred to the University Hospital with suspected necrotizing soft tissue infection.

Upon arrival, the patient presented with a bluish hue, crepitation and paresis of the right shoulder, right upper and lower extremity and pain around the lumbar area. The abdomen and back area had no signs of crepitation, and the abdomen was soft and pain free upon palpation. Her systolic blood pressure was around 110-120 mmHg without circulatory support but with cold periphery and tachypnea. Blood test results revealed clear signs of severe septic shock with leukopenia, lactatemia and acidosis. Her white blood cell count was 1.4 E9/l, lactate 6.8 mmol/l, base excess -9.4 mmol/l, P-TT (thrombin time) 26%, CK (creatine kinase) 14689 U/l and C-reactive protein (CRP) 463 mg/l.

Empirical antibiotic therapy was started immediately with intravenous clindamycin 600 mg every six hours, meropenem 1000 mg every eight hours and a single 1000 mg dose of vancomycin. The patient was rapidly taken into the operation theatre for surgical exploration and debridement, which revealed massive myonecrosis of the right upper and lower extremities. Bacterial cultivations and gram stains were taken from the affected tissues. Almost all hamstring and adductor muscles were in necrosis had to be removed. In the shoulder and upper extremity, most of the triceps, trapezius and deltoid had to be removed, as well as large parts of skin. Skin on the right side and lower back was also incised and during surgery, but no clear signs of myonecrosis of the lower back and abdominal wall were clinically evident.

After surgery, clindamycin and meropenem were continued intravenously. The gram stains revealed a substantial number of gram-negative bacilli and scant in amount of gram -positive bacilli. The patient had an increasing need of inotropic support, deepening acidosis, was anuric and was transferred to an intensive care unit. A body CT-scan was taken, which

revealed a large gas collection in the retroperitoneum, extending from the level of the right kidney to the psoas and iliacus muscles, as well as ascites, thickening and gas in the wall of the colon ascendens (figure 1). A second-look revision and lumbotomy were performed. The right side of transversus abdominis, the iliacus and part of the psoas muscles were necrotic and were removed.

After the second operation the patient was transferred to the ICU and a continuous dialysis was started. A control CT scan was performed the next morning. It revealed gas bubbles around the right piriformis, psoas and gluteus minimus and medius muscles. The tissue sample and blood bacterial cultures revealed *C. septicum* infection and sepsis. The patient was taken a third time to the operation theatre. The psoas and sartorius muscles were found necrotic and were removed. An explorative laparotomy was also performed. The wall of the caecum and colon ascendens were found to be somewhat edematous and thickened, which was interpreted secondary to the retroperitoneal infection and the intestine was left intact.

The state of the patient continued to deteriorate and need of inotropic support continued to increase without any clinical signs of spreading myonecrosis. A second –look laparotomy was performed on the third day. The caecum and terminal ileum now had visible bluish spots. An ileocecal resection was performed, and the abdomen was left open. The next day a temporary protective ileostomy was carried out and the abdomen was temporarily closed with vacume-assisted wound therapy (VAC). The abdomen was closed two days later with the ileostomy left intact.

After the ileocecal resection, the patient's overall situation started to improve. The need for inotropic support ceased, the lactate levels and P-TT normalized and the CRP dropped from 422 to 226. During the following days, the patient underwent two further

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revisions, but no more major tissue resections had to be performed. The pathological examination from the caecum revealed necrosis. No signs of neoplasy were found.

After the triceps and thigh myectomies, the patient had exposed radial and sciatic nerve and large skin defects (figures 2a and 2b). When the patient's overall situation improved, the tissue defect of the right upper arm was covered with a pedicular latissimus dorsi flap and the sciatic nerve was covered with a free latissimus dorsi flap. The patient also underwent several further smaller revision procedures and skin transplantations. No amputation surgery was needed.

The patient spent approximately a month at the intensive care unit and was then transferred to a bed ward unit. Her kidneys recovered fully. She was released to a rehabilitation unit after three months. Her temporary ileostomy has been closed. She is now living at home with the help of a personal assistant and has returned to work. Her major problems remain paresis and scar contracture in the affected extremities with diminished range of movement (figures 3a and 3b). She is still going through rehabilitation and visiting the outpatient clinic regularly.

Discussion

The *C. septicum* has traditionally associated with gas gangrene caused by trauma during warfare and natural disasters. In the recent years, there seems to have been an increase in reported cases of spontaneous *C. septicum* gas gangrene [1], although exact data is lacking. In their literature review, Srivastava et al [2] identified 94 cases of *C. septicum* gas gangrene since 1956 to 2016. The overall mortality rate in their study was 67% and a significant number of patients died within 24 hours from arrival. In the literature, spontaneous *C. septicum* gas

gangrene has a strong association with an underlying malignancy, most often colorectal cancer or hematological malignancy [2-3, 5-6]. The bacteria usually gain access into the bloodstream or tissues by penetrating intestinal wall, most commonly the cecum or the colon ascendens. A defect in the mucosal barrier due to colorectal malignancy or neutropenia secondary to a hematological malignancy or immunosuppression may be contributing factors to this opportunistic infection. In contrast to most of the case studies in the literature [2-3,5-6], our patient did not have neutropenia or immunosuppression, and the pathological examination of the resected caecum did not have signs of occult malignancy. The patient had however robot-assisted renal resection years earlier, which had required the mobilization and reattachment of the right hemi colon to the posterior peritoneal wall, which can be hypothesized to have been a contributing factor to the infection. What triggered the spontaneous infection four years later remains unknown and highlights the multifactorial and opportunistic nature of *C. septicum* gas gangrene. No *C. septicum* was found in the bacterial samples taken from the patient's abdominal cavity.

The ability of the *C. septicum* strain to produce toxins, especially alpha-toxin has been shown to be a major contributor to the ability of this bacterium to cause myonecrosis by decreasing microvascular perfusion in the affected muscle tissue and thus, opportunistic infection [4, 7]. However, the identification of such virulence factors is not in clinical use at our unit and thus the ability of this particular strain to produce alpha-toxin remained unknown.

The onset of symptoms is often insidious, and the rarity of the disease makes the initial diagnostics challenging. There is often no time to waste on imaging studies as the patients often present to the hospital in septic shock. Once a gas gangrene is suspected, this rapidly advancing, and often fatal infection should be managed without delay with rapid surgical exploration and debridement of the affected tissue. While extensive myonecrosis often leads to amputation [6., 8.-9.], with rapid debridement, both affected limbs were saved.

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The source of the infection is often unknown in the beginning and empiric wide spectrum antibiotics should be commenced immediately upon arrival. Bacterial cultures should be taken both from the blood and the affected tissues, as well as gram stains from the tissues during the operation. In our patient's case, the initial gram stains showed both a substantial number of gram-negative bacilli and a smaller amount of gram-positive bacilli. However, the cultures showed that the causing agent in all tissue and blood cultures was *C. septicum* which is a gram-positive bacterium. Gram stains may be unreliable from samples taken from necrotic tissues and may stain gram negative, even if the bacteria are gram positive. The choice of antibiotics in our case was initially empirical and generally used for necrotizing soft tissue infections. Once *C. septicum* was identified, it was found to be susceptible to both clindamycin and meropenem, and these antibiotics were continued. *C. septicum* has also been found to be less susceptible to vancomycin than beta-lactams and clindamycin [10].

Our patient's state started to improve once the source of the infection was detected and removed. Our case demonstrates the difficulty of establishing the source, as clear clinical signs of necrosis in the colon developed days after the onset of the bacterial translocation and progressive gas gangrene. Our case demonstrates that if a patient has *C. septicum* gas gangrene without preceding trauma, colorectal origin should be suspected, even without a known malignancy or immunosuppression. Repeated CT imaging studies and surgical exploration are warranted, as well as a multi professional approach combining plastic and gastrointestinal surgery, infectious disease, intensive care and radiological expertise.

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None relevant to this manuscript.

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Declaration of competing interest

On behalf of all authors, the corresponding author states that there is no conflict of interest.

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Figure 1. A CT -scan revealed a large gas collection in the right retroperitoneum.



Figure 2a. Right thigh after partial hamstring and adductor myectomies.



Figure 2b. Right upper arm after surgical debridement and myectomies.



Figure 3a. The tissue defect in the right thigh was covered with a free latissimus dorsi microvascular flap and skin transplantations.



Figure 3b. The tissue defects in the right arm were covered with a pedicular latissimus dorsi flap and skin transplants. There is still some scar contracture in the right elbow.

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Highlights

- We present a case of *Clostridium septicum* gas gangrene in a healthy individual
- Our patient presented with severe septic shock and myonecrosis
- Patient's state improved when the origin of infection in the intestine was removed
- Despite extensive myonecrosis, no limb amputations had to be performed

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Conflict of interest

The authors have no conflict of interest to declare.

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