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Case report

# *Clostridium sporogenes* bacteremia in an immunocompetent patient

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ABSTRACT

Of the 200 *Clostridium* spp. known to exist, approximately 30 have been associated with human disease. Commonly found in soil, marine sediment and mammalian intestinal tracts, these gram-positive bacilli are known to cause infections ranging from cellulitis to septicemia. Isolates that are identified by clinical microbiology laboratories include *Clostridium* perfrigens species in 20–40% of cases. However, when *Clostridium sporogenes* is identified, is rarely considered to be pathogenic. We present a case of *Clostridium sporogenes* bacteremia secondary to lower limb cellulitis and osteomyelitis in an immunocompetent patient.



## Case presentation

A 66-year-old woman with a history of morbid obesity, hypertension, hyperlipidemia, non-insulin dependent diabetes mellitus and coronary artery disease was admitted to our hospital for sepsis secondary to lower extremity ulceration and osteomyelitis.

Two weeks before this admission, the patient contacted family members for assistance and was found to be immobilized in the collapsed floor of her mobile home and without access to hydration for long time. Despite the squalid living condition of her home, the patient initially refused outside assistance before requesting medical attention. She was then transported by emergency medical services to our emergency department.

On examination, the patient appeared to be anxious. The temperature was 99.8o F, pulse 109 beats per minute, blood pressure 128/60 mm Hg, and respiratory rate 18 breaths per minute. Skin examination showed multiple necrotic ulcers with brown discharge located in her bilateral lower extremities, left heel and sacral decubitus area. Electrocardiograph showed atrial fibrillation with rapid ventricular response. Computed tomography of the thorax and abdomen yielded no acute abnormalities.

On admission to the surgical intensive care unit, vancomycin and piperacillin-tazobactam were administered intravenously for empiric coverage of common pathogens implicated in sepsis and clinical gas gangrene. Complete blood count was significant for a white cell count of 23.6k per mm3, hemoglobin 9.7 g/dL, and platelet count of 601k per mm3. Comprehensive metabolic panel was significant for sodium 128 mEq/L, bicarbonate 18 mEq/L, urea nitrogen 46 mg/dL and creatinine 2.03 mg/dL. Lactic acid was 2.76 mmol/L. Cultures of urine and blood were send to the clinical microbiology laboratory and orthopedic and infectious disease services were consulted.

Blood cultures grew *Clostridium sporogenes* in two out of two bottles that was obtained from one site (one aerobic and one anaerobic bottle) and urine cultures grew *Enterococcus* spp. (with colony forming units count more than **200,000**). Antimicrobials were switched to daptomycin, ertapenem and clindamycin. Repeat blood cultures were negative after 5 days of incubation. Clinical gas gangrene with severe destruction to the subcutaneous tissue was documented affecting the whole planter surface of the left foot as well as parts of the right foot. General surgery was consulted, who recommended below knee amputation of the left leg and right foot disarticulation. Patient refused the amputations. Despite the treatment with antimicrobial agents, patient clinical conditions continued to deteriorate. At that time, the patient refused all medical management, was placed on comfort measures and expired shortly thereafter.

## Discussion

*Clostridium sporogenes* is an anaerobic, gram-positive bacillus that comprises a part of the normal intestinal flora. First described in 1908, *C. sporogenes* has been isolated from the gastrointestinal tracts of both healthy individuals as well as those with chronic colitis [1]. Sporadic infections manifest in a wide variety of pathologies, including septic arthritis, empyema, and gas gangrene [2–5].

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Clostridial species represent a widely divergent group from strict anaerobes to aerotolerant species, and from pathogens producing virulent toxins to harmless saprophytes [6]. *Clostridium* sp. may be involved in a wide variety of infections and is a common cause of enteritis and enterotoxaemia humans [7]. The causes of these diseases are usually endogenous (e.g. brain abscess, pneumonia, intra-abdominal abscess, cholecystitis, bacteremia) and arise from the microflora of the host. However, others may be exogenous, such as food poisoning, pseudomembranous colitis, tetanus, botulism and gas gangrene [8]. One review found that about two thirds of the patients have been older than 65 years [9]. The most common underlying conditions in fore-mentioned review were diabetes, malignancy and neutropenia.

Of the 23 reported cases of *Clostridium sporogenes*, 16 involved bacteremia, 1 involved a pyogenic liver abscess, 2 involved empyema, 1 involved septic arthritis, and 2 involved septicemia [2–4,10,11]. Gorbach et al. reviewed reports of 87 clostridial soft tissue infections and found *C. sporogenes* to be implicated in only 3 cases [12]. In 130 reported cases of gas gangrene, *C. sporogenes* was identified in only one case [13]. In a review of 136 cases of clostridial bacteremia in cancer patients by Bodey et al., 12 cases were identified as *C. sporogenes* [14].

Mortality rates associated with clostridial bacteremia have been reported to be as high as 34% and 55% for monomicrobial and polymicrobial infections, respectively [14]. Thus, prompt initiation of appropriate antimicrobial therapy is critical in reducing the mortality of clostridial bacteremia/septicemia. This is critical when there are associated underlying conditions including alcoholism, intra-abdominal surgery and necrosis of small and/or large bowel. While the exact underlying pathogenesis of *C. sporogenes* remains unclear but is suspected to involve the production of a hemorrhagic toxin and proteinases [15–17]. In our case, the diagnosis was made through blood cultures obtained prior to empiric treatment with intravenous piperacillin-tazobactam and vancomycin.

The success of the treatment of established gas gangrene in clinical practice has depended largely upon early diagnosis and prompt surgical intervention as means to control the source of infection. Urgent, thorough surgical debridement is mandatory to improve survival, preserve limbs, and prevent complications [12]. Several types of antibiotics, including penicillin, clindamycin, rifampin, metronidazole, chloramphenicol, tetracycline, and erythromycin have been shown to be effective in vitro or in animal studies. Historically in humans, penicillin G has been recommended in doses of between 10 and 24 million units per day. Currently, a combination of penicillin and clindamycin is widely used for treating clostridial gas gangrene. The rationale for using penicillin in combination with clindamycin is that some strains of *Clostridium* are resistant to clindamycin but susceptible to penicillin. Clindamycin is thought to be the superior drug for reducing toxin formation [18].

Other, non-clostridial bacteria are frequently found in gas gangrene tissue cultures, so treatment that is active against Gram-positive (e.g. penicillin or cephalosporin), Gram-negative (e.g. amino- glycoside, cephalosporin, or ciprofloxacin), and anaerobic organ- isms (e.g. clindamycin or metronidazole) should be combined in the antibiotic therapy until the results of bacteriological culture are known [18].

Use of multiple drugs active against anaerobes is not necessary and puts the patients at risk for additional drug toxicities. No data or guidelines support the use of two anti-anaerobic drugs in clinical practice. In some cases, double anaerobic coverage is preferred by many clinicians, for example metronidazole can be added to another agent with anaerobic activity when being used to treat *clostridium difficile* infection. Another situation is clindamycin which can be added to another agent with anaerobic activity when being used for the treatment of necrotizing fasciitis [19]. Even in the case of single agents that cover all 3 categories of bacteria, (eg, broad-spectrum penicillins) Dual antibiotic therapy is recommended for all necrotizing soft-tissue infections given observed synergism in animal models [20].

First line treatment of confirmed *C. sporogenes* is traditionally with penicillins. In a study performed by Roberts et al., *C. sporogenes* was found to have 100% susceptibility to penicillins (amoxicillin-clavulanate and piperacillin-tazobactam), cephalosporins (cefoxitin, cefotetan, and ceftriaxone), clindamycin, carbapenems (imipenem and meropenem) as well as metronidazole [21] Blood cultures obtained after the initiation of antimicrobial treatment was negative for *C. sporogenes* after 5 days of incubation, nevertheless due to high suspicion for being a source of infection, amputation of the patient's foot was recommended. This recommendation, along with any form of medical treatment, was refused by the patient, who expired within a few days of treatment cessation.

## Conclusion

*Clostridium sporogenes* is a rare clinical pathogen and thus its discovery as the bacteremic agent in an immunocompetent patient made this case an unusual one. As with any patient suspected of being septic, obtaining cultures and routine susceptibility tests and initiating antimicrobial therapy in a timely manner are critical for obtaining an optimal outcome. However, without a rapid diagnostic test for *Clostridium* spp., prompt diagnosis is often difficult resulting in broad empiric therapy. Fortunately, *Clostridium* species remain susceptible to many antibiotics used in the treatment of bacteremia, osteomyelitis and sepsis but may not prevent progression to death.

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## Ethics approval

Our institution does not require ethical approval for reporting individual cases or case series.

## Author agreement

We all authors certify that we have seen and approved the final version of the manuscript being submitted. We warrant that this article entitled "*Clostridium sporogenes* Bacteremia in an Immunocompetent Patient "is our original work, hasn't received prior publication and isn't under consideration for publication elsewhere.

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