



Extraintestinal *Clostridioides difficile* infection

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ABSTRACT

Clostridioides (Clostridium) difficile is the major cause of healthcare antibiotic-associated diarrhoea. However, extra-intestinal manifestations of *Clostridioides (Clostridium) difficile* infection (CDI) (including bacteremia and tissue infection) are extremely rare. We report a case of extraintestinal CDI after surgery. The isolate of *C. difficile* was not the PCR ribotype 027. However, this isolate produced toxins A and B. The patient underwent a follow-up examination 30 days after discharge, which showed complete recovery. This case report adds to existing knowledge of CDI.

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Introduction

Clostridioides (Clostridium) is an anaerobic bacillus that produces spores and *C. difficile* is widely detected in humans, animals and environmental specimens [1]. The frequency of *C. difficile* infection (CDI) has been increasing for years and it has become a common hospital-acquired infection [2]. *C. difficile* is transferred by the faecal-oral route. The common risk factors of CDI and the clinical symptoms are antimicrobial therapy, old age and high fever with various degrees of diarrhea and possibly life-threatening colitis [3]. Different assays can be used to diagnose and detect CDI, but no single assay confirms CDI [4,5]. Vancomycin, fidaxomicin and metronidazole are used to treat CDI [6]. Extraintestinal manifestations of CDI are extremely rare. This case report will update physicians on the scientific knowledge of CDI.

Case report

On 5 April 2019, a 28-year-old man was admitted to the hospital with comminuted fracture of the middle segment of the right tibia and an oblique fracture of the upper segment of the right fibula (Fig. 2). After repeated manipulative reduction, the fracture could

not be aligned properly. Considering that soft tissue may be embedded in the broken end of the fracture, a right tibial fracture reduction and internal fixation operation was performed. Cephalosporin (500 mg q 8 h) was used to prevent infection 30 min before the operation and Cefuroxime sodium for injection was used to prevent infection for 72 h after the operation.

On 8 April 2019, the patient suddenly developed a high fever (39 °C) at night, leukocytes 12,200/μL, (83 % neutrophils), C-reactive protein [CRP] 177.63 mg/L and procalcitonin [PCT] 0.06 ng/mL). HIV, hepatitis B virus and hepatitis C virus were negative. A blood culture was sent to detect microbes.

On 9 April, the patient developed a fever with a body temperature of 39 °C. The infectious blood indicators were: leukocytes 12,900/μL, (88 % neutrophils) and CRP 154.32 mg/L. The blood culture revealed a Gram-positive bacillus (Fig. 1). The wound secretion, the stool of the patient detected by polymerase chain reaction (PCR) and enzyme immunoassay, respectively. The following day, *C. difficile* was detected in wound secretions using the Xpert[®] *C. difficile*, VIDAS[®] *C. difficile* GDH and VIDAS[®] *C. difficile* Toxin assays. The results showed that this *C. difficile* isolate produced Toxins A and B, but it was not ribotype 027. At the same time, the wound secretions were cultured on chromID *C. difficile* agar medium (Biomerieux Diagnostics, La Balme-les-Grottes, France) under anaerobic conditions (86 % N₂, 7 % H₂, and 7 % CO₂) at 37 °C. Some blank colonies with entire edges formed on the agar media after 24 h (Fig. 3). The blood and stool specimens of the patient were negative for *C. difficile*. The patient was immediately transferred to a single room and treated with vancomycin 1000 mg q 12 h. His fever subsided on 15 April. However, the skin around the

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Fig. 1. The blood culture revealed a Gram-positive bacillus.



Fig. 2. X-ray examination of this patient. It is shown that comminuted fracture of the middle segment of the right tibia, oblique fracture of the upper segment of the right fibula.

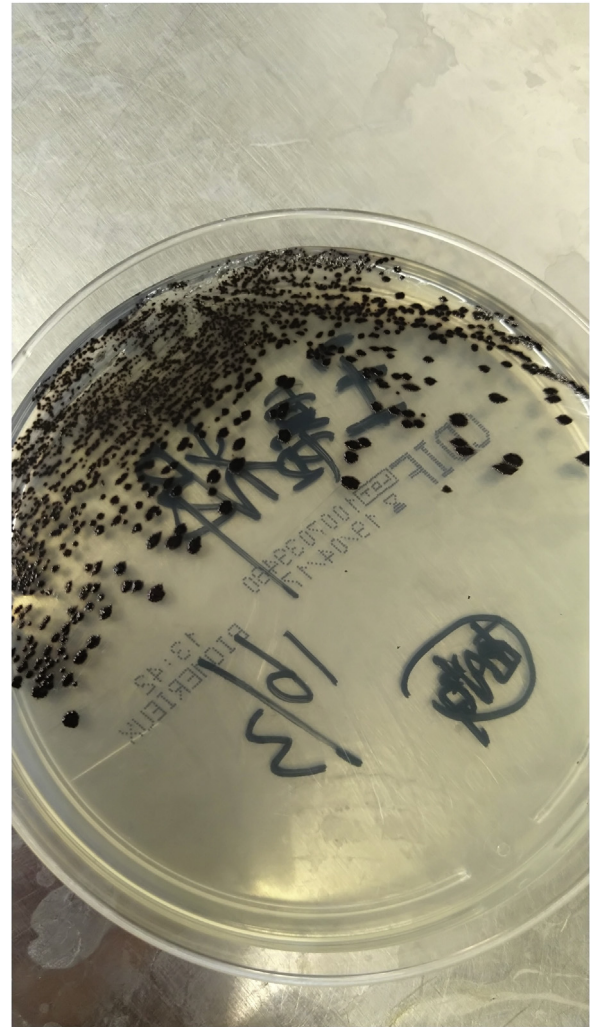


Fig. 3. The wound secretion was cultured on chromID *C. difficile* agar (CDIF) medium (Biomérieux® diagnostics, France) in anaerobic conditions (86% N₂, 7% H₂ and 7% CO₂) at 37 °C for detecting *C. difficile*. After 24 hours, some blank colonies with entire edges formed on the agar media after 24 h.

wound was red with a yellowish fluid exudation. Swelling was observed in the right leg wound, so wound debridement and removal of internal fixation was performed. A pathological examination of the necrotic tissues revealed flaky necrosis, and hyperplastic granulation tissue and suppurative inflammation were observed in the focal areas. A bacteriological examination revealed a large number of *C. difficile*. The plasma concentration of vancomycin was 4.7 µg/mL. Combined with Metronidazole sodium chloride (0.5 g q 12 h), was added as well as oral *Bifidobacterium* triplex live bacteria tablets were administered to regulate floral microbiology.

On 18 April, no fever was detected in the patient, and the infection indices were: leukocytes 10,100/µL, (80 % neutrophils), erythrocyte sedimentation rate 89 mm/h, CRP 32.17 mg/L and PCT 0.14 ng/mL. The patient was treated with vancomycin (1000 mg q 12 h) combined with metronidazole sodium chloride injection (0.5 g) q 12 h until April 31. CRP was > 0.5 mg/L, and PCT was > 0.05 ng/mL. The symptoms of infection subsided. The wound and stool specimens were negative for *C. difficile* at the 30 days follow-up examination. The outcome of this patient was good.

Discussion

The incidence, severity, mortality and healthcare costs associated with CDI are increasing, making *C. difficile* a major threat to public health⁵. Severe cases of CDI were increasingly reported in Canada, the United States and Europe during the early 2000s [5]. In particular, people with an adequate immune response can get infected and be asymptomatic carriers.

Patients with different characteristics (age, different types of antimicrobial drugs) may have different symptoms⁶. The present case only developed a fever without diarrhea or colitis. Studies show that expand on extraintestinal CDI (including bacteremia and tissue infection) are extremely rare [7]. The CDI of the tissue was treated with a combination of metronidazole and vancomycin for 14 days parenterally⁷. The patient did not develop a recurrence of CDI at the follow-up examination.

There are many different methods to detect the three different targets: *C. difficile* toxin (EIA, cytotoxin), *C. difficile* (GDH, cytotoxin culture) and toxin B gene (PCR) [8,11]. In this case, we used several methods to detect the microbial isolate. This *C. difficile* produced toxins A and B but was not PCR ribotype 027 [9,10,13], Toxins A and B act on the colonic epithelium and immune cells and induce a complex cascade of cellular events that result in fluid secretion, inflammation and tissue damage. However, the action of these toxins in muscle tissue is unclear [12,14]. Whereas CDI is ignored in China. We hope this case report promotes a greater understanding of CDI.

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Ethical approval

Ethical approval was obtained from the Shaanxi provincial people's hospital Ethics Committee

Declaration of Competing Interest

None to declare.

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Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:<https://doi.org/10.1016/j.idcr.2020.e00921>.

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