Septic shock due to *Yersinia pseudotuberculosis* infection in an adult immunocompetent patient: a case report and literature review

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**Abstract**

**Background:** *Yersinia pseudotuberculosis* infection can occur in an immunocompromised host. Although rare, bacteremia due to *Y. pseudotuberculosis* may also occur in immunocompetent hosts. The prognosis and therapeutic strategy, especially for immunocompetent patients with *Y. pseudotuberculosis* bacteremia, however, remains unknown.

**Case presentation:** A 38-year-old Japanese man with a mood disorder presented to our hospital with fever and diarrhea. Chest computed tomography revealed consolidation in the right upper lobe with air bronchograms. He was diagnosed with pneumonia, and treatment with intravenous ceftriaxone and azithromycin was initiated. The ceftriaxone was replaced with doripenem and the azithromycin was discontinued following the detection of Gram-negative rod bacteria in 2 sets of blood culture tests. The isolated Gram-negative rod bacteria were confirmed to be *Y. pseudotuberculosis*. Thereafter, he developed septic shock. Doripenem was switched to cefmetazole, which was continued for 14 days. He recovered without relapse.

**Conclusions:** We herein report a case of septic shock due to *Y. pseudotuberculosis* infection in an adult immunocompetent patient. The appropriate microorganism tests and antibiotic therapy are necessary to treat patients with *Y. pseudotuberculosis* bacteremia.

**Keywords:** Azithromycin, Bacteremia, Cefmetazole, Ceftriaxone, Doripenem, Septic shock, *Yersinia pseudotuberculosis*
infection. We herein report the first case of septic shock due to *Y. pseudotuberculosis* infection in an adult immunocompetent patient. The patient was successfully treated with the appropriate antibiotics.

**Case presentation**

A 38-year-old Japanese man with a mood disorder was admitted to the emergency department of Oita University Hospital (Oita, Japan) for complaints of fever and diarrhea. Ten days prior to presentation at the emergency department, he experienced appetite loss and vomiting a few days after attending a riverside barbecue and eating half-roasted foods. He was receiving oral ethyl loflazepate and paroxetine hydrochloride hydrate therapy for mood disorder and alcoholism. The patient had a fever and watery diarrhea 3 days prior to admission. His body temperature was 38.8 °C, blood pressure 111/70 mmHg, pulse 112 beats/min, and he had an SpO₂ of 100% at 3 L/min with a nasal mask on admission. Although he was awake without any stimuli, he was unable to recall his name or date of birth. No murmur was detected on heart examination. No crackles were auscultated in either lung field. Laboratory tests revealed an elevated white blood cell count (11,840/μL), hypoalbuminemia (2.6 g/dL), decreased serum iron level (22 μg/dL), decreased serum unsaturated iron-binding capacity level (162 μg/dL), decreased transferrin saturation (TSAT) level (12%), elevated C-reactive protein level (9.58 mg/dL), and an elevated procalcitonin (18.8 ng/mL). A chest X-ray showed an infiltrative shadow in the right upper lung field. Whole body computed tomography showed no remarkable finding except for consolidation with air bronchograms in the right upper lung lobe. The patient was diagnosed with community-acquired pneumonia, and treatment with intravenous ceftriaxone (2 g every 24 h) and azithromycin (500 mg every 24 h) was initiated. On day 3, 2 sets of blood culture tests revealed the presence of Gram-negative rod bacteria (Fig. 1-a); therefore, the ceftriaxone was replaced with doripenem (500 mg every 8 h) and the azithromycin was discontinued. On day 4, the Gram-negative rod bacteria were identified as *Y. pseudotuberculosis*, using the VITEK 2 system (bioMérieux, Marcy l’Etoile, France) with 99% probability. Furthermore, matrix-assisted laser-desorption/ionization time-of-flight mass spectrometry (Bruker Daltonics, Billerica, MA, USA) was used to identify the bacteria as *Y. pseudotuberculosis* with highly probable species identification (score value, 2.32). On day 5, the patient’s blood pressure decreased to 80/50 mmHg (mean arterial pressure 60 mmHg). Blood gas analysis revealed an elevated lactate level (4.1 mmol/L). The hypotension persisted despite adequate volume resuscitation, and norepinephrine as a vasopressor was started. The patient was diagnosed with septic shock due to *Y. pseudotuberculosis* infection. On the basis of susceptibility testing of *Y. pseudotuberculosis* using a dry plate (Eiken, Tokyo, Japan) with a conventional microdilution method and analysis by an image analyzer (Koden IA40MIC-i, Koden, Tokyo, Japan), the strain was found to be sensitive to ampicillin, ampicillin/sulbactam, cepotiam, ceftazidime, cefmetazole, meropenem, gentamicin, and levofloxacin. A sputum culture test was negative. A stool culture test detected *Escherichia coli* and *Streptococcus spp*, but no *Y. pseudotuberculosis*. On day 7, his fever was reduced and the norepinephrine was discontinued. Desquamation of the fingers was observed (Fig. 1-b). Two sets of blood culture tests showed negative results. On day 9, the treatment regimen was changed to cefmetazole (2 g every 8 h) and continued for a total of 14 days. On day 10, a chest X-ray showed complete improvement of the infiltrative shadow in the right upper lung field. On day 17, he was discharged from the hospital. Further characteristics of the *Y. pseudotuberculosis* strain was performed because of the clinical importance of virulence factors of this strain. *Y. pseudotuberculosis* isolate was of serotype 6 using serotyping.
scheme based on O-antigen. To evaluate the pathogenicity of this isolate, variants of Y. pseudotuberculosis-derived mitogen (YPM) superantigens were investigated in the strain using PCR with the following primers: ypmA [5′-CATCTTTCTCGGATAGCG-3′ (forward) and 5′-GATGTTCAGAGCTATTGTT-3′ (reverse)] and ypmB [5′-CTCCAGATTACGACATT-3′ (forward) and 5′-CATCTTTCCCATCGATCTTTA-3′ (reverse)] [4]. The PCR test using isolated bacteria showed positivity of ypmA. Combined with the results of serotype 6 and genetic detection of Yersinia pseudotuberculosis-derived mitogen A (YPMa), Y. pseudotuberculosis strain belonged to a genetic group 3 (Far East systemic pathogenicity type) [5]. We finally diagnosed with Far East scarlet-like fever (FESLF) caused by Y. pseudotuberculosis complicated septic shock.

**Discussion and conclusions**

We report a case of septic shock due to Y. pseudotuberculosis infection in an adult immunocompetent patient. Y. pseudotuberculosis infection in humans was first described in 1883 [6]. It is a Gram-negative rod bacterium and can grow in temperatures as low as 4°C [2]. The incubation period for intestinal Y. pseudotuberculosis infection is approximately 3 to 7 days [7]. Cases of Y. pseudotuberculosis infection, including gastroenteritis, pseudoappendicitis, bacteremia, pharyngitis, erythema nodosum, reactive arthritis, and syndromes mimicking Kawasaki disease, have been reported [2, 5, 8]. Risk factors for Y. pseudotuberculosis infection are exposure to contaminated food or water, as well as underlying medical conditions such as hepatic cirrhosis, HIV infection, malignancy, anaplastic anemia, thalassemia, iron overload, and diabetes mellitus [9, 10]. The mortality of bacteremia due to Y. pseudotuberculosis is reported to be as high as 75% [11]. Nine cases of Y. pseudotuberculosis bacteremia in adult immunocompetent patients were reported from 1911 through 1994 [2]. Of the 9 patients, 6 (66%) died. Four cases reported from 1995 to 2020 and our case of Y. pseudotuberculosis bacteremia in an adult immunocompetent patient are summarized in Table 1 [12–15]. All 5 patients survived. Although the case numbers of Y. pseudotuberculosis bacteremia in adult immunocompetent patients are limited, the prognosis of recent cases of Y. pseudotuberculosis bacteremia in adult immunocompetent patients might be better than that of the previous cases. The better outcome may be related to advances in diagnostic techniques and antibiotic therapy. Further studies are required to establish the prognosis of Y. pseudotuberculosis bacteremia in adult immunocompetent patients. Alcohol consumption is known to result in an iron overload, which could be a predisposing factor for systemic Y. pseudotuberculosis infection. Although serum ferritin level was not examined in our case, low serum iron and TSAT levels implied the low possibility of iron overload. Thus, we considered the patient would be immunocompetent.

FESLF caused by Y. pseudotuberculosis infection is a severe inflammatory disease that occurs sporadically and outbreaks in Russia and Japan [5]. FESLF patients with Y. pseudotuberculosis infection can be complicated with desquamation at the distal portion of the extremities in convalescent phase [16, 17]. Desquamation is seen in 83% of Y. pseudotuberculosis infection cases in childhood [17]; however, few cases have reported desquamation as a complication of Y. pseudotuberculosis infection in adults [16, 18]. Further studies are required to establish the epidemiology of desquamation in Y. pseudotuberculosis infection in adults.

In our case, Y. pseudotuberculosis strain was of serotype 6 and harbored superantigen gene ypmA. Y. pseudotuberculosis

**Table 1** Cases of Yersinia pseudotuberculosis bacteremia in adult immunocompetent patients. "Septic shock" is defined based on a clinical construct of sepsis with persistent hypotension requiring vasopressors to maintain a mean arterial pressure of ≥65 mmHg and having a serum lactate level > 2 mmol/L despite adequate volume resuscitation.

| Author            | Age/Sex | Probable portal of entry | Contaminated food or water exposure | Septic shock | Treatment | Outcome | Reference |
|-------------------|---------|--------------------------|------------------------------------|--------------|-----------|---------|-----------|
| Ljungberg et al.  | 54/M    | Unknown                  | Unknown                            | No           | PCG→ CTRX→ CPFX | Survived | [12]      |
| Ressler et al.    | 68/F    | Skin and soft tissue     | Unknown                            | No           | Unknown   | Survived | [13]      |
| Lai et al.        | 33/M    | Gastrointestinal tract   | Unknown                            | No           | MFLX→ CPFX | Survived | [14]      |
| Mashiba et al.    | 22/F    | Unknown                  | None                               | No           | CEZ→ FOM→ IPM/CS | Survived | [15]      |
| Our case          | 38/M    | Gastrointestinal tract   | Undercooked food                   | No           | CTRX→ DRPM→ CMZ | Survived |           |

Age (years old) and sex (F, female; M, male). Abbreviations: CEZ cefazolin, CMZ cefmetazole, CPFX ciprofloxacin, CTRX ceftriaxon, DRPM doripenem, FOM fosfomycin, IPM/CS imipenem/cilastatin, MFLX moxifloxacin, PCG penicillin G.
has been classified into serotypes 1 to 15 [5]. Most European
Y. pseudotuberculosis isolates are of serotypes 1 to 3, whereas
serotypes 4 to 15 are primarily found in Asia [5]. YPMa is a
superantigenic toxin produced almost by Far Eastern strains
[4] which is involved in the pathogenesis of severe inflammatory
disease from patient with FESLF. Thus, the clinical
isolate from our patient was compatible with the that from
FESLF patients.

The definitions of sepsis and septic shock were
changed in 2016 [3]. Septic shock can be defined with
persistent hypotension requiring vasopressors to maintain
a mean arterial pressure of ≥65 mmHg and a serum
lactate level > 2 mmol/L despite adequate volume resuscita-
cion. In the previous diagnostic criteria, septic shock
was defined as sepsis with hypotension despite adequate
fluid resuscitation [19]. Thus, septic shock according to
the new definition is more critical than that based on
the previous criteria. Lai et al. reported a case of Y. pseu-
dotuberculosis infection in an adult patient who developed
to septic shock [14], but their case was reported before 2016 and it is unclear whether their case fulfilled
the new septic shock criteria [3]. To our knowledge,
according to the new septic shock criteria, our case could
be the first case of septic shock due to Y. pseudotuberculo-
sis infection in an adult immunocompetent patient.

Y. pseudotuberculosis exhibits greater susceptibility to
antimicrobials other than macrolides. In a murine
model, fluoroquinolone therapy is effective against Y.
pseudotuberculosis infections whereas beta lactam
therapy is associated with lower survival or a poor
clinical response [20, 21]. The best antimicrobial therapy
for Y. pseudotuberculosis infection, however, is not yet
established. Further studies are needed to determine the
appropriate treatment for Y. pseudotuberculosis infec-
tions with bacteremia.

In our case, the illness developed a few days after the
patient attended a barbecue. For prevention, it is import-
ant to take into account whether or not contaminated
food and water were consumed raw and to exclude the
possibility of secondary contamination due to under-
cooked food and unboiled water. Although stool culture
did not detect Y. pseudotuberculosis in our case, blood-
stream infection could originate from intestinal infection.
Vulnerability of intestinal tract leading to bacteremia
might be caused by mucosal damage due to inflammation
of Y. pseudotuberculosis infection and intestinal edema
came from hypoalbuminemia.

In conclusion, we herein report a case of septic shock
due to Y. pseudotuberculosis infection in an adult
immunocompetent patient. This report will help to raise
awareness among clinicians that Y. pseudotuberculosis
bacteremia should be included in the differential diagno-
sis when patients exhibit fever and diarrhea after consuming undercooked food.

Abbreviation
Y. pseudotuberculosis: Yersinia pseudotuberculosis

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TH and SN drafted the manuscript. TH, RT, HF, KH, SN, TS, and OS
contributed to deciding the patient’s treatment. HH analyzed the virulence
factors of clinical isolate. All authors have read and approved the manuscript.

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Ethics approval and consent to participate
The need for approval was waived off by the Institutional Review Board of
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Consent for publication
Written informed consent was obtained from the patient on publication
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Competing interests
The authors declare that they have no competing interests.

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