Fatal community-acquired *Bacillus cereus* pneumonia in an immunocompetent adult man: a case report

Ryosuke Ishida 1*, Kazunori Ueda 1, Tadashi Kitano 1, Tomohiko Yamamoto 2, Yasuyoshi Mizutani 4, Yutaka Tsutsumi 5, Koji Imoto 3 and Yuji Yamamori 1

**Abstract**

**Background:** *Bacillus cereus* is a gram-positive rod bacterium that is responsible for food poisoning. It is naturally widely distributed, and thus often contaminates cultures. Although it is rarely considered responsible, it can cause serious infections under certain conditions. However, lethal infections, especially in immunocompetent patients, are rare.

**Case presentation:** A healthy 60-year-old man developed community-acquired *B. cereus* pneumonia and alveolar hemorrhage unveiled by abrupt chest pain and hemoptysis with no other advance symptoms. *B. cereus* induced silent alveolar destruction without any local or systemic inflammatory response. Although the lesion resembled lung anthrax, there was no evidence of *Bacillus anthracis* toxin.

**Conclusions:** Some isolates of *B. cereus* can cause anthrax-like fulminant necrotizing pneumonia in immunocompetent patients. If this type of *B. cereus* were used as a means of bioterrorism, it may be quite difficult to recognize as bioterrorism. We should keep *B. cereus* in mind as a potential pathogen of fulminant human infectious disease.

**Keywords:** *Bacillus cereus*, Community-acquired infection, Anthrax-like toxin

**Background**

*Bacillus cereus* is a ubiquitous, gram-positive rod bacterium that is responsible for food poisoning in humans [1, 2]. *B. cereus* is naturally widely distributed, and thus often contaminates cultures. Although it is rarely responsible for serious infections, previous reports have demonstrated that it can cause serious infections under certain conditions [1, 2]. However, lethal infections, especially in immunocompetent patients, are rare. Recently, it has been shown that some *B. cereus* contain the plasmid coding *Bacillus anthracis* toxin genes, which induces toxin-mediated severe necrotizing pneumonia [2, 3]. We report a case of fatal community-acquired *B. cereus* pneumonia and alveolar hemorrhage in a healthy man, unveiled by abrupt chest pain and hemoptysis with no other advance symptoms. Here, *B. cereus* induced silent alveolar destruction without any local or systemic inflammatory response. Since pathological findings showed anthrax-like lung lesion, we tried to determine whether this *B. cereus* strain contained *B. anthracis* toxin genes using real-time polymerase chain reaction (PCR).

**Case presentation**

A 60-year-old man presented with sudden severe right shoulder and flank pain and numbness of the right hand. The patient had a history of working in his home garden every day. He had no subjective symptoms prior to the day of admission, and no past medical history other than hypertension, which was managed with medication. The patient called an ambulance 3 h after the onset of symptoms and was able to get into the ambulance unassisted. He was transported to a nearby hospital. At the hospital, he developed hemoptysis and hypoxemia with severe forced breathing and tachypnea. He was tracheally...
intubated and transferred to our emergency department by
air ambulance helicopter 6 h after the onset of symptoms.

On examination in our emergency department, a
course crackle with right lateral dominance was audible.
A small volume of blood was continuously suctioned
through the tracheal tube, although bronchoscopic
examination did not reveal any source of bleeding. The
patient’s blood pressure was 132/87 mmHg, pulse was
109 beats per minute and body temperature was 36.7 °C.
He was mechanically ventilated with spontaneous
breathing at a rate of 14 breaths per minute under sed-
at. No skin eruptions or lesions were observed.

Upon examination of chest computed tomography
(CT), we saw infiltration predominant in the right upper
lobe and spreading to the right middle and lower lobe
and left hilar area (Fig. 1). Peripheral blood was collected
for laboratory examination. Arterial blood gas analysis
showed a pH of 7.174, with a partial pressure of carbon
dioxide of 62.4 mmHg, a partial pressure of oxygen of
94.3 mmHg, a base deficit of −7.4, under the condition
of end-expiratory pressure at 10 cm H₂O, and a fraction
of inspired oxygen of 0.5, indicating acute respiratory
failure. Other laboratory data were normal, including
blood cell count, coagulation, and biochemistry, includ-
ing inflammatory biomarkers, other than a slight eleva-
tion in serum creatinine level (1.37 mg/dL).

Electrocardiography showed a sinus rate of 86 beats
per minute, with an obvious ST segment elevation in the
inferior leads. Echocardiography also showed severe
hypokinesis of the cardiac inferior wall. The patient’s
serum troponin T level was elevated (0.487 ng/mL).

The patient’s history was obtained from his family, and
showed only hypertension. His current medications in-
cluded enalapril, carvedilol, and amlodipine. He had no
known allergies and no recent travel history. He did not
smoke and there was no history of unusual ingestions.
The Triage DOA® intoxication screening test result was
negative.

From the laboratory results and other tests, there were
two contradictory clinical concerns: revascularization of
the coronary artery and alveolar hemostasis. As the eti-
ology of the alveolar hemorrhage was unknown, we were
obliged to seek the pathogenesis under mechanical ven-
tilation, with no obvious indicators for a hemostatic ap-
proach. Thus, after discussion, we decided to prioritize
the revascularization of the coronary artery. After
heparinization, coronary angiography confirmed 99% se-
vere stenosis with a flow delay (thrombolysis in myocar-
dial infarction grade 2 flow) of the mid right coronary
artery at segment 2. Thrombus aspiration was per-
formed, followed by implantation of a drug-eluting stent
(DES). To minimize the bleeding risk, we delayed ad-
ministration of antiplatelet drugs, aspirin and prasugrel,
until the time of definite decision to implant the DES.

Next, transcatheter arterial embolization was per-
formed to treat the alveolar hemorrhage. Although we
did not detect overt extravasation by angiography, we
believed that the location of the hemorrhage was a
branch of the right bronchial artery, which we embolized
using a gelatin sponge. However, we were unable to con-
trol the alveolar hemorrhage, which increased and blew
out from the tracheal tube, making it very difficult to
maintain oxygenation and circulation. The patient died
12 h after the onset of symptoms. No antibiotics were
administered during treatment.

Autopsy was performed with the family’s consent im-
mediately after the patient’s death.

The following day, additional laboratory blood exams
revealed that negative for the anti-neutrophil cytoplas-
mic antibody, anti-nuclear antibody, and anti-glomerular
basement membrane antibody. Levels of lung surfactant
proteins A and D, as well as KL-6, were normal. Later,

B. cereus was cultured from the sputum sample suc-
tioned through the tracheal tube.

Immunohistochemistry of B. cereus and real-time PCR
for pXO1-like plasmid from lung tissue were performed

Fig. 1 Chest CT showing infiltration predominantly in the right upper lobe and spreading to the right middle and lower lobe and left hilar area, suggesting alveolar hemorrhage
to confirm that the bacterium was *B. cereus* and whether this bacterium produced anthrax-like toxin.

The lungs were fixed in 20% formalin for 24 h and embedded in paraffin, followed by pathological examination. *B. cereus* immunostaining was performed using anti-*Bacillus cereus* rabbit polyclonal antibody (Abcam, Cambridge, UK).

Next, we performed DNA extraction and real-time PCR for *B. anthracis* toxin plasmid. Two pieces of 10 μm-thick Formalin fixed paraffin embedded (FFPE) sections were collected in Eppendorf tubes. DNA was extracted from these sections with the use of Nucleospin DNA FFPE XS kit (Macherey-Nagel, Düren, Germany), according to the manufacturer’s instruction. For detecting infection with *B. cereus* containing pXO1-like plasmid, lethal factor (LF) gene (Genbank M29081.1) and protective antigen gene (PAG) (Genbank AF268967.1) were amplified by real-time PCR. For amplifying LF, two primer sets were prepared.: LF1, 5′- CAGCTTTAT GCACCGGAAGC-3′ (forward) and 5′- CGCTCCAGT GTTGATAGTG-3′ (reverse), generating a product of 148 bp; and LF2, 5′- TCGCTTAAGGAACATTCC ACA -3′ (forward) and 5′- GCTTCGGTGCAATAAAG CTG-3′ (reverse), generating a product of 144 bp. LF was amplified using the primers 5′- CAGGCTCGA CAGGAGTAA -3′ (forward) and 5′- TCACTAGGA TTAAACCGGCCG -3′ (reverse), generating a product of 118 bp. PCR reactions were carried out in a 25-μL final volume containing 2 μL of sample DNA, 12.5 μL of 2× reaction mixture (QuantiTect SYBR Green PCR Kits; Qiagen, Hilden, Germany) and 0.2 μM primers. The real-time PCR was performed with Rotor Gene Q (Qiagen), with an initial holding step at 95°C for 15 min, followed by 50 cycles of three-step PCR (94°C for 15 s, 55°C for 30 s, and 72°C for 30 s) with SYBR Green fluorescence monitoring to detect amplification. The melting curve was examined to check for contamination. As a positive control, genomic DNA of *Bacillus anthracis* (JNBP01251) was provided by the Gifu Type Culture Collection, Graduate School of Medicine, Gifu University.

Histologic sections of the lung, especially of the right upper lobe, demonstrated necrotizing hemorrhagic pneumonia similar to anthrax, with tremendous proliferation of gram-positive rods. The bacteria were diffusely gram-positive. Additionally, hemorrhagic diffuse alveolar damage within the hyaline membrane that was probably due to acute respiratory distress syndrome was also observed throughout the lungs. The bacteria reacted to the *B. cereus* antibody, and did not react to *Pseudomonas aeruginosa* and *Escherichia coli* antibodies. There was no infiltration of neutrophils. There was also no deposition of immunoglobulins or complements on the alveolar walls by immunofluorescence, excluding a diagnosis of vasculitis. *B. cereus* was also confirmed from the sputum culture. Therefore, *B. cereus* necrotizing pneumonia was confirmed pathologically (Fig. 2).

In the real-time PCR, amplification was obtained in the positive control (*B. anthracis* DNA), but not in the patient sample or the negative control (no template).

**Discussion and conclusion**

*Bacillus cereus* infection generally causes food poisoning, although it can cause fulminant disease in an immunocompromised host. Miyata and colleagues summarized 16 *B. cereus* pneumonia cases and concluded that most of these cases occurred in patients with hematological disorders or alcohol abuse [4]. However, it has been previously shown that, even in immunocompetent patients, *B. cereus* may induce serious necrotizing infections [1]. For example, Sliman et al. [5] determined that localized infection by *B. cereus* in the eye or viscera, such as pneumonia, may precipitate severe necrotizing infection with profound morbidity. Generally, *B. cereus* and *Bacillus anthracis* genomes have a high homology [6, 7]. Recently, it has been shown that some isolates of *B. cereus* contain *B. anthracis* toxin genes, which are accountable for toxin-mediated severe necrotizing pneumonia [2, 3]. Hoffmaster et al. [8] demonstrated that *B. cereus* isolated from patients with life-threatening pneumonia had a circular plasmid called pBCXO1. This plasmid shows 99.6% similarity with the plasmid pXO1, which encodes a *B. anthracis* toxin. Furthermore, previous reports presented two healthy welders in Louisiana [9] and two healthy metalworkers in Texas [10] who died of *B. cereus* pneumonia, and the pXO1 plasmid was confirmed in the Texas cases.

In the present case, there was no local infiltration of neutrophils, suggesting the observed necrotizing pneumonia was toxin-mediated and less inflammatory. However, we could not demonstrate that this *B. cereus* produced anthrax toxin.

Our pathological findings are consistent with lung anthrax [11]. We speculate that some *B. cereus* may produce toxins different from those produced by *B. anthracis*, but cause corresponding symptoms. This might be responsible for fatal *B. cereus* pneumonia. Here, we present some previous cases of fatal *B. cereus* pneumonia (Table 1). Our case is unique in that it was less inflammatory, displayed few symptoms, and was rapidly progressive. In previous reports, the subjects presented with symptoms such as nausea, vomiting, fever, chill, or white blood cell count elevation, suggesting bacterial infection, and infection was diagnosed in other cases at a high incidence [8, 9].

Unfortunately, we were unable to save our patient. However, we believe that there are factors in this case that may benefit clinicians in future cases, allowing them to save the patient’s life. At the initial presentation,
physical examination and laboratory data indicated severe hypoxemia due to alveolar hemorrhage of unknown etiology and lack of inflammatory response. The patient had no previous indications of illness, had a regular routine, and the symptoms developed suddenly. Therefore, we did not consider infectious disease as an etiology. Rather, we considered a systemic disease, such as drug-induced alveolar hemorrhage or vasculitis.

In retrospect, the best treatment would have been immediate isolation of the right upper lobe, followed by optimal antibiotics. Additionally, selective blocking of the right upper bronchus may have delayed the increased expansion of the blood to the other lobe. However, we did not have sufficient information to determine that such a procedure was indicated, i.e., we could not determine that the lesion was localized within the right upper lobe.

The comorbid ST-elevation myocardial infarction (STEMI) complicated the case, presenting conflicting symptoms that required immediate attention (revascularization of the coronary artery and alveolar hemostasis). Since visible bleeding was minor, we estimated that the alveolar hemorrhage was controllable, and thus first treated the coronary artery. After discussion, we concluded that we could not continue the treatment while ignoring the inferior STEMI induced by severe stenosis at mid right coronary artery, which has high mortality rate [12]. Thus, we concluded that anti-platelet therapy was imperative. Venovenous extracorporeal membrane oxygenation could not be performed because of continuous massive bleeding.

The patient first presented with sudden severe right shoulder and flank pain. This may have been caused by acute myocardial infarction. However, his hemoptysis occurred simultaneously. Community-acquired pneumonia (CAP) has been previously reported to be associated with cardiovascular complications at a high incidence. Violi et al. reported that 32.2% of CAP patients experienced cardiovascular events after hospitalization, including 8% who experienced myocardial infarction. The risk increases as the Pneumonia Severity Index increases [13]. Although the mechanism is not totally understood, the clinical implications are significant.
elucidated, impaired endothelial function [14], activation of coagulation [15], and activation of platelets [16] are possible candidates. We speculate that the invasion of the B. cereus infection may have triggered the myocardial infarction. In conclusion, we report a case of severe necrotizing pneumonia caused by B. cereus. This is a rare case, as the patient was immunocompetent and asymptomatic until onset. Additionally, the environmental background of infection is totally different from those of previous reports. Some isolates of B. cereus can cause anthrax-like fulminant necrotizing pneumonia in immunocompetent patients. If this type of B. cereus were used as a means of bioterrorism, it may be quite difficult to recognize as bioterrorism. This is also a public health concern. Although we were not able to make a diagnosis in this case, we should keep B. cereus in mind as a potential pathogen of fulminant human infectious disease.

Abbreviations
CAP: community-acquired pneumonia; CT: computed tomography; DES: drug-eluting stent; FFPE: Formalin fixed paraffin embedded; LF: lethal factor; PAg: protective antigen; PCR: polymerase chain reaction; STEMI: ST-elevation myocardial infarction

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Availability of data and materials
The datasets used and analyzed in this case report are available from the corresponding author on reasonable request.

Authors’ contributions
RI treated the patient and wrote the manuscript as a corresponding author. KU, TK, KL, YY treated the patient and edited the draft of the manuscript. TY performed pathological evaluation. YM designed and performed the PCR assay. YT designed and performed pathological evaluation and PCR assay. All authors read and approved the final manuscript.

Authors’ information
Not applicable.

Ethics approval and consent to participate
Not applicable.

Consent for publication
We obtained written agreement for publication of this case report from the patient’s family.

Competing interests
The authors declare that they have no competing interests.

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