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CASE REPORT

Fatal outcome of *Bacillus cereus* septicaemia

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ABSTRACT

Bacillus cereus is a ubiquitous environmental micro-organism which is often a contaminant of clinical cultures. Infections due to *B. cereus* are described, but mostly in immunocompromised patients. We report a fatal outcome of *B. cereus* septicaemia in an immunocompetent patient with a mechanical mitral valve.

KEYWORDS

Bacillus cereus, fatal outcome, fever of unknown origin, immunocompetent, septicaemia

What was known on this topic?
Bacillus cereus can cause deep-seated infections, such as endocarditis, in immunocompromised patients or intravenous drug users resulting in high morbidity and even mortality. In immunocompetent patients only cases of catheter-related infections have been published. These patients all fully recovered upon catheter removal and antibiotic therapy.

What does this add?
Our study adds that in immunocompetent patients with foreign body material the possibility of deep-seated infections must be carefully evaluated when *B. cereus* or other low pathogenic bacteria are cultured from blood. When a deep-seated infection is not considered in this patient group, this may result in premature discontinuation of antibiotic therapy, subsequent treatment failure and, as in our case, death. Furthermore, our study emphasises that in order to prove a deep-seated infection, early molecular comparison of bacterial strains retrieved from different samples may lead to the right diagnosis.

INTRODUCTION

Bacillus cereus is a ubiquitous environmental, gram-positive, facultative anaerobic, spore-forming rod, which is commonly considered a contaminant when cultured from clinical specimens. *Bacillus* species are commonly found in soil, dust, water, fomites and on mucous membranes of healthy people.[1,2] *B. cereus* produces a variety of toxins and is a potential pathogen being able to cause serious infections such as food poisoning, pneumonia, septicaemia, central nervous system infection and endocarditis.[3,4] We report a case of *B. cereus* septicaemia in a 74-year-old immunocompetent male with fatal outcome.

CASE REPORT

A 74-year-old male patient was referred to our university hospital because of fever of unknown origin (FUO). His medical history included a prosthetic mitral valve replacement, a percutaneous transluminal coronary angioplasty with stent placement, both 12 years earlier, and an out-of-hospital cardiac arrest 16 weeks earlier.
The patient had been admitted to the cardiology ward of another hospital three times in the past four months with symptoms of progressive shortness of breath, recurrent fever after discontinuation of antibiotic therapy, night

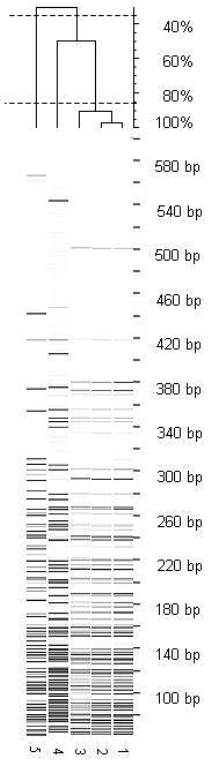
sweats, pancytopenia and eventually septic shock. The patient was treated with vancomycin and gentamicin for suspected endocarditis, and in different courses with clarithromycin, ceftriaxone, ciprofloxacin and co-amoxiclav for a lung infiltrate proven by CT scan. No pathogenic micro-organisms were cultured from sputum or blood. Blood cultures were taken during different hospital admissions and after discontinuation of antibiotics. Despite antibiotic treatment he became septic and was treated with vancomycin and gentamicin. A transoesophageal echocardiography (TEE) revealed no evidence of endocarditis. After one week the patient again developed fever. All antibiotic treatment was stopped and the patient was referred to our hospital because of FUO.

Cultures of blood, urine, sputum, pleural fluid and faeces were negative for pathogenic micro-organisms, including *Mycobacterium tuberculosis*. Polymerase chain reaction on a throat swab and serology for *Mycoplasma pneumoniae* were negative. Serology showed re-activation of Epstein-Barr virus. Tests for hepatitis A, B and C virus, cytomegalovirus, HIV and *Coxiella burnetii* were negative. Pleural fluid was negative for malignant cells, and showed no signs of inflammation (white blood cells $0.6x10^9$/l, lactate dehydrogenase 136 U/l). After eight days without antibiotic treatment a ciprofloxacin-sensitive *Klebsiella pneumoniae* was cultured from sputum. The patient was treated with ciprofloxacin 500 mg twice daily for 16 days. During this treatment his condition improved and his fever disappeared, but the fever returned after termination of the treatment.

Because of a recent stay in Turkey, a bone marrow aspiration was performed to rule out leishmaniasis, brucellosis, mycobacteria and fungi. Culture of the aspirate yielded *Bacillus* sp. which was considered a contaminant. Ten days after the bone marrow aspiration one of six blood culture bottles yielded *Bacillus* sp., also considered a contaminant. However, four days later three out of four additional blood culture bottles yielded *Bacillus* sp. Only now a deep-seated infection with *Bacillus* sp. was suspected. Tested by disk diffusion isolates were susceptible to ciprofloxacin, clindamycin, vancomycin and gentamicin. The patient was treated with vancomycin and ciprofloxacin. A TEE in our hospital revealed no signs of endocarditis. The condition of the patient worsened, with shock and respiratory insufficiency and he was admitted to the intensive care unit for supportive care. He developed multi-organ failure and died despite maximal supportive therapy within 24 hours. No permission for autopsy was given.

The *Bacillus* isolates from bone marrow and blood cultures were identified by matrix-assisted laser desorption and ionisation mass spectrometry time of flight (MALDI-TOF) as *B. cereus*. All blood culture isolates were identical (*figure 1*) by amplified fragment length polymorphism (AFLP).[5]

Figure 1. *Amplified fragment length polymorphism (AFLP) of patient's B. cereus isolates*



Strains with >85% homology are considered identical. 35% homology is the cut-off for isolates considered to belong to the same species. Lane 1-3 patient's blood isolates from three different days; lane 4 B. cereus NCTC 11143; lane 5 TY2666 B. thuringiensis clinical isolate.

DISCUSSION

We describe a case of fatal *B. cereus* septicaemia in an immunocompetent patient. *B. cereus* is a well-known ubiquitous micro-organism and a frequent contaminant of clinical samples.[6] Although *B. cereus* has some pathogenic potency, it is mostly associated with food poisoning due to toxin production.[7] Infrequently, septicaemia, pneumonia, meningitis, and endocarditis are caused by *B. cereus*.[3,4] The majority of these infections occur in immunocompromised patients, intravenous drug users, or newborn babies. However, some patients with *B. cereus* bacteraemia are immunocompetent. Two case reports describe central catheter associated *B. cereus* bacteraemia in an immunocompetent patient.[8,9] Both patients recovered upon catheter removal and antibiotic treatment. Two outbreaks of nosocomial *B. cereus* bacteraemia have been described with 18 and 11 patients, respectively.[10,11] These articles do not clearly mention the immune status of all patients, but it appears that some patients were immunocompetent. Most cases were associated with central catheters and some even with contaminated intravenous fluid.[11]

We concluded that our elderly patient was immunocompetent, because he had no history of recurrent infections, nor was he taking immunosuppressive medication. Recent CT scans did not show signs of malignancy and an extensive panel of autoimmune markers was negative. In addition to this, the pathology report on his bone marrow was in agreement with ongoing *B. cereus* septicaemia. *B. cereus* was late to be recognised as a causative pathogen due to several factors. First, all blood cultures collected during the first three admissions in the other hospital remained negative. Also no *Bacillus* species were reported as contaminants. The first positive blood culture in our hospital yielded *B. cereus* in only one out of six bottles. Due to these factors, adequate treatment was stopped after a short period. Our patient had a mechanical mitral valve, which made him more susceptible to endocarditis. According to the Duke criteria, the diagnosis was possible infective endocarditis.[12] Despite the fact that with repeated TEEs no definite diagnosis could be made, endocarditis is still the most probable diagnosis. A nosocomial infection introduced in our hospital can not be ruled out because blood cultures in the other hospital yielded no micro-organisms.

B. cereus endocarditis is associated with prosthetic valves or pacemaker leads.[13] With the increasing age of patients, more and more patients will have artificial cardiac valves. These patients are probably more susceptible to deep-seated infections with micro-organisms of low virulence. In immunocompetent patients with artificial material, positive blood cultures with *Bacillus* species should be carefully evaluated even when the TEE does not show signs of an endocarditis. When a response on antimicrobial treatment is observed, longer treatment duration must be considered.

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