

A cluster of *Bacillus cereus* bacteremia cases among injection drug users

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Bacillus cereus is a ubiquitous spore-forming organism that is infrequently implicated in extraintestinal infections. The authors report three cases of *B cereus* bacteremia among injection drug users presenting within one month to an urban tertiary care hospital. Treatment with intravenous vancomycin was successful in all three cases. While temporal association suggested an outbreak, molecular studies of patient isolates using pulsed-field gel electrophoresis did not suggest a common source. A review of the association of *B cereus* infections with heroin use and treatment of this pathogen is provided.

Key Words: *Bacillus cereus*; Bacteremia; Contamination; Heroin; Injection drug users

Bacillus cereus is a spore-forming Gram-positive bacillus that is pervasive in nature. This organism is commonly implicated in food-poisoning outbreaks associated with contaminated rice, and typically produces a self-limited emetic or diarrheal illness. Extraintestinal infections caused by *B cereus* are rare and studies are limited mainly to case reports. Bacteremia, temporally associated with injecting heroin, has been sporadically reported in the literature (1-3). Only one previous study has positively linked (through molecular analysis) a *B cereus* infection with a contaminated source of heroin (4). In the present report, we describe a cluster of *B cereus* bacteremia among three injection drug users presenting independently within one month.

CASE PRESENTATIONS

Case 1

A 41-year-old male injection drug user was brought to the emergency department unresponsive, febrile and hypotensive. Physical examination showed numerous track marks but no obvious source of infection. Initial investigations revealed a white blood cell count of $19.3 \times 10^9/L$; urinalysis, chest x-ray and abdominal computed tomography were all unremarkable. Fluid resuscitation, vasopressor support and empirical antibiotic therapy with intravenous (IV) piperacillin/tazobactam, vancomycin and clindamycin were initiated. Following resuscitation, the patient provided a vague history: he was well until the day of admission, at which time he developed a headache, severe fatigue and generalized malaise. His most recent heroin use had been the night before symptom occurrence. His medical history was significant for hepatitis C and previous episodes of bacteremia related to injection drug use. Blood cultures collected on admission grew *B cereus* (four of four bottles) and *Serratia marcescens*. The patient's antibiotics were

Un groupe de cas de bactériémie à *Bacillus cereus* chez des consommateurs de drogue injectable

Le *Bacillus cereus* est un organisme sporulé omniprésent qui est parfois responsable d'infections extra-intestinales. Les auteurs rendent compte de trois cas de bactériémie à *B cereus* chez des consommateurs de drogue injectable qui ont consulté au cours du même mois dans un hôpital urbain de soins tertiaires. Dans les trois cas, un traitement intraveineux à la vancomycine a donné de bons résultats. L'association temporelle laissait suggérer une éclosion, mais des études moléculaires d'isolats de patients par électrophorèse en champ pulsé n'évoquaient pas une source commune. Les chercheurs proposent une analyse de l'association des infections à *B cereus* à la consommation d'héroïne et du traitement de cet agent pathogène.

changed to IV vancomycin and ciprofloxacin. Blood cultures were persistently positive for *B cereus* until day 14 of admission. On day 29, the patient developed a small antecubital abscess that was drained and cultured *B cereus*. A transthoracic echocardiogram showed no signs of endocarditis. The patient received a total of six weeks of IV vancomycin and was discharged home.

Case 2

Nine days following the admission of case 1, a 49-year-old man with a history of daily heroin and crystal methamphetamine injection drug use presented to hospital with confusion and agitation. He was afebrile, with no obvious focus of infection on history or physical examination. His medical history was significant for recently diagnosed HIV infection and hepatitis C. Initial laboratory results showed a white blood cell count of $13.1 \times 10^9/L$. Empirical therapy with IV piperacillin/tazobactam and vancomycin was initiated. Blood cultures collected on admission grew *B cereus* and *Lactobacillus*, and the patient was switched to IV vancomycin and ciprofloxacin. A transthoracic echocardiogram showed evidence of a vegetation on the mitral valve. Three subsequent blood cultures were positive for *B cereus*; blood cultures eventually cleared on day 14 of admission. IV vancomycin was continued for a total duration of eight weeks and the patient was discharged.

Case 3

Twenty days after case 1 was admitted to hospital, a 33-year-old man with a history of heroin and cocaine injection drug use presented to the emergency department with confusion. He was afebrile and his physical examination was unremarkable. His medical history included hepatitis C and previous episodes of methicillin-resistant *Staphylococcus*

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aureus infective endocarditis, one of which necessitated a tricuspid valve replacement. The patient left hospital against medical advice, but was called to return the following day when blood cultures returned positive for Gram-positive bacilli, subsequently identified as *B cereus*. Repeat blood cultures were drawn and IV vancomycin therapy was initiated. Only the initial blood culture (one of two bottles) grew *B cereus*, and all subsequent blood cultures were negative. A transthoracic echocardiogram showed no evidence of endocarditis. The patient received a total of two weeks of IV vancomycin and was discharged home.

Molecular analysis

The *B cereus* isolates from the present cluster of three cases were submitted to the British Columbia Public Health Microbiology and Reference Laboratory for pulsed-field gel electrophoresis (PFGE) analysis to determine genetic relatedness. PFGE was performed for *B cereus* using *Sma*I restriction endonuclease for digestion and based on the parameters described by Liu et al (5). The PFGE fingerprint patterns indicated that the isolates were most likely not genetically related.

Additionally, the Vancouver Police Department was able to provide five samples of confiscated heroin (dry powder) for microbiological analysis. The samples of confiscated heroin were randomly chosen and were not related to the patients who presented to hospital. Of the five samples of heroin provided, three grew *B cereus* from microbiological culture. Coagulase-negative staphylococci (three of five) and *Escherichia vulneris* (one of five) were also recovered in culture. Given the preliminary findings from the PFGE performed on the clinical isolates of *B cereus*, the organisms recovered from the heroin samples were not submitted for further genetic analysis.

A common source for the cluster was not confirmed.

DISCUSSION

B cereus has been reported as a cause of extraintestinal infections, including those of the musculoskeletal, ocular, respiratory, cardiovascular and central nervous systems (6). Injection drug use is often attributed as an etiological factor, with reports of cellulitis (4), endophthalmitis and panophthalmitis (3,7,8), and endocarditis (1,6,9,10). The prognosis of bacteremia and native valve endocarditis with *B cereus* is typically good, with prompt antibiotic therapy of adequate duration being suitable for recovery (2). Conversely, high morbidity and mortality have been observed with prosthetic valve endocarditis, and authors of a review on the subject recommend prompt valve replacement in conjunction with IV antibiotics (11).

No guidelines exist for treatment of invasive *B cereus* infections, and reports in the literature describe clinical recovery with two to four weeks of IV antibiotics for bacteremia, and four to six weeks for endocarditis (2). Published susceptibility reports describe complete susceptibility of

B cereus to vancomycin, quinolones, gentamicin, carbapenems and tigecycline; intermediate susceptibility to clindamycin, tetracycline and erythromycin; and high-level resistance to trimethoprim/sulfamethoxazole, penicillins and cephalosporins (12).

In the present study, case 1 was treated with a prolonged six-week course of IV vancomycin for *B cereus* bacteremia because of persistently positive blood cultures for the first 14 days. Case 2 was treated for mitral valve endocarditis with an eight-week course of IV vancomycin and his blood cultures cleared over a two-week period. Although case 3 had a prosthetic tricuspid valve, there was no evidence of endocarditis and only a single initial positive blood culture. He received a two-week course of IV vancomycin, despite the possibility that this was a culture contaminant.

All patients in the cluster shared the risk factor of injection drug use, having recently injected heroin. *B cereus* infections have been sporadically associated with injection drug use, particularly with heroin. These rare occurrences were first reported (9) and reviewed (1) in the 1970s. *B cereus*, a known contaminant related to drug use, is resistant to heat and capable of surviving in harsh environments. A report from 1983 conducted in Washington, DC, found that nearly one-half of injection paraphernalia and 32% of heroin samples were contaminated with *Bacillus* species (13). The microbial burden was significantly higher on the injection paraphernalia than the heroin itself, and brown heroin (mainly from Mexico) was found to have a higher burden compared with white heroin (mainly from overseas). The authors speculated that heroin users experience frequent transient episodes of *Bacillus* species bacteremia, which are rarely of clinical significance.

In the literature, one case exists with a largely conclusive link of a *B cereus* infection to contaminated heroin (4). A patient with cellulitis provided a heroin sample, and both his wound aspirate and heroin cultured *B cereus*, which was found to be indistinguishable through PFGE. In our cluster, PFGE did not identify relatedness among the patients' isolates. Possible explanations for our cluster not having a common source include increasing microbial burden of heroin in general, supported by the burden found on the randomly acquired heroin or, particularly, contaminated injection paraphernalia among users.

CONCLUSION

B cereus infections are an underappreciated cause of bloodstream infections in injection drug users, for which the treatment requires prompt identification and antibiotic coverage. Our observation of three unrelated but temporally associated cases of *B cereus* infection in heroin users suggests that suspicion of *B cereus* infection in this patient population may become increasingly warranted.

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