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Two unrelated episodes of *Bacillus cereus* bacteremia in a neonatal intensive care unit

Bacillus cereus is an ubiquitous environmental bacterium, isolated in rare instances from invasive clinical specimens.¹ *B. cereus* is gaining notoriety as an opportunistic human pathogen associated with severe local and systemic infections among immunosuppressed hospitalized patients.² Premature infants are highly susceptible to infection because of their poorly developed innate and adaptive immune systems and prolonged invasive procedures, such as mechanical ventilation and central catheterization. Most of the literature-reported cases concerned infections of the bloodstream, lungs, and central nervous system.^{3,4}

In August 2011, blood cultures positive for *B. cereus* were obtained from 2 premature babies. Both infants were hospitalized in the same neonatal intensive care unit at the public hospital in Strasbourg, France.

The first of these 2 premature babies was born at 24 weeks and 5 days of gestation and weighed 650 g. An umbilical venous catheter and a percutaneous central venous catheter were implanted for the maintenance of hydration and the administration of drugs and parenteral nutrition. This neonate presented several complications during his stay. He suffered refractory hypoxemia at the age of 19 days, requiring high-frequency ventilation. Progression to chronic bronchial dysplasia led to corticosteroid (betamethasone) treatment for 25 days. The infant also presented a stage-II intraventricular hemorrhage, with bleeding of the vermis, requiring neurologic monitoring. When the patient was 32 days old, a blood culture positive for *B. cereus* was obtained from the arterial catheter. No other bacterial pathogens were found. This episode was accompanied by an inflammatory syndrome, with a C-reactive protein concentration of 92.6 mg/L and an interleukin-6 concentration of 391 ng/L (normal value, <23 ng/L). Treatment with cefotaxime, vancomycin, and amikacin was administered for 10 days, with a favorable outcome.

The second premature infant was born at 26 weeks and 5 days of gestation and weighed 615 g. An umbilical venous catheter, an intubation, and an injection of pulmonary surfactant were required at birth. On day 5, signs of infection were observed, with apnea, bradycardia, and gray complexion. Clinical examination revealed a major inflammatory syndrome, with a C-reactive protein concentration of 107 mg/L; interleukin-6 concentration of

13,283 ng/L; anemia, with a hemoglobin concentration of 10 g/dL; and severe thrombocytopenia. The right atrium had a fleecy appearance on echocardiography, and a cranial ultrasound scan highlighted space-occupying lesions suggestive of brain abscesses. Two blood cultures were set up: the first from a sample taken from the peripheral catheter on day 5 and the second from a sample taken from the central catheter on day 6. Both were positive for *B. cereus*. The child died at the age of 6 days from multiple organ failure and pulmonary and cerebral abscesses.

In the 2 clinical cases discussed here, the detection of *B. cereus* in consecutive invasive specimens (blood cultures) and the absence of other pathogenic bacteria in these cultures strongly suggest that this opportunistic pathogen was responsible for the symptoms observed in these infants. The strains isolated from the blood cultures of the 2 newborns were compared. The phylogenetic relationships between these 2 isolates of *B. cereus* were analyzed with the M13-polymerase chain reaction assay.⁵ The 2 isolates were found to be different. We also determined the toxin profiles of the 2 isolates. The primary toxins of *B. cereus* are hemolysin BL (Hbl), nonhemolytic enterotoxin (Nhe), cytotoxin K (Cyt k), and cereulide.⁶ Neither isolate produced enterotoxin Hbl (oxid kit) or the emetic toxin cereulide (absence of the *ces* gene). These isolates also lacked the *cytK* gene. However, both produced the Nhe toxin (Tecra kit), with a high production index at 37°C. Moreover, both isolates were highly cytotoxic to human epithelial cells. Thus, each of the 2 isolates possessed at least 1 virulent toxin and had microbiologic activities conferring a high virulence potential,^{6,7} potentially accounting for the disease observed in these 2 cases.

In conclusion, we relate 2 cases of *B. cereus* bacteremia in premature infants that caused serious complications in the first newborn and the death of the second child from multiple organ failure and pulmonary and cerebral abscesses. In the 2 clinical cases, *B. cereus* was detected in 2 consecutive invasive specimens, and both infants were hospitalized simultaneously in the same neonatal intensive care unit. However, there was no clear link between these outcomes: the 2 *B. cereus* strains were genetically different, and the source of contamination was not identified. A hypothesis is that both neonates could have been infected via the point of entry of the umbilical catheter, which was not protected by a dressing, and may therefore have been exposed to environmental contamination. Changes in care practices relating to umbilical central venous catheters should therefore be introduced.

The widespread ignorance of *B. cereus* and of its pathogenic potential makes it difficult to diagnose the infections it causes. As a result, the management of these conditions is often both late and inadequate. Thus, we believe that reporting the cases of *B. cereus* infections among patients, and in particular among the really fragile and exposed neonate population, will help to gain information on this still poorly recognized pathogen and to develop new therapeutic approaches that will protect exposed patients.

N.R. and L.B. contributed equally to this work.
Conflicts of interest: None to report.

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