Severe Bacillus cereus infection in a neonatal intensive care unit

Abstract: Infections of the central nervous system (CNS) in neonates with very low birth weight (VLBW) may have major clinical consequences due to their immunocompromised status. Bacillus cereus is a rare pathogen that can cause serious infection in these patients and is associated with a high mortality rate. We report the case of an extremely preterm neonate who developed severe infection of the CNS caused by B. cereus with progressive neurological deterioration despite broad spectrum antibiotic treatment. She died at the age of 16 months. In conclusion, we wish to increase the awareness among health care practitioner about the possibility of infection due to B. cereus in sick neonates and its devastating course in this population.

Keywords: Bacillus cereus; immunocompromised; infection; neonate; preterm.

Case presentation

A female neonate (second twin) weighing 529 g, whose parents were young, nonconsanguineous, and healthy, was born by spontaneous vaginal delivery after 24 weeks of gestation. The Apgar score was 8 at 1 min and 9 at 5 min. Prior to the delivery, her mother received ampicillin for suspected chorioamnionitis (confirmed by pathological examination of the placenta), and one course of dexamethasone to aid in fetal lung surfactant production. Except for premature labor, her pregnancy had been otherwise normal.

The neonate was admitted to the neonatal intensive care unit immediately after birth. She experienced respiratory distress that was treated with exogenous surfactant and needed prolonged mechanical ventilation. As a secondary to umbilical arterial catheter placement, she developed vasospasm of the left lower extremity that improved partially after withdrawal of the catheter. Doppler ultrasound showed normal blood flow. On day 8, she showed signs of necrotizing enterocolitis with perforation and an abdominal drain was inserted; she received antibiotic therapy with vancomycin, cefotaxime, and metronidazole. She received prolonged parenteral nutrition (until day 50) and as a consequence presented with neonatal cholestasis treated with ursodeoxycholic acid and liposoluble vitamins.

Despite these events, the neonate presented a favorable outcome from day 60, without central venous catheter (peripherally inserted central catheter) from day 50. At this time, she was fed powdered infant formula by nasogastric tube. Transfontanellar ultrasound (TU) showed dilatation...
of the lateral ventricles with periventricular hyperechogenicity of the parenchyma without evidence of cystic change.

On day 74, the patient started episodes of apnea and bradycardia that needed mechanical ventilation and seizures that were treated with phenobarbital and continuous infusion of midazolam. Her clinical condition continued to worsen progressively with right facial paralysis, left hemiparesis, marked irritability, gastric bleeding, anemia, thrombocytopenia, increased cholestasis, and hypoalbuminemia. Laboratory studies showed increased C-reactive protein (203 mg/L maximum), leukocytosis with \(14.3 \times 10^3/\mu L\) white blood cells (4.1\( \times \)10^3/\mu L neutrophils and 4.2\( \times \)10^3/\mu L lymphocytes) and cerebral spinal fluid (CSF) pleocytosis (4545 cells/\mu L) with 72,000/\mu L RBCs, 66% neutrophils, and 21% lymphocytes, low CSF glucose level, and 1.11 g/L protein. The Gram stain was negative. Suspecting infection of CNS, antibiotic therapy with vancomycin and meropenem was started (after blood culture). On day 75, TU was repeated showing signs of ventriculitis (Figure 1) and periventricular leukomalacia (Figure 2). The echocardiogram was normal.

Meanwhile, \textit{B. cereus} was isolated in the blood culture (antibiotic susceptibility results were not available). CSF culture was negative. She maintained the need for mechanical ventilation and inotropic support with dopamine and dobutamine. Serial TUs were performed and showed worsening of the described lesions.

Her neurological status was progressively deteriorating and on day 90, a brain MRI was performed showing cystic dilatation of the 4th ventricle (Figure 3) and macrocystic leukomalacia (Figure 4). A neurosurgeon was consulted who opined that there was no indication for drainage of the described 4th ventricle lesion.

She completed 35 days of antibiotic treatment (until CSF pleocytosis, blood leukocytosis, and C-reactive protein became normal), with negative control blood and CSF cultures, maintaining treatment with phenobarbital. Electroencephalogram confirmed multifocal epileptiform activity.

She was stable until day 122 when her neurologic status declined with progressive increase in head circumference with bulging fontanelle and dehiscence of

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**Figure 1** Ventricular CSF with intraventricular septa and thickened ependyma due to ventriculitis.

**Figure 2** Involvement of the periventricular white matter with marked hyperechogenicity and multiple microcysts, suggesting periventricular leukomalacia.

**Figure 3** Cystic dilatation of the 4th ventricle with severe compression of the brainstem and cerebellar parenchyma.
cranial sutures. TU was repeated and it showed marked transtentorial growth of the posterior fossa cyst causing compression of the supratentorial ventricular system. At this point, it was decided to place an external ventricular drain with the goal of symptom relief that was removed after 14 days. CSF was xanthochromic but it did not show pleocytosis and the culture was negative.

On day 131, the patient showed signs of CNS infection with decreased spontaneous activity and CSF pleocytosis with low CSF glucose level. She was administered a new course of antibiotic therapy with vancomycin and cefotaxime.

The patient was discharged on day 148 and she presented decreased spontaneous activity, uncoordinated movements of the limbs with tremors, and no social interaction. She remained under regular neonatology, neurosurgery, physical medicine, and nutrition follow-up, but she needed several hospitalizations during this time, Ommaya reservoir placement, and anticonvulsant therapy. She died at the age of 16 months due to progressive neurological and clinical deterioration with oliguric renal failure.

Discussion

There are only a few reports of severe and often fatal infections in neonates with B. cereus in recent years, indicating that this bacterium is an uncommon but potentially serious pathogen [2, 3]. Despite this small number, it seems likely that the actual occurrence of this organism is more common as a true pathogen than the published literature would suggest. This can occur because it is usually designated as a contaminant even when the organisms are isolated from sterile sites such as blood or CSF [2, 5].

In neonates, B. cereus can lead to systemic infections with bacteremia, sepsis, and endocarditis as well as localized infections of the CNS, respiratory tract, eye, wounds, and soft tissue, causing extensive damage and necrosis of infected tissues due to the toxins produced [1].

Neonatal meningoencephalitis caused by B. cereus is rare. In most cases, the infection is fatal because of extensive damage and necrosis of the infected tissue caused by the toxins produced by B. cereus. In the literature, there are only a few published cases of infections with B. cereus in preterm neonates; however, all of them followed a devastating course: one had cerebral palsy as a late sequel and all the others died [6].

Our case also demonstrates the value of serial sonography to detect brain destruction in a neonate with signs of sepsis and/or convulsions and normal early scans.

Lequin et al. [6] described three cases of preterm neonates with severe hemorrhagic meningoencephalitis due to infection caused by B. cereus. All three had uneventful initial days with normal routine brain sonography. After the infection they showed, similar to our patient, white matter central necrosis, intraventricular septa, and thickened ependyma due to ventriculitis and signs of hemorrhagic destruction of white matter in magnetic resonance images. In our patient, the imaging characteristics and CSF analysis (hemorrhagic meningoencephalitis) are therefore consistent with findings in the literature of severe infection caused by B. cereus in preterm neonates, which allow us to presume that the infection due to B. cereus was responsible for the clinical deterioration presented.

The autopsy findings in the literature were characterized by a high incidence of intracranial hemorrhage [7]. The reason why B. cereus is associated with intracranial hemorrhage remains unknown, but it may suggest that B. cereus has an invasive tendency in the CNS. It is known to produce not only enterotoxin, causing food poisoning, but also hemolysin and phospholipase [4]. The in vivo role of these enzymes is not entirely clear, but could be associated with successful local infections and be important in the establishment of severe systemic diseases. Autopsy findings (softened brain tissue or brain lysis) also support the hypothesis that enzymes play an important role in meningitis caused by B. cereus in the neonate [7].

The drug of choice for these infections appears to be vancomycin [1]. However, in our neonate antibiotic treatment remained ineffective with progressive neurologic deterioration. Antibiotic susceptibility results, which...
could be extremely useful information for optimizing treatment, were not available because the microbiologists considered *B. cereus* as a contaminant and they did not perform susceptibility tests.

All the CSF cultures showed negative results which could be explained by the fact that due to the patient’s clinical instability at the time clinical deterioration occurred LP was performed under antibiotic treatment.

In this case, the infection occurred when the central venous catheter and other invasive devices had already been removed, which is not in agreement with other reported cases [1, 3]. However, feeding was performed by nasogastric tube which could raise the hypothesis of the gastrointestinal tract as the most likely site of origin of the infection, although the bacterium was not isolated in the milk used.

After isolation of *B. cereus* from the blood culture, the infection control committee of our hospital was informed and an exhaustive search for the origin of the bacterium was performed in our unit, including investigations on the handling of bottles and nasogastric tubes used in feeding, as well as the conditions of storage, but unfortunately they were not able to prove the source of the infection.

In conclusion, we wish to increase the awareness among health care practitioners about the possibility of infection caused by *B. cereus* in sick neonates. The health care practitioners and clinical microbiologists must give serious consideration to the significance of a *B. cereus* isolate from a clinical specimen, especially if the patient is immunocompromised, because the outcome may be devastating as it happened in this case. Given the possible role of toxins in the severe tissue damage that is typical of infections caused by *B. cereus*, the rapid progression of the infection and the inability of antibiotics alone to stop the disease process, alternative forms of intervention need consideration, including measures that address the role of toxins.

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**References**


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