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Meningoencephalitis caused by *Bacillus cereus* in a neonate

在新生兒中由蠟樣芽胞桿菌引起的腦膜炎

We report on a newborn boy, who was delivered at 26 weeks' gestation by emergency caesarean section because of a prolapsed cord and breech presentation. Grade IV hyaline membrane disease subsequently developed, for which a surfactant was given. On day 8, there were frequent apnoeic attacks, and on day 30, marked irritability developed, as did intermittent stiffening of all four limbs. The anterior fontanelle was bulging and tense, and the cerebrospinal fluid was found to be turbid. Gram staining of the cerebrospinal fluid and blood revealed Gram-positive bacilli. Subsequent culturing yielded *Bacillus cereus*, which was sensitive to amikacin and vancomycin. Severe cerebral oedema developed, however, and computed tomography of the brain showed bright cortical sulci, suggestive of meningitis. The baby died on day 37, and post-mortem histological examination of the brain showed extensive liquefactive necrosis with abundant neutrophilic infiltration. Since infection with *Bacillus cereus* is rapidly fatal, early recognition of infection by this organism is important.

我們報告一名因產婦臍帶脫垂和臀先露而在妊娠26週時由緊急剖腹產手術的男嬰。患者接著發生了IV玻璃樣膜病，為此使用了表面活性劑。在第8天，有頻繁的窒息發作；在第30天，出現顯著的過敏，四肢間歇性僵硬。前顱腫脹緊張，並發現腦脊髓液是混濁的。腦脊髓液和血液的革蘭染色顯示革蘭陽性桿菌屬，隨後的培養物生長出對愛米戰素和萬古戰素敏感的蠟樣芽胞桿菌，嚴重的大腦水腫出現，而電腦的腦X光斷層照相術顯示明亮的皮質溝，證明有腦膜炎。這名男嬰死於第37天。腦死後組織學檢查顯示帶有大量中性白細胞浸潤的廣泛液化壞死。因為蠟樣芽胞桿菌傳染是快速致命的，對這生物傳染的早期識別很重要。

Key words:

Bacillus cereus;
Bacillaceae infections;
 Brain/pathology;
 Infant, newborn;
 Meningoencephalitis

關鍵詞：

蠟樣芽胞桿菌；
 芽胞桿菌科傳染；
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Introduction

Bacillus cereus, a Gram-positive or Gram-variable, aerobic spore-forming rod, is ubiquitous in the environment. The organism is often regarded as a contaminant of specimens received by the microbiology laboratory, and a positive growth of *B. cereus* is often disregarded by clinicians and microbiologists.

Although meningitis caused by *B. cereus* in neonates is rare, it is usually fatal. A review of the English-language literature yielded seven reports of *B. cereus* meningoencephalitis (Table).¹⁻⁷ This report describes a fatal case of neonatal meningitis due to *B. cereus* infection, which resulted in infarction and liquefactive necrosis of the whole brain. Such a case of meningoencephalitis in neonates has never been reported in Hong Kong. We also report the findings from ultrasonography and computed tomography (CT) studies of the brain in this case.

Table. Reports in the literature of infection of the central nervous system with *Bacillus cereus*

Study	Sex/gestation/ weight	Age at onset	Predisposing factors	Nature of infection	Treatment	Outcome
Leffert et al, ¹ 1970	Not reported	18 weeks	Dandy-Walker cyst, ventricular shunt	Meningitis	Ampicillin, gentamicin, shunt removal	No sequelae
Raphael and Donaghue, ² 1976	Not reported	8 months	Ventricular shunt	Meningitis	Ampicillin, gentamicin, shunt removal	No sequelae
Turnbull et al, ³ 1977	Female/ 32 weeks/ 1.32 kg	4 days	Necrotising enterocolitis, cerebral haemorrhage	Meningitis	Ampicillin, gentamicin	Died
Hendrickx et al, ⁴ 1981	Female/ 32 weeks	8 days	Respiratory distress syndrome, central line	Meningitis	Ampicillin, gentamicin, erythromycin	Died
Feder et al, ⁵ 1988	Female/ 32 weeks/ 1.5 kg	7 weeks	Infected intravenous catheter	Meningitis	Chloramphenicol	Cerebral palsy
Patrick et al, ⁶ 1989	Female/ 26 weeks/ 0.83 kg	7 days	Bilateral thalamic haemorrhage	Encephalitis	Vancomycin, amikacin	Died
Weisse et al, ⁷ 1991	Male/ term/ 3.7 kg	3 weeks	None	Meningitis	Gentamicin, chloramphenicol	No sequelae
Weisse et al, ⁷ 1991	Male/ 36 weeks/ 2.71 kg	5 days	Myelomeningocele sac ruptured	Meningitis	Vancomycin	No sequelae
Present report, 1997	Male/ 26 weeks/ 1.5 kg	4 weeks	Bronchopulmonary dysplasia, dexamethasone used	Meningitis	Vancomycin, amikacin	Died

Case report

A baby boy (twin 1) was born in the Tuen Mun Hospital on 12 October 1997 to a Nepalese primigravida by emergency caesarean section at 26 weeks' gestation because of a prolapsed cord and breech presentation. His birthweight was 1.58 kg. At birth, he was flaccid and cyanotic, had bradycardia, and was not breathing spontaneously. He was resuscitated with endotracheal intubation and mechanical ventilation, and he showed a good response. Apgar scores were 3, 6, and 8 at 1, 5, and 10 minutes, respectively. Umbilical arterial and venous catheters were placed soon after birth, and both were removed on day 15.

Physical examination revealed a normal preterm baby with no dysmorphic features. Grade IV hyaline membrane disease subsequently developed, for which two doses of beractant 4 mL/kg as surfactant (Survanta; Abbott Laboratories, Chicago, United States) were given. Hypotension also developed on the first day, which required dopamine infusion. Empirical antibiotics (penicillin and netilmicin) were administered. His condition was complicated by patent ductus arteriosus and frequent apnoeic attacks on day 8. The patent ductus arteriosus closed after a course of

indomethacin was given. He was given parenteral nutrition via peripheral venous access until day 19, when milk feeding was fully established.

The baby required prolonged mechanical ventilation and he developed signs suggestive of bronchopulmonary dysplasia. Dexamethasone 0.5 mg/kg was given every 6 hours for 5 days from day 22 and the dose was tapered thereafter. Serial bedside ultrasonography of the brain on days 1, 3, 7, and 14 revealed no evidence of intracranial haemorrhage. Until day 26, there was no positive growth from repeated blood cultures. Culture of surface swabs yielded either commensals or non-haemolytic *Streptococcus* species and *Staphylococcus aureus*, which were sensitive to initial antibiotic treatment.

On day 30, the baby developed marked irritability and intermittent stiffening of his limbs. The anterior fontanelle was bulging and tense. Microbiological investigations included cultures of urine, tracheal aspirate, blood, and cerebrospinal fluid (CSF). A complete blood count showed leukocytosis—that is, a white blood cell count (WBC) of 21.2 x 10⁹/L (normal range, 6.0-18.0 x 10⁹/L). Neutrophils were found to be predominant and the CSF was found to be turbid.

Light microscopic examination of the CSF revealed an elevated WBC of 3.2×10^5 /L, with 80% polymorphs; the levels of protein and glucose were 2.3 g/L and <1 mmol/L, respectively. Urgent Gram-staining examination showed the presence of Gram-positive bacilli in both the blood and CSF samples. Ampicillin and cefotaxime were given empirically. Subsequent cultures of the CSF and blood yielded *B cereus*, which was sensitive to amikacin, chloramphenicol, imipenem, meropenem, and vancomycin but resistant to penicillin, cefotaxime, ceftriaxone, and ceftazidime. Cultures from urine and tracheal aspirate did not show any positive growth. On day 31, the antibiotics were changed to amikacin 7.5 mg/kg three times daily and vancomycin 15 mg/kg four times daily. However, severe cerebral oedema developed and ultrasonography of the brain on day 30 showed a hyperechoic region in the right parietal lobe with a mass effect on the lateral ventricle and midline shift to the left. A CT scan of the brain performed on the same day also showed a diffuse area of low attenuation in the right parietal lobe compressing the ventricle and displacing it into the left side. The cortical sulci appeared bright on the CT scan, suggestive of meningitis (Fig 1).

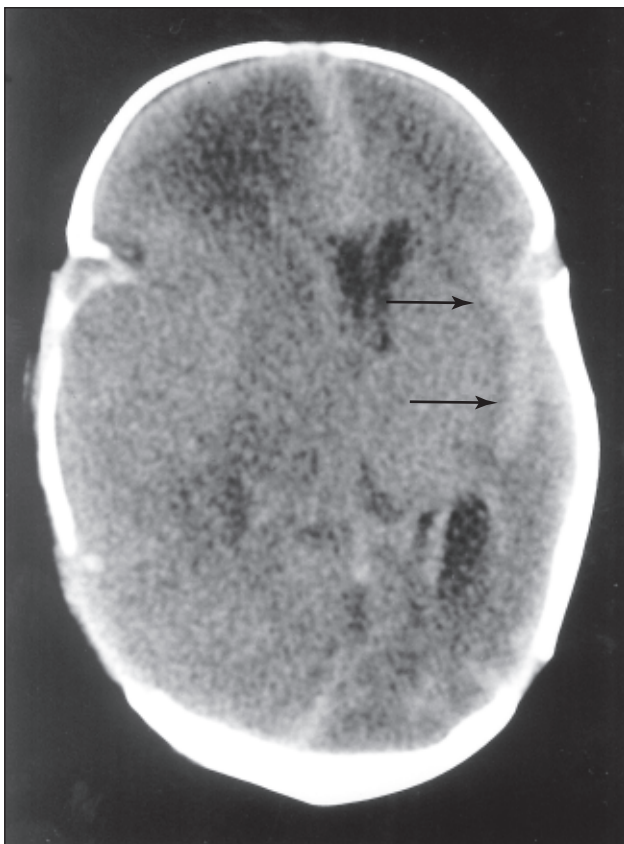


Fig 1. An axial non-contrast computed tomogram of the brain on day 30 showing low attenuation involving the right frontal, parietal, and occipital lobes. Similar changes are also shown on the left, but to a lesser extent. Note the increase in density of the left Sylvian fissure (arrows) and cortical sulci, suggestive of meningitis.

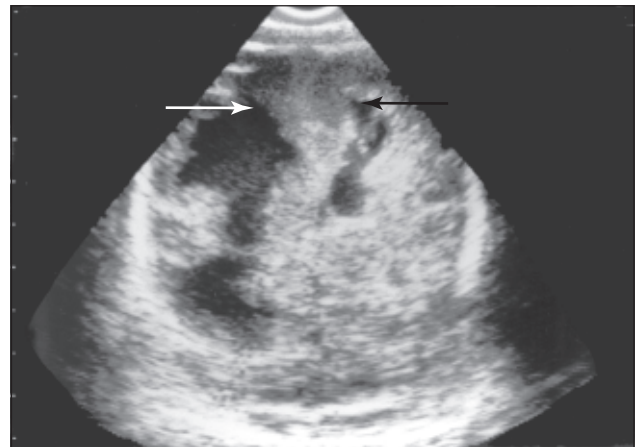


Fig 2. A coronal ultrasonogram on day 37 showing liquefactive necrosis in the right parietal (white arrow) and left frontal area (black arrow).

Although stabilisation was attempted with fluid restriction, mechanical hyperventilation, and the use of mannitol and anticonvulsants, the baby developed brain death with fixed and dilated pupils, absence of gag reflex, and total areflexia. The electroencephalogram showed severely depressed background activity and an ultrasound examination of the brain on day 37 showed an area of liquefactive necrosis in the right parietal region (Fig 2). The baby died on day 39. The post-mortem examination revealed that the brain was unusually soft and friable, with a loss of normal anatomical structures. Histological examination of the brain showed extensive liquefactive necrosis with abundant neutrophilic infiltration. Gram staining, however, did not reveal Gram-positive bacilli.

Discussion

Bacillus cereus is a ubiquitous organism, which can readily contaminate the hospital environment, including uniforms of health care workers, patients' dressings, or intravenous catheters. The organism mainly causes infection in immunocompromised patients or those with invasive devices fitted, such as endotracheal intubation tubes and central venous lines.⁸ Infection can occur following burns or as wound sepsis; systemic infections can lead to meningoencephalitis, pneumonia, endocarditis, bacteraemia, or toxin-induced food poisoning.⁹ *Bacillus cereus* is susceptible to aminoglycosides, clindamycin, chloramphenicol, and erythromycin, but resistant to β -lactam antibiotics such as penicillins and cephalosporins.¹⁰

This case report illustrates two important points. Firstly, the presence of Gram-positive bacilli in the blood or CSF is frequently regarded as contamination by *Bacillus* species. Even if the presence of the bacilli is considered important, as in the clinical setting of

meningitis in this patient, infection with *Listeria monocytogenes* is usually presumed. The standard empirical treatment for neonatal meningitis with high-dose ampicillin and cefotaxime covers *Listeria* species but not *B cereus*, thus leaving the patient unprotected against infection by this organism. Secondly, meningitis caused by *B cereus* is a serious infection. As illustrated in the Table, the nine cases so far reported (including this case) comprised four deaths and one case of serious neurological sequelae.

Because *B cereus* produces toxins, which include a necrotising enterotoxin, phospholipases, proteases, and haemolysins,¹¹ it causes extensive damage and necrosis of infected tissues. These features were demonstrated in this case by the ultrasonography and CT findings. Liquefactive necrosis is not commonly seen in neonatal meningitis, which usually demonstrates thickening of the meninges (in meningitis) or ventricular walls (in ventriculitis). Basal meningitis may also produce ventricular dilatation. In contrast, the post-mortem examination of this patient showed widespread liquefactive necrosis, which was particularly noticeable in the cerebral cortex and basal ganglia. The same finding was also described by Hendrickx et al in their case report.⁴

Clinicians need to be aware of *B cereus* as a potential pathogen in predisposed patients. When Gram-positive bacilli are found in the blood or CSF, the possibility of *B cereus* septicaemia or meningitis needs to be considered, especially for neonates receiving prolonged parenteral nutrition that requires the insertion of a long-term central venous catheter. In neonatal meningitis caused by Gram-positive bacilli, *Listeria monocytogenes* infection is the most common cause, and ampicillin and cefotaxime are usually given. This

regimen, however, does not adequately cover *B cereus*, which is resistant to most β -lactam antibiotics. Clinicians must ensure that they receive the culture and antibiotic susceptibility results, and that they change to the appropriate antibiotics, such as vancomycin and an aminoglycoside as soon as possible. Since the infection is rapidly fatal, we wish to emphasise that early recognition of infection by this organism is important for preterm neonates.

References

1. Leffert HI, Baptist JN, Gidez LI. Meningitis and bacteremia after ventriculoatrial shunt-revision: isolation of a lecithinase-producing *Bacillus cereus*. *J Infect Dis* 1970;122:547-52.
2. Raphael SS, Donaghue M. Infection due to *Bacillus cereus*. *Can Med Assoc J* 1976;115: 207.
3. Turnbull PC, French TA, Dowsett EG. Severe systemic and pyogenic infections with *Bacillus cereus*. *Br Med J* 1977;1: 1628-9.
4. Hendrickx B, Azou M, Vandepitte J. *Bacillus cereus* meningo-encephalitis in a pre-term baby. *Acta Paediatr Belg* 1981;34: 107-12.
5. Feder HM, Garibaldi RA, Nurse BA, Kurker R. *Bacillus* species isolates from cerebrospinal fluid in patients without shunts. *Pediatrics* 1988;82:218-20.
6. Patrick CC, Langston C, Baker CJ. *Bacillus* species infections in neonates. *Rev Infect Dis* 1989;11:612-5.
7. Weisse ME, Bass JW, Jarrett RV, Vincent JM. Nonanthrax *Bacillus* infections of the central nervous system. *Pediatr Infect Dis J* 1991;10:243-6.
8. Barrie D, Wilson JA, Hoffman PN, Kramer JM. *Bacillus cereus* meningitis in two neurosurgical patients: an investigation into the source of the organism. *J Infect* 1992;25:291-7.
9. Drobniewski FA. *Bacillus cereus* and related species. *Clin Micro Rev* 1993;6:324-38.
10. Coonrod JD, Leadley PJ, Eickhoff TC. Antibiotic susceptibility of *Bacillus* species. *J Infect Dis* 1971;123:102-5.
11. Turnbull PC, Jorgensen K, Kramer JM, Gilbert RJ, Parry JM. Severe clinical conditions associated with *Bacillus cereus* and the apparent involvement of exotoxins. *J Clin Pathol* 1979;32: 289-93.