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CASE REPORT PEER REVIEWED | OPEN ACCESS

Paenibacillus thiaminolyticus sepsis and meningoencephalitis in a 37-day old preterm infant

Kristen Bastug, Ashajyothi M Siddappa, Stacene Maroushek

ABSTRACT

Introduction: The *Paenibacillus* genus consists of saprophytic organisms that are commonly associated with soil, water, plants, feces, and diseased insect larvae. Human infection is rare. This disease typically occurs in immunocompromised hosts, adults with a history of intravenous drug use, and hosts with prosthetic medical devices. There are a limited number of case reports describing *Paenibacillus* infections in neonates. This is the second published instance of pediatric meningoencephalitis caused by *Paenibacillus thiaminolyticus* in a preterm infant with intrauterine drug exposure.

Case Report: A 37-day-old male infant with a history of prematurity of 33 weeks completed gestation presented to the Emergency Department for acute onset poor feeding, poor color, and unresponsiveness at home. Examination revealed cyanosis, apnea, and hypotonia. Vital signs were significant for hypotension and hypothermia. Initial labs revealed a metabolic acidosis, elevated C-reactive protein, normal complete white blood cell count, and a negative viral respiratory pathogen panel. Aerobic blood culture and cerebrospinal fluid (CSF) culture were positive for *P. thiaminolyticus* within 24 hours. Cranial ultrasound and magnetic resonance imaging revealed changes concerning for liquefactive meningoencephalitis. The infant was admitted to the neonatal intensive care unit (NICU) and ultimately discharged home on a "do not resuscitate/do not intubate" status and later died at 11 months of age.

Conclusion: *Paenibacillus* species are common environmental organisms but can cause devastating disease in neonates. This is the second reported case of a preterm infant with *P. thiaminolyticus* infection and in-utero drug exposure (IUDE), supporting that prematurity and IUDE may be risk factors for severe disease.

Keywords: Bacillus, Meningitis, *Paenibacillus thiaminolyticus*, Prematurity

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INTRODUCTION

The *Paenibacillus* genus contains approximately 200 rod-shaped, endospore forming, gram variable, aerobic or facultatively anaerobic bacteria with a 16S rDNA sequence and a peritrichous flagella. *Paenibacillus* species are common saprophytic organisms associated with soil, water, plants, feces, and diseased insect larvae [1, 2]. They produce many antimicrobial compounds and are considered beneficial for crop growth. One species, *P. larvae*, causes large-scale liquefactive destruction of bee colonies in a disease known as American Foulbrood. Human infections are rare. This disease typically occurs in immunocompromised hosts, adults with a history of

intravenous drug use, and hosts with prosthetic medical devices. Few cases are described in children and neonates [3]. We present a case report of *P. thiaminolyticus* sepsis and meningoencephalitis in a preterm infant with intrauterine drug exposure. This report is the second published instance of pediatric meningoencephalitis caused by *P. thiaminolyticus* [4]. While *P. thiaminolyticus* infection is rare, this case offers supportive evidence that devastating disease is possible in neonates.

CASE REPORT

A 37-day-old male infant with a corrected gestational age of 38 weeks presented to the Emergency Department for poor feeding, poor color, and unresponsiveness. Examination revealed cyanosis, apnea, and hypotonia. He was resuscitated with intubation and intravenous fluids, and was treated with ampicillin (300 mg/kg/day divided every 6 hours), cefepime (150 mg/kg/day divided Q8 hours), and gentamicin (5 mg/kg Q24 hours) for empiric antimicrobial coverage. Labs were notable for a normal glucose, total white blood cell count was 10.8 10^3/uL, absolute neutrophil count was 1.9 10^3/uL, and c-reactive protein (CRP) was 123 mg/L (Table 1). Respiratory viral panel including COVID-19 was negative. His blood culture was positive for *P. thiaminolyticus* within 12 hours. The cerebrospinal fluid (CSF) culture was also positive for *P. thiaminolyticus* (Table 2). A chest X-ray revealed a right upper lobe infiltrate concerning for pneumonia. A cranial ultrasound was abnormal (Figure 1), revealing abnormal echogenic parenchyma throughout the bilateral cerebral hemispheres involving subcortical and deep white matter of the frontal lobes.

Previous medical history was reviewed. The infant was admitted to the neonatal intensive care unit (NICU) immediately after birth for prematurity. The infant was delivered via urgent cesarean section at 33 weeks and 4/7 days gestation due to decreased fetal movement and fetal distress. The mother was a G5P3 (3 term deliveries, 1 abortion, and one ectopic pregnancy). The pregnancy was complicated by hyperemesis gravidarum syndrome, intrauterine growth restriction, seizure disorder, homelessness, bipolar disorder, and polysubstance use including alcohol, methamphetamines, heroin, and cocaine. The infant's mother was enrolled in a treatment program for one month prior to delivery. Maternal medication history included lurasidone (40 mg oral p.m. and 20 mg oral a.m.), prenatal vitamin (1 mg oral daily), metoclopramide (10 mg oral daily), and hydroxyzine (25 mg oral as needed). Prenatal testing at 22 weeks gestational age was within normal limits and included hepatitis B surface antigen, rapid plasma reagin (RPR), hepatitis C antibody, and human immunodeficiency virus (HIV) antigen-antibody combination. The mother was found to be a carrier for group B streptococcus (GBS) with a previous pregnancy. Intrapartum antibiotics were not administered to the mother. The birth weight was 1371 grams, and he was small for gestational age (SGA). APGAR scores were 5 and 8 at 1 and 5 minutes of age, respectively, and he required positive pressure ventilation at delivery. He was subsequently admitted to the NICU and treated empirically for neonatal sepsis with ampicillin and tobramycin for 48 hours. Laboratory results on admission were significant for normal CRP, normal complete blood count (CBC), and a positive meconium toxicology screen for cocaine and tetrahydrocannabinol (THC). Placental pathology revealed early evidence of chorioamnionitis. His blood cultures remained negative for bacterial growth. He was discharged on day of life 22 at a corrected gestational age of 36 weeks with a weight of 1970 grams.

Culture sensitivity results for the infant's *P. thiaminolyticus* infection revealed ampicillin susceptibility. He received 21 days of ampicillin following the first negative blood culture (hospital day 1). A brain magnetic resonance image (MRI) with contrast

Table 1: Serologic results during the acute phase of hospitalization

	Reference range	Day 1	Day 2	Day 4
White blood cell count (k/cmm)	5–19	10.78	14.09	27.70
Absolute neutrophil count (k/cmm)	0.9–9.3	1.94	3.24	14.96
Hemoglobin (g/dL)	10–18	10.3	9.6	7.6
C-reactive protein (mg/L)	0–5.0	123	132	72

Table 2: Cerebrospinal fluid analysis on admission and day 5 of hospitalization

	Admission	Day 5
Appearance	Bloody	Yellow
Clarity	Clear	Hazy
Red Blood Cell (cells/uL)	<1000	1000
Nuclear count (cells/uL)	9152	1021
Neutrophil (%)	74	80
Lymphocyte (%)	2	9
Macrophage (%)	25	10
Protein (mg/dL)	975	475
Glucose (mg/dL)	25	<2
Gram stain	Gram negative rods	Gram negative rods
Final culture result	*P. thiaminolyticus*	Negative

performed on hospital day 2 of admission showed leptomeningeal enhancement and findings concerning for necrotizing/liquefactive meningoencephalitis (Figure 2), in addition to bilateral ischemic strokes involving the thalami and occipital lobes. Brain magnetic resonance angiography (MRA) was without significant stenosis or aneurysm. A repeat brain MRI was obtained at the end of antibiotic treatment (day 25 of admission) and showed evidence of progressive supratentorial cerebral cystic encephalomalacia and subfalcine herniation (Figure 3). An electroencephalogram (EEG) was abnormal with generalized cerebral dysfunction and several rhythmic runs of electrographic seizures. The infant was discharged home on day 27 of admission, feeding well orally with his respiratory status stable on room air. His physical exam at discharge was significant for an enlarged head circumference, full bulging fontanelle, alert neurologic status with high-pitched cry, tremors, and upper and lower extremity hypertonicity. The infant was discharged home on a "do not resuscitate/do not intubate" status and later received a ventriculoperitoneal shunt placement. In the outpatient setting he experienced recurrent difficulties with seizure activity and feeding problems. He was admitted for respiratory failure at 11 months of age and subsequently passed away.

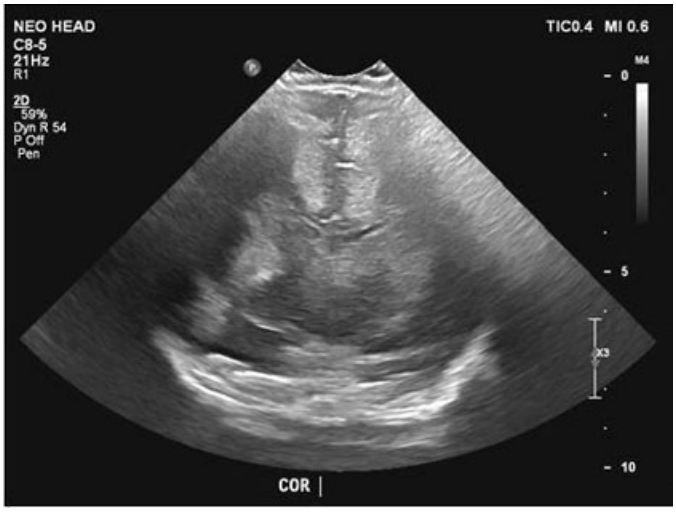

Figure 1: Cranial ultrasound. Suboptimal evaluation due to significant amount of artifact. Grossly abnormal echogenic parenchyma throughout both cerebral hemispheres, particularly involving the subcortical and deep white matter of the frontal lobes.

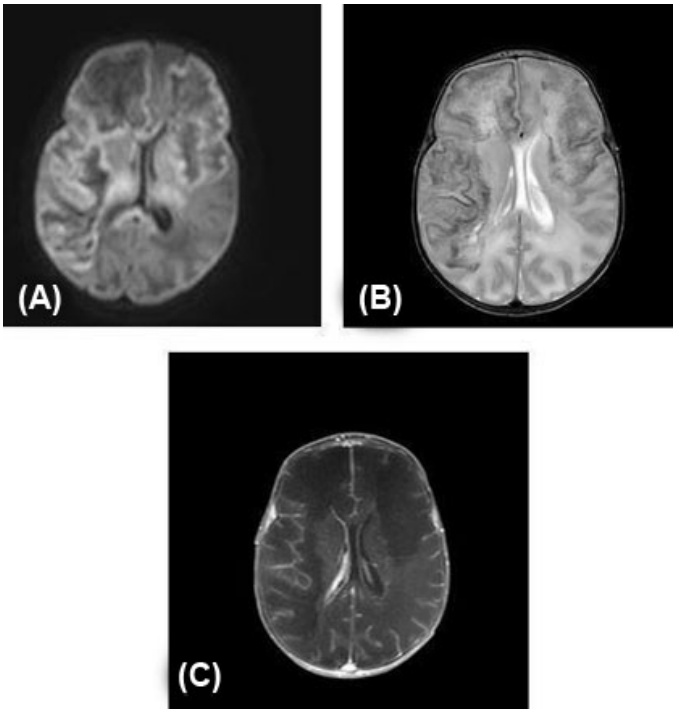

Figure 2: Brain magnetic resonance image with contrast. Transverse images obtained on admission, day of life 37. (A) Diffusion-weighted image showing infarctions involving the bilateral thalami and bilateral occipital lobes. (B) T2 image showing areas of liquefaction and hemosiderin staining in the bilateral frontal lobes and right temporal parietal lobes concerning for necrotizing/liquefactive meningoencephalitis. (C) T1 GAD images show extensive leptomeningeal enhancement.

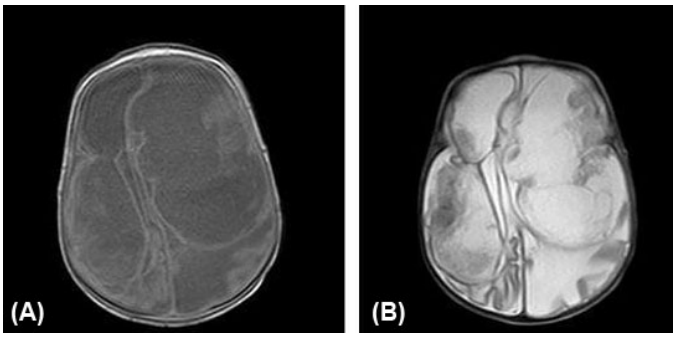

Figure 3: Brain magnetic resonance image with contrast. Transverse images obtained on day of life 62. (A) (T1-weighted) and (B) (T2-weighted) images show progressive supratentorial cerebral liquefactive/cystic encephalomalacia. The involved peripheral rims of cerebral parenchyma surrounding these cystic areas demonstrate scattered microhemorrhages.

DISCUSSION

Paenibacillus species recovered from human specimens have historically been considered nonpathogenic environmental organisms. However, specimens with positive culture results should not be immediately attributed to environmental contamination. In a case report, Hunt et al. [4] describe a preterm infant born at 35 weeks gestational age. The infant was treated in the emergency room at 25 days of life for cardiopulmonary arrest. Medical history was significant for limited prenatal care and intrauterine exposure to methamphetamine, marijuana, and tobacco. Cerebrospinal fluid analysis was indicative of purulent meningitis, and blood culture at 23 hours was positive for *P. thiaminolyticus*. The infant

was treated with ampicillin, gentamicin, and cefepime but suffered clinical deterioration. Palliative care was initiated, and supportive cares were withdrawn on day 4 of admission.

Another case report by DeLeon et al. [5] reported a 4-week-old female infant born at 33 5/7 weeks gestation who presented with a 1-day history of lethargy and refusal of feeds. She had evidence of cerebritis and edema on neuroimaging. The blood culture and CSF culture grew *Paenibacillus alvei*. A brain MRI two weeks later demonstrated cystic encephalomalacia. The infant died five months after hospital discharge.

In another case, Wiedermann [3] reported a 20-day-old full term female that was admitted with irritability and a fever. She was subsequently diagnosed with purulent meningitis. The CSF gram stain showed gram-variable rods initially thought to be listeria monocytogenes. Her blood and CSF cultures were further examined, and the causative organism was determined to be *Bacillus alvei* (later reclassified to *Paenibacillus alvei*) based on morphologic and biochemical characteristics. She was ultimately treated with 21 days of ampicillin and was discharged home without subsequent neurodevelopmental abnormalities.

Case reports of *Paenibacillus* infections in the adult population also exist [6–9]. *Paenibacillus larvae* bacteremia has been reported in intravenous drug users who had self-injected methadone prepared with honey containing *P. larvae* spores [7]. Paenibacillus larvae causes a highly infectious and lethal liquefactive disease in honeybees known as "American Foulbrood." Honeybee larvae are infected by ingesting *P. larvae* spores in their food. The spores germinate inside the honeybee larvae, killing the honeybee host and releasing millions of *P. larvae* spores [10].

The gram-variable nature of *Paenibacillus* species can make gram stain identification difficult with crystal violet staining. The two methods best used for identification of *Paenibacillus* species are: (1) 16S rRNA sequencing and (2) matrix-assisted laser desorption/ionization time-of-flight (MALDI-TOF) mass spectrometry [2]. A recent study utilized next generation metagenomic sequencing to evaluate CSF and blood samples of 100 Ugandan infants with post-infectious hydrocephalus, and *P. thiaminolyticus* was found to be the dominant pathogen [11]. This supports that *P. thiaminolyticus* may be more pathogenic than previously described. Further investigations are needed to better understand the risk factors and prevalence of *Paenibacillus* infections.

CONCLUSION

There is a paucity of literature describing *Paenibacillus* infections in neonates. To date, this is the second published case report of *P. thiaminolyticus* meningoencephalitis in a preterm neonate with intrauterine drug exposure (IUDE), suggesting that prematurity and IUDE may be risk factors for severe disease. While *P. thiaminolyticus* infection is rare in humans, it has been discovered as a dominant pathogen in Ugandan infants with post-infectious hydrocephalus. Our case offers supportive evidence that *P. thiaminolyticus* can cause devastating disease in neonates and that this organism may be more pathogenic than previously described.

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Author Contributions

Kristen Bastug – Design of the work, Analysis of data, Interpretation of data, Drafting the work, Revising the work critically for important intellectual content, Final approval of the version to be published, Agree to be

accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

Ashajyothi M Siddappa – Conception of the work, Design of the work, Acquisition of data, Analysis of data, Interpretation of data, Drafting the work, Revising the work critically for important intellectual content, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

Stacene Maroushek – Conception of the work, Design of the work, Acquisition of data, Analysis of data, Interpretation of data, Drafting the work, Revising the work critically for important intellectual content, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

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Conflict of Interest
Authors declare no conflict of interest.

Data Availability
All relevant data are within the paper and its Supporting Information files.

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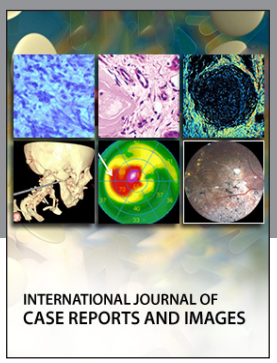

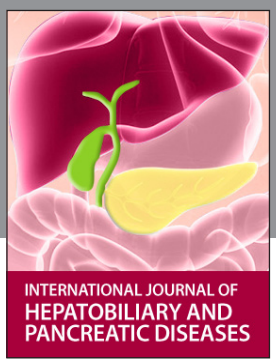

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