Invasive *Bordetella pertussis* Infection in Infants: A Case Report

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Infants are more likely to develop severe pertussis. We report a malignant pertussis case in a 2-month-old boy with respiratory failure, severe pneumonia, septic shock, and encephalopathy. *Bordetella pertussis* was detected from nasopharyngeal secretions by polymerase chain reaction, as well as both blood and cerebrospinal fluid samples via metagenomics next-generation sequencing.

**Keywords.** bacteremia; *Bordetella pertussis*; encephalopathy; pneumonia; whooping cough.

Pertussis, commonly known as whooping cough, is a highly contagious disease caused by *Bordetella pertussis*. To the best of our knowledge, there are currently rare reports of invasive pertussis through blood. We report a case of severe pertussis in a Chinese infant with detection of *B pertussis* in both blood and cerebrospinal fluid (CSF).

**CASE PRESENTATION**

A 2-month-old boy was referred to the emergency department of our hospital on March 18, 2022, because of mild cough, fever (37.8°C), and malaise for 1 day after close contact with his 7-year-old brother who had a cold. He was born very preterm (31 weeks + 5 days), with a low birth weight of 1700 grams. He was hospitalized for 25 days after birth due to neonatal pneumonia, coagulation dysfunction, intracranial hemorrhage (grade I, absorption phase), and neonatal pathologic jaundice. He had only been vaccinated with Bacillus Calmette-Guerin. He received symptomatic treatments of mask oxygen inhalation, ipratropium bromide atomization. However, the clinical symptoms deteriorated rapidly, with tachypnea and low oxygen saturation even with the oxygen mask. He was transferred to the Pediatric Intensive Care Unit (PICU) for further management.

On admission, the patient’s body temperature was 37.3°C, heart rate was 172 beats per minute, respiratory rate was 56 breaths per minute, and blood pressure was 96/50 mmHg. He presented with a puffy nose, triple concave signs, and mild cyanosis of the lips. The Glasgow Coma Score was 13 (E4, V3, M6). The oxygen saturation was 93% with the support of an oxygen mask. Pulmonary auscultation revealed rough breath sounds and wheezing in both lungs. He had an umbilical hernia on the abdomen and an anterior fontanelle bulge. He presented with a low response and screaming after stimulation. A computed tomography scan of the chest showed multiple plaques, streaks, solid shadows, and indistinct reticular shadows in both lungs. Magnetic resonance imaging of the brain showed that the bilateral frontal, parietal, and temporal extracranial spaces were slightly wider, and no obvious abnormality was found in the brain parenchyma. Echocardiography revealed no abnormalities. Routine blood tests revealed a hemoglobin level of 84 g/L, red blood cell count of 3.05 × 10¹²/L, white blood cell count of 6.5 × 10⁹/L, neutrophil count of 3.59 × 10⁹/L, lymphocyte count of 2.16 × 10⁹/L, and platelet count of 280 × 10⁹/L. Liver and kidney function tests were normal. The infant was diagnosed with respiratory failure, severe pneumonia, septic shock, and encephalopathy. Antibiotic therapy with meropenem, vancomycin, and leviteracetam was applied to treat pulmonary and intracranial infections. After 3 hours of PICU admission, the patient deteriorated, with worsening dyspnea, groans, gray face, cold limbs, and speckles all over the body. Bilateral crackles were detected by lung auscultation. The capillary refill time was 5 seconds. Oxygen saturation dropped to 54%. Blood gas analysis revealed a lactate level of 7.07 mmol/L. Procalcitonin was 14.29 ng/mL. The patient was further managed with symptomatic therapies, including invasive ventilator-assisted ventilation, norepinephrine, mannitol, fructose glycerol, immunoglobulin, and fresh frozen plasma.

Viral nucleic acid extracted from bronchial alveolar lavage fluid (BALF) specimens and examined by multiplex quantitative real-time polymerase chain reaction (PCR) assay for respiratory viruses, including respiratory syncytial virus, parainfluenza virus (PIV) 1, PIV 2, PIV 3, human adenovirus, influenza A (Flu A), Flu B, human metapneumovirus, rhinovirus, boca virus, and novel coronavirus was negative. Serological tests of *Mycoplasma pneumonia*, *Chlamydia trachomatis*, and cytomegalovirus immunoglobulin (Ig)M and/or IgG were negative. Sputum bacterial cultures were negative. The tuberculin test of tuberculin
Meanwhile, a blood sample and a CSF sample were subjected to dehydrogenase; m-NGS, metagenomics next-generation sequencing; RBC, red blood cell; abbreviations: CRP, C-reactive protein; CSF, cerebrospinal fluid; LDH, lactate dehydrogenase; m-NGS, metagenomics next-generation sequencing; RBC, red blood cell; WBC, white blood cell.

### Table 1. Results of Blood Testing, CSF Assay, and m-NGS

| Items                        | Day 0 | Day 5 | Normal Value |
|------------------------------|-------|-------|--------------|
| **Blood testing**            |       |       |              |
| WBC (x10^9/L)                | 6.5   | 27.2  | 4.3–14.2     |
| Lymphocyte (x10^9/L)         | 2.16  | 8.89  | 2.4–9.5      |
| Neutrophil (x10^9/L)         | 3.59  | 14.55 | 0.6–7.5      |
| CRP (mg/L)                   | 15.7  | 21.2  | 0–8          |
| **CSF assay**                |       |       |              |
| Appearance                   | Red   | Colorless, clear | Colorless, clear |
| Protein qualitative          | Positive | Negative | Negative |
| RBC, cells per mm^3          | 17,000 (fresh RBCs) | 420 (fresh RBCs) | 0–1 |
| WBC, types, cells per mm^3   | 34 (polymorphs, 61.0%; lymphocytes, 30.0%; monocytes, 9.0%) | 0 | 0–15 |
| Glucose, mmol/L              | 5.30  | 5.50  | 2.8–4.5      |
| Protein, mg/L                | 1190.0| 1250.0| 80–430       |
| Chloride, mmol/L             | 124.0 | 129.0 | 120–130      |
| LDH, U/L                     | 62    | 25    | 5–35         |
| Bacterial culture            | Negative | Negative | Negative |
| Pathogen smear               | Negative | Negative | Negative |
| **m-NGS**                    |       |       |              |
| Blood (species/reads count)  | Bordetella pertussis; 620 |
| CSF (species/reads count)    | Bordetella pertussis; 210 |

Abbreviations: CRP, C-reactive protein; CSF, cerebrospinal fluid; LDH, lactate dehydrogenase; m-NGS, metagenomics next-generation sequencing; RBC, red blood cell; WBC, white blood cell.

### DISCUSSION

Pertussis has long been considered to be a toxin-mediated disease because it occurs without fever or other evidence of inflammatory illness, and histopathologic changes of the upper respiratory tract of patients with fatal pertussis are often relatively normal unless there is a secondary bacterial infection [2]. However, the exact pathogenesis involved in pertussis severity remains poorly understood [3]. It is currently believed that *B. pertussis* adheres to the airways and releases a series of toxins, including pertussis toxin (PT), adenylate cyclase toxin, dermonecrotic toxin, filamentous hemagglutinin, and fimbriae. The predominant toxin is PT, which inhibits signaling through a subset of G protein-coupled receptors in mammalian cells, leading to leukocytosis with lymphocytosis linked with severe and lethal pertussis disease [4, 5].

*Bordetella pertussis* colonizes the epithelial cells of the human respiratory tract and is usually isolated from the nasopharynx. Invasive infection caused by *B. pertussis* has rarely been reported thus far, with only 4 cases of *B. pertussis* bacteremia in adult patients with immunocompromised diseases (1 had granulomatosis with polyangiitis, 2 had multiple myeloma, and 1 had human immunodeficiency virus infection) [6]. All patients suffered from paroxysmal cough and presented clinical manifestations of pneumonia. *Bordetella pertussis* in nasopharyngeal specimens, BALF, or lung biopsy samples was detected by PCR, and bacteremia was confirmed by a positive blood culture of *B. pertussis* [6]. In our reported case, *B. pertussis* was first observed in the patient’s nasopharyngeal specimen by targeted multiplex real-time PCR and was further detected in blood and CSF by m-NGS. To our knowledge, there are currently no reports of *B. pertussis* being detected in either blood or
cerebrospinal fluid. In this case, no pathogenic bacteria were found in blood or cerebrospinal fluid cultures, which may be related to the use of antibiotics before admission, whereas m-NGS is less affected by prior antibiotic exposure.

As an unbiased and comprehensive method for the detection and taxonomic characterization of microorganisms, m-NGS has become an attractive strategy in the detection of pathogens in the last decade. Numerous studies have demonstrated the success of m-NGS in the diagnosis and tracking of infectious diseases. However, limitations of m-NGS, such as sensitivity, interpretation, antimicrobial susceptibility, laboratory workflow, and cost, are barriers for its application in clinical practice [7]. Thus, clinicians should understand both the benefits and limitations of m-NGS when applying it to clinical practice.

CONCLUSIONS

Pediatricians should be aware of invasive *B pertussis* infection in children with severe pertussis.

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