

Case Report

Meningitis and bacteremia caused by *Haemophilus influenzae* Type e in an immunocompetent child

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Abstract

Haemophilus influenzae infection is a well-known cause of severe invasive disease in adults and children. But the incidence of the common serotypes is type b, f, and a. There is very little information on the invasive disease of *Haemophilus influenzae* type e (Hie) in China, especially in children. We report a case of an immunocompetent child with a clinical diagnosis of bacterial meningitis and bacteremia caused by Hie. The literature on infection, especially meningitis caused by Hie, is reviewed.

Key words: *Haemophilus influenzae* type e; invasive disease; bacterial meningitis.

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Introduction

Some recent reports of invasive *Haemophilus influenzae* disease in children and the elderly have shown that *Haemophilus influenzae* can cause pneumonia, meningitis, septicemia, septic arthritis, genitourinary infections, and endocarditis. [1]. Based on the research of polysaccharide capsule antigens, *H. influenzae* strains can be classified as encapsulated (denoted serotypes a–f) and unencapsulated (NTHi). Serotype b (Hib) is the most common strain of *H. influenzae*, causing 95% of severe invasive diseases, especially in children [2]. With the introduction of Hib conjugate vaccines, the threat of invasive Hib infection among children has dramatically decreased in many countries, regardless of development level or economic status [3]. Unfortunately, the incidence of invasive disease caused by non-Hib serotypes, which are not cross-protected by the Hib vaccine, has increased in recent decades [4,5]. Hif and Hia are the most common non-b strains in some countries [6].

Little knowledge is available concerning the epidemiological, microbiological, and clinical significance of Hie. Limited Hie infection has been obtained from reports of sporadic clinical cases of meningitis, pneumonia, peritoneal infection, and bacteremia [7]. To our knowledge, reports regarding the invasive disease of Hie are negligible in China, especially in children. We report a case of an immunocompetent child who was clinically diagnosed

with bacterial meningitis with bacteremia caused by *H. influenzae*. The serotype of *H. influenzae* was identified, and the importance of monitoring non-vaccine-preventable *H. influenzae* strains for effective surveillance of invasive *H. influenzae* disease was discussed.

Case Report

The patient was an 11-year-old boy with hearing loss that presented to a local hospital with fever and headache. He was subsequently admitted to Children Hospital, Shanxi, China, on November 11, 2018, with a four-day history of fever, headache, frequent vomiting, and refusal of food. He had no history of rash, allergy, trauma, blood transfusion, or contact with animals.

Initially, on examination, he was febrile (temperature of 41 °C) with tachypnea, weakness, and photophobia. Physical examination revealed a heart rate with 92 beats/min sinus rhythm and a respiratory rate of 24 breaths/min. Brudzinski's sign was positive. The remainder of the physical examination findings, including the fundus, was unremarkable. The patient was empirically started on intravenous cefotaxime and vancomycin. Blood routine test (BRT) and routine examinations of cerebrospinal fluid were conducted in our hospital (Table 1).

BRT and routine examination of CSF were conducted in our hospital (Table 1). The examination of CSF revealed 6.0351×10^{10} leukocytes/L (85%

neutrophils), 2.7 g/L of protein, 0.29 mmol/L of glucose and 12.97 mmol/L of lactate. The results of CSF routine examination also support the conjecture of bacterial meningitis. The renal and liver function tests were normal; levels of serum calcium, troponin T, immunoglobulins, and total complement were within normal limits; and the computed tomography of the head was normal. On the day of admission, a CT scan of the head revealed unremarkable.

The day after hospital admission, the presence of *H. influenzae* was confirmed in blood and CSF cultures. *H. influenzae* isolate was serotyped as type e using the slide agglutination method with polyclonal serotype-specific antisera (BD, New Jersey USA). Real-time polymerase chain reaction (RT-PCR) was performed for confirmation. Using the nitrocefin disc method, *H. influenzae* isolate was found to be β -lactamase producing, ampicillin-resistant. Vancomycin was stopped after culture results arrived. Anti-infection therapy (cefotaxime, 4g/day) was continued following the sensitivity results (β -lactamase producing, ampicillin-resistant, but susceptible to other tested antimicrobial drug (cefotaxime, ceftriaxone, meropenem, levofloxacin, azithromycin, etc.), and dexamethasone (20 mg/day for three days) was simultaneously administered intravenously.

A favorable clinical outcome without sequelae was achieved, and laboratory results returned to normal after 21 days of antibiotic therapy. The patient was discharged home without sequelae. No

neurodevelopmental disabilities were detected in the six-month follow-up.

Discussion

Recently, there has been an increase in reports of invasive disease caused by non-type b *H. influenzae* in both adults and children [8]. The most common serotypes have been serotype f and NTHi. Interestingly, the distribution of non-b invasive demonstrates geographic variations [9]. Hia meningitis has been reported mainly in Canada, the United States, and Australia. Hif has been mainly distributed in Brazil and England, while Hie has been distributed primarily on England, Italy, and Spain [7,10,11]. To the best of our knowledge, infection with non-type b *H. influenzae* has been very limited in China in recent years, although non-type b *H. influenzae* is a significant cause of invasive infection in other parts of the world [10]. In contrast to disorders in childhood, invasive Hie infections in adults usually occur in individuals with an underlying disease [11]. We encountered a case of bacterial meningitis with bacteremia due to Hie in an immunocompetent child.

The clinical symptoms of the patient showed relatively stable when he was admitted to our hospital. This observation is less like a study showing that Hie appears to cause more severe clinical disease and poor infection-attributable outcomes by evaluating invasive infection with Hie and Hif among children in England [11]. Thus, even in the post-Hib conjugated vaccine era,

Table 1. Results of sequential laboratory tests during the clinical course of *H. influenzae* meningitis in a child admitted to Children Hospital in Shanxi, China.

Test type	Hospitalization day					Reference range	
	1		2	7	14		21
	Adm	Adm+12h					
Blood							
Leukocytes, $\times 10^9$ cells/L	14.3	12.26		13.18		9.01	$3.5-9.5 \times 10^9$
Neutrophils %□	94.3	88.8		77.0		75.0	40-75%
Lymphocytes, $\times 10^9$ cells/L	0.46	0.59		2.39		1.53	$1.1-3.2 \times 10^9$
Platelets, $\times 10^9$ cells/L	268	219		345		332	$100-300 \times 10^9$
Hemoglobin, g/L		130		138		140	110-140 g/L
CRP, mg/L	> 200	> 200		36.12		13.11	0-10 mg/L
PCT, ng/mL		6.80		0.62		<0.05	< 0.05 ng/mL
Blood culture		Hie					
CSF							
Leukocytes, 10^6 cells/L			60,351		96	121	
Neutrophils, %			85		2	3	
Lymphocytes, %			15		98	97	
Protein, g/L			2.7		0.3	0.22	0.15-0.45 g/L
Glucose, mmol/L			0.29		2.44	2.63	2.8-4.5 mmol/L
PCT, ng/mL			6.06		< 0.05		
Gram stain			NM		NM	NM	
Culture			Hie		NG	NG	

* Adm: at admission (previous hospital); Adm + 12h: 12 hours after admission; CRP: C-reactive protein; CSF: cerebrospinal fluid; Hie: *Haemophilus Influenzae* type e; NA: not applicable; NG: no growth; NM: no microorganisms.

physicians should consider other *H. influenzae* serotypes, including non-typeable serotypes, when encountering patients with severe/moderate infections, such as bacterial meningitis.

As shown in Table 1, inflammatory parameters slightly decreased in the first 12 hours after admission. These results may be related to the use of antibiotics. In this case, although the patient's symptoms were moderately severe, the infection was quickly brought under control, and he gradually recovered fully after hospitalization. This outcome was due to the correct prediction of pathogens and the use of effective antibiotics. Thus, effective empiric therapy is essential for the treatment and prognosis of patients. The antibiotic resistance of non-b types of *H. influenzae* is a matter of concern and is vital in guiding empirical therapy.

Previous studies [12,13] have shown that Non-type b *H. influenzae* infection is associated with significant morbidity in the pediatric population. The knowledge of non-type b *H. influenzae* as an important pathogen in the pediatric population is constantly improving. The contribution of non-type b *H. influenzae* to invasive disease in children is not well understood. In this paper, we report our case of invasive *H. influenzae* type e infection whose clinical and drug resistance features may provide some valuable information for Hie invasive disease. We want to emphasize that extensive monitoring of the circulating non-vaccine-preventable strains is crucial for an effective surveillance of invasive *H. influenzae* disease.

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