

Case Report

***Haemophilus influenzae* serotype e meningitis in an adult**

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Abstract

The incidence of *Haemophilus influenzae* type b (Hib) invasive disease has declined significantly in countries with routine infant Hib immunization. Accordingly, infections caused by other *H. influenzae* serotypes or by encapsulated *H. influenzae* strains are of growing interest. *H. influenzae* serotype e (Hie) is a rare cause of infection. Invasive Hie infections reported in adults are generally in individuals who had previous underlying conditions, in contrast to infections in childhood. We present the first report of Hie meningitis in Turkey. It is of interest that meningitis due to this organism occurred as a complication of transsphenoidal hypophysectomy, which to our knowledge has never been documented. Further identification of *H. influenzae* strains isolated from patients with invasive disease, especially those with predisposing factors and/or who have been vaccinated, is essential.

Key words: *H. influenzae* serotype e, meningitis, transsphenoidal hypophysectomy

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Introduction

Six antigenically and biochemically distinct capsular polysaccharide subtypes (a-f) of *H. influenzae* have been identified. Although, historically, type b encapsulated strains have been of primary clinical and immunologic importance because of their association with invasive infection, including meningitis, the other encapsulated strains can also cause invasive disease [1]. We report a case of Hie meningitis complicating transsphenoidal hypophysectomy.

Case Report

A 24-year-old female presented to the emergency department with fever, severe headache, nausea and vomiting. Medical history revealed that she had undergone a transsphenoidal hypophysectomy operation one week prior to presentation. On physical examination, the findings were as follows: temperature, 39 °C; blood pressure, 120/90 mmHg; pulse rate, 110/minute. Alteration of consciousness and neck stiffness were found, and Kernig's and Brudzinski's signs were positive. Results of laboratory investigations were as follows: WBC count: 17,700/mm³ with 73% bands; platelet count: 503,000; and biochemical tests were normal. All four of the blood cultures obtained showed no growth.

Cerebrospinal fluid (CSF) examination revealed the following: leucocyte count 700/mm³; protein 300 mg/dL; glucose 25 mg/dL (simultaneous blood glucose level was 130mg/dl); and high CSF pressure.

Intravenous vancomycin (500mg every 6 hours) and meropenem (2g every 8 hours) were commenced as drugs of choice for empirical therapy of suspected post-operative meningitis. A Gram negative coccobacillus was isolated from the CSF cultures and the organism exhibited typical characteristics of *H. influenzae* by traditional identification methods. Identification was confirmed by API NH (Biomérieux, Marcy l'Etoile, France) as *H. influenzae*. To identify the biotype and serotype, a chocolate agar plate was sent to the *Haemophilus* National Reference Laboratory (HNRL) of Refik Saydam National Hygiene Center, Turkey. For biotyping, the urease, spot indole and ornithine decarboxylase tests were performed. Urease positivity, indole and ornithine decarboxylase negativity showed that the *H. influenzae* isolate was biotype III. A slide agglutination test (Difco Laboratories, Detroit, USA) using monoclonal sera for types a, b, c, d, e, f was performed to determine the serotype of the isolate. The findings showed that the isolate was type e and the organism was finally identified as *H. influenzae* serotype e biotype III.

Antibiogram-susceptibility testing results of the isolate revealed no resistance to ampicillin, cefotaxime, ciprofloxacin or chloramphenicol. Computerized tomograms demonstrated air and soft tissue density in the sellar plane. On the second day of treatment, the patient was afebrile and her mental function had improved. On the fifth day, therapy was changed to intravenous ceftriaxone (2 g every 12 hours) in keeping with the antibiotic susceptibility report. After two weeks of parenteral antibiotic therapy, the patient showed full recovery and was discharged.

Discussion

H. influenzae is a small (1µm x 0.3µm), pleomorphic, Gram negative coccobacillus. Six serotypes, designated a to f, are based on antigenically distinct capsular polysaccharide types. Hib is the most virulent organism and it causes approximately 95% of serious *H. influenzae* systemic infections. The rate of nasopharyngeal colonization as well as the invasive disease due to this organism has dramatically decreased with the use of conjugate vaccines in many countries [1]. However, other capsulated non Hib serotypes have been reported to cause invasive diseases such as bacteremia, meningitis, pneumonia, and cellulitis [2-11].

Invasive infections due to Hie presented as sporadic cases in most reports [2, 6-11]. Clinical and epidemiological features of Hie infections strikingly resemble those associated with invasive Hib disease. According to the number of the published cases, meningitis due to non- Hib seems to be rare. In the majority of reports, infants were infected because they are more prone to invasive diseases and usually no predisposing factor is determined in this age group [6]. Al-Tawfiq reviewed 14 cases of Hie meningitis reported between 1976 and 2006 and showed that nine of the cases were in those younger than 16 years and a predisposing factor was determined in only one patient [9]. Because of the widespread coverage of routine immunization of children against Hib, reporting infections due to other serotypes and nontypable strains of *H. influenzae* has become more important in order to characterize the clinical and epidemiologic features of non-Hib disease in the Hib vaccine era.

In contrast to infections seen in childhood, the invasive Hie infections reported in adults are generally associated with previous underlying conditions. Five adult cases of invasive Hie diseases in Italy were described by Cerquetti *et al.* with

meningitis occurring in two patients and the majority of patients (4 of 5) having severe underlying conditions [12]. Campos *et al.* [3] described 26 cases of infection due to Hie that occurred in Spain after introduction of the Hib vaccination. The clinical presentation of all patients included cases of invasive and non-invasive disease. Only one patient presented with meningitis. The majority of cases occurred in patients aged older than 16 years and approximately half of the patients had previous underlying conditions [3]. These reports suggest that Hie is an opportunistic pathogen but the data do not indicate that the incidence of Hie colonization increased after introduction of the Hib vaccine [3,12].

In this report we present a case of Hie meningitis in an adult following transsphenoidal hypophysectomy. *H. influenzae* is not an expected cause of infection after neurosurgery; however, nasopharyngeal colonization of this organism can cause meningitis after a transsphenoidal procedure. Post-operative meningitis complicating transsphenoidal hypophysectomy is more likely if the defect produced in sella turcica is not adequately sealed [13]. In contrast to Hib-meningitis, infections with non-Hib mostly spread to meninges directly from a local focus [7]. We have reported the case of a Turkish woman with Hie meningitis, which is the first case reported from Turkey. While predisposing factors such as craniocerebral injury, cerebrospinal leaks, or ventriculoperitoneal shunts and respiratory infections have been reported before [7,12], it is of interest that, to our knowledge, this is the first report of Hie meningitis complicating transsphenoidal hypophysectomy.

Although not determined in our case, increasing ampicillin resistance in both beta lactamase positive and negative *H. influenzae* isolates are reported worldwide [2,3]. Ceftriaxone is the suggested regimen in the treatment of *H. influenzae* meningitis because of its potent bacteriocidal activity and penetration into the subarachnoid space. Only Hib serotypes have been reported as a cause of meningitis reported in Turkey [14], and as the clinical features and treatment regimen of *H. influenzae* infections are similar, serotyping of isolates is not routinely conducted. However, we recommend further identification and susceptibility tests of *H. influenzae* strains isolated from invasive disease of patients, especially those with predisposing factors and/or who have been vaccinated.

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