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HAEMOPHILUS INFLUENZAE MENINGITIS IN A ADULT: A RARE ETIOLOGY OF MENINGITIS – CASE REPORT

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ABSTRACT

Haemophilus influenzae is a gram-negative bacterium that commonly causes meningitis in children, rarely in adults, particularly in immunocompetent individuals. Most adult cases occur in those with predisposing conditions such as chronic diseases and immunosuppression. We describe a case of meningitis caused by *Haemophilus influenzae* in an immunocompetent 66-year-old male. The patient received treatment with ceftriaxone and he was discharged in good clinical condition, with no neurological deficits. *Haemophilus influenzae* meningitis in adults underscores the importance of considering this rare pathogen in the differential diagnosis of bacterial meningitis.

Keywords: *Haemophilus influenzae*, meningitis, lumbar puncture

INTRODUCTION

Haemophilus influenzae is a gram-negative bacterium that can cause a wide range of localized and invasive infections in humans, such as epiglottitis, pneumonia, septicemia, and meningitis.[1] Historically *H. influenzae* used to be the most common cause of bacterial meningitis, and primarily a disease of infants and young children.[2,3] With the introduction of the *H. influenzae* type B (*Hib*) vaccine in the late 1980s, the incidence of Hib-related diseases significantly declined, especially in pediatric populations. However, invasive *H. influenzae* infections in adults, particularly meningitis, remain rare and often occur in individuals with predisposing factors such as immunosuppression, recent head trauma, or cerebrospinal fluid leaks.[4] Patients ≥ 65 years of age with invasive *H. influenzae* disease have higher case-fatality ratios than children. [5] Up to 20% of patients who survive Hib-meningitis have long-term neurological sequelae, such as hearing loss. [6]

In this case report, we present an unusual case of *H. influenzae* meningitis in an adult male with hypertension but no other apparent risk factors. We discuss the clinical presentation, diagnostic process, and successful management of the case, underlining the importance of early recognition and the role of polymerase chain reaction (PCR) in confirming the diagnosis. This case underscores the need for vigilance in identifying rare etiologies of meningitis and demonstrates the critical impact of timely intervention on patient outcomes.

CASE REPORT

A 66-year-old male with poorly controlled hypertension presented to the emergency department with a 2-day history of headache followed by fever and vomiting. The patient's family reported that his symptoms had worsened rapidly over the past 24 hours, leading to difficult speaking and decreased responsiveness. He had no history of Hib vaccination and no known immunosuppressive therapy.

After a neurological examination that revealed positive meningeal signs, and a CT scan, which excluded acute neurological disorder a suspicion for meningitis was set. Further testings for definitive diagnosis and infection identification followed.

On a day of admission in our clinic, he had a high fever (39°C) and he was confused, disoriented, with positive meningeal signs. His vital signs included blood pressure of 154/90mmHg, respiratory rate of 17 breaths/min, and pulse rate of 109 beats/min. The remainder of the systemic examination was unremarkable.

Results of the initial laboratory studies were as follows results: leucocytosis $14,9 \times 10^9/L$ (ref.ranges $4.0 - 10.0 \times 10^9/L$) with a domination of polymorphonuclear leucocytes, erythrocyte sedimentation rate 90 mm/h, and C-reactive protein 131 mg/L (ref.ranges 0 – 10 mg/L), the rest of his serum biochemistry values were normal.

A lumbar puncture was performed, and cerebrospinal fluid (CSF) analysis revealed: pleocytosis of 7594 cells/mm³ (90% polymorphonuclear), elevated protein level (14.30 g/L), and low CSF glucose level (1.0 mmol/L) at glycemia 7.3mmol/L (Table 1). Because an initial diagnosis of bacterial meningitis was made, the patient was immediately started on empiric intravenous antibiotics, including ceftriaxone and vancomycin. *Haemophilus influenzae* was detected from cerebrospinal fluid by molecular method (PCR) and the culture was negative thus vancomycin was discontinued, and monotherapy with ceftriaxone continued for a total of 14 days. Dexamethasone was also administered for 4 days. The patient responded well to treatment, the fever resolved, and he gradually regained full orientation. A second and third lumbar puncture were performed on the 3th and 14th hospital day and the cerebrospinal fluid findings improved significantly. The patient was discharged in good clinical condition, with no neurological deficits and normal cerebrospinal fluid results. (Table 1)

Data/Indicators	Day 1	Day 3	Day 14
CSF	Cloudy	Cloudy	Clear
Pandy	+	+	-
Leucocytes/mm ³	7594	406	15
Polymorphonuclear %	90	80	-
Protein g/L	14,3	2.85	0,50
Glycose mmol/L	1.0	2.5	2.3
Lactate mmol/L	13.62	5.03	2.17
Culture	Negative	Negative	Negative
PCR CSF	H.influenzae	-	-

At a follow up visit one month later, the patient remained symptom free, with no evidence of long-term cognitive impairment or relapse of infection.

DISCUSSION

Haemophilus influenzae type B (*Hib*) was once a leading cause of bacterial meningitis in children prior to the widespread adoption of Hib vaccination. However, its incidence in adults remains rare, accounting for only a small fraction of bacterial meningitis cases. This case is particularly noteworthy as it occurred in an otherwise immunocompetent adult with hypertension, a condition not typically associated with increased susceptibility to *H. influenzae* infections.

Adult-onset *H. influenzae* meningitis often presents similarly to other bacterial meningitis etiologies, with symptoms including headache, fever, neck stiffness, and altered mental status. [7] The overlap in clinical presentation underscores the need for comprehensive diagnostic evaluation. While Gram stain and cultures are traditional diagnostic tools, they may fail to identify the pathogen, as seen in this case. Molecular diagnostics, particularly PCR, have proven indispensable in such scenarios due to their speed, high sensitivity and specificity.[8]

Treatment of *H. influenzae* meningitis involves prompt administration of third-generation cephalosporins, such as ceftriaxone or cefotaxime. [9]. In this case, the patient responded well to 14 days of intravenous ceftriaxone, with no residual neurological deficits.

This case emphasizes several critical points: the utility of PCR in identifying rare pathogens when conventional methods fail, the importance of early empiric antibiotic therapy in bacterial meningitis, and the role of vigilant clinical monitoring and management of comorbidities. Continued surveillance and research into adult cases of *H. influenzae* meningitis are necessary to better understand risk factors, optimal diagnostic strategies, and treatment protocols for this uncommon but potentially life-threatening condition.

CONCLUSION

Haemophilus influenzae meningitis in adults underscores the importance of considering this rare pathogen in the differential diagnosis of bacterial meningitis. Early diagnosis and prompt initiation of appropriate antibiotic therapy remains essential for successful outcome. PCR was essential in diagnosing this case, underscoring the value of molecular diagnostics in identifying pathogens when traditional methods are inconclusive. Hib vaccination should be considered in adults with risk factors to prevent such rare but serious infections.

REFERENCES:

1. van de Beek D, Brouwer M, Hasbun R, Koedel U, Whitney CG, Wijdicks E. Community-acquired bacterial meningitis. *Nat Rev Dis Primers*. 2016 Nov 3;2:16074. doi: 10.1038/nrdp.2016.74.
2. Brouwer MC, Tunkel AR, van de Beek D. Epidemiology, diagnosis, and antimicrobial treatment of acute bacterial meningitis. *Clin Microbiol Rev*. 2010 Jul;23(3):467-92. doi: 10.1128/CMR.00070-09.
3. Schuchat A, Robinson K, Wenger JD, Harrison LH, Farley M, Reingold AL, Lefkowitz L, Perkins BA. Bacterial meningitis in the United States in 1995. Active Surveillance Team. *N Engl J Med*. 1997 Oct 2;337(14):970-6. doi: 10.1056/NEJM199710023371404.
4. Chekrouni N, Koelman DLH, Brouwer MC, van der Ende A, van de Beek D. Community-acquired *Haemophilus influenzae* meningitis in adults. *J Infect*. 2021 May;82(5):145-150. doi: 10.1016/j.jinf.2021.03.016. Epub 2021 Mar 25. PMID: 33774020.
5. MacNeil JR, Cohn AC, Farley M, Mair R, Baumbach J, Bennett N, Gershman K, Harrison LH, Lynfield R, Petit S, Reingold A, Schaffner W, Thomas A, Coronado F, Zell ER, Mayer LW, Clark TA, Messonnier NE. Current epidemiology and trends in invasive *Haemophilus influenzae* disease--United States, 1989-2008. *Clin Infect Dis*. 2011 Dec;53(12):1230-6. doi: 10.1093/cid/cir735. PMID: 22080119.
6. Center for Disease Control and Prevention, Atlanta, Georgia. Available at: <https://www.cdc.gov/hi-disease/clinicians.html>. August 21, 2024
7. Domingo P, Pomar V, de Benito N, Coll P. The spectrum of acute bacterial meningitis in elderly patients. *BMC Infect Dis*. 2013 Feb 27;13:108. doi: 10.1186/1471-2334-13-108.
8. Liu Q, Jin X, Cheng J, Zhou H, Zhang Y, Dai Y. Advances in the application of molecular diagnostic techniques for the detection of infectious disease pathogens (Review). *Mol Med Rep*. 2023 May;27(5):104. doi: 10.3892/mmr.2023.12991. Epub 2023 Apr 7.
9. Tunkel AR, Hartman BJ, Kaplan SL, Kaufman BA, Roos KL, Scheld WM, Whitley RJ. Practice guidelines for the management of bacterial meningitis. *Clin Infect Dis*. 2004 Nov 1;39(9):1267-84. doi: 10.1086/425368. Epub 2004 Oct 6. PMID: 15494903.