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Case report

# Haemophilus influenzae serotype a meningitis in an elderly patient: A case report and literature review

Harika Kalangi [a,*], Anjali Anne Ajit [a], Bernard Camins [b], Stanley R. Yancovitz [a]

[a] Department of Medicine, Division of Infectious Diseases, Mount Sinai Morningside/West/Beth-Israel, 1111 Amsterdam Ave, New York, NY 10025, USA
[b] Department of Medicine, Division of Infectious Diseases, Icahn School of Medicine at Mount Sinai, One Gustave Levy Place Box 1090, New York, NY 10029, USA

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ABSTRACT

*Haemophilus influenzae* is a gram-negative bacterium that encompasses a diverse group of strains with varying pathogenic potentials. Classified into six serotypes (a-f), it has been historically associated with a range of infections, including respiratory tract infections, bacteremia, meningitis, and others. Of particular significance is *H. influenzae* type b (Hib), which was a leading cause of invasive diseases in children prior to the introduction of the Hib vaccine. The Hib vaccine has revolutionized the prevention of severe bacterial infections and has drastically reduced the incidence of Hib. *Haemophilus influenzae* serotype a (Hia) has now emerged as a significant contributor to bacterial meningitis leading to morbidity and mortality. It remains a notable concern among elderly patients, despite its historical association with children. This shift in demographic susceptibility is accompanied by distinct clinical characteristics and challenges in diagnosis. Here we report a case of Hia meningitis and bacteremia in a previously healthy elderly patient, who responded to ceftriaxone treatment. Efforts to address the global burden of Hia meningitis include robust surveillance and potential vaccine development, aiming to mitigate its impact on vulnerable populations.

## Introduction

*H. influenzae* is a group of gram-negative bacteria that encompasses a spectrum of serotypes with varying clinical significance. These serotypes are classified based on their distinct capsule antigens, denoted alphabetically from a to f [1]. Historically, Hib has been associated with invasive diseases such as meningitis and sepsis, primarily affecting infants and young children. Vaccination efforts targeting Hib have led to remarkable reductions in associated morbidity and mortality.

Post-Hib vaccine era epidemiology has changed significantly in the United States and other serotypes. Since 2008, the non-b serotypes like Hia have gained attention as they are now associated with significant morbidity and mortality, particularly in certain populations [2–4].

Certain groups, such as infants and the elderly over 65 years with comorbidities like heavy alcohol use, diabetes, hypertension, smoking, and chronic obstructive pulmonary disease may be more susceptible to severe infections caused by Hia. With increasing age, the prevalence and severity of invasive Hia in older adults increases but may be less severe if treated early [5].

Hia colonization typically begins in the upper respiratory tract, including the nasopharynx, where the bacteria can adhere to mucosal surfaces and evade immune responses. It is associated with Hib-like invasive diseases that range from localized infections to severe systemic illnesses including meningitis, pneumonia, septic arthritis, osteomyelitis, and bacteremia [6].

Hib vaccines do not provide cross-protective immunity against other serotypes. Research into the epidemiology, virulence factors, and treatment strategies for Hia-related invasive diseases continues to evolve. A comprehensive understanding of these factors is essential for guiding public health efforts, improving clinical outcomes, and reducing the global burden of invasive diseases caused by Hia.

Herein we report a case of Hia meningitis in an elderly patient who was successfully treated with a 14-day regimen of ceftriaxone.

## Case presentation

Our patient is a 71-year-old, elderly female with no significant past medical history. She is an ex- smoker and has had seasonal allergies for the past 30 years. She presented to the emergency department with complaints of nausea, vomiting, presyncope and inability to walk. One

* Correspondence to: Mount Sinai Morningside-West Hospital Center, Icahn School of Medicine at Mount Sinai, 440 West 114th Street, New York, NY 10025, USA.
*E-mail addresses:* harikakalangi1693@gmail.com, harika.kalangi@mountsinai.org (H. Kalangi), anjalianne.ajit@mountsinai.org (A.A. Ajit), bernard.camins@mountsinai.org (B. Camins), stanley.yancovitz@mountsinai.org (S.R. Yancovitz).

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week prior, she was in her normal state of health. The patient is a retired second-grade teacher and only reported nasal congestion and sinusitis a week before her hospitalization.

In the emergency department, the patient was alert, oriented and in no respiratory distress. She was afebrile, hypotensive, and quickly responded to intravenous fluids.

A physical examination showed no evidence of nuchal rigidity or focal neurological deficits. The patient's cardiovascular and respiratory function were unremarkable. There were no signs of macular rash or petechial rash.

The patient underwent initial labs outlined in Table 1. The rest of the labs were within normal limits.

A Chest radiograph showed no focal consolidation. Contrast enhanced computed tomography (CT) scan of the brain was negative for any signs of bleeding or edema.

On day two of hospital admission, the leukocytosis increased (22 K/uL) and her platelet count decreased 109 K/uL. She was more lethargic, irritable, and physical examination now revealed nuchal rigidity and photophobia. Blood cultures were drawn, and ceftriaxone, vancomycin, ampicillin, and acyclovir were administered. A lumbar puncture procedure was performed and revealed a cloudy cerebrospinal fluid (CSF) with an opening pressure of 32 cm of water. The results of the CSF analysis are shown in Table 2.

CSF Gram stain was negative and bacterial cultures were no growth. CSF meningitis/encephalitis panel polymerase chain reaction (PCR) detected *Haemophilus influenzae*.

The initial blood cultures now confirmed growth of *Haemophilus influenzae* serotype a which was susceptible to all tested antibiotics (Table 3).

The repeat blood cultures showed negative results. She continued ceftriaxone and the remaining antimicrobials were stopped. Dexamethasone was also added for 48 hrs. Clinically, the patient was stable with a declining white count. Ceftriaxone was administered for 14 days to the patient. The patient experienced overall clinical improvement and was discharged home without any neurological sequelae.

## Discussion

Hia disease has been increasing in incidence in US as well as in other countries, including Canada, Brazil, Australia, and some European countries [2,3]. The highest rates of invasive Hia have been observed in indigenous populations like North American Indians and Alaskan native children. These rates are comparable to the pre-Hib vaccine era. Asymptomatic colonization can play a role in transmission, contributing to its persistence in these communities [4].

Hia has emerged as a notable pathogen causing invasive diseases, particularly among the elderly population. While it has historically been associated with infections in younger individuals, recent observations suggest a shifting demographic susceptibility associated with increased mortality, highlighting the importance of understanding its impact on older adults [5].

Invasive diseases caused by Hia encompass a spectrum of illnesses, including meningitis, bacteremia, and sepsis [6].

As the age increases, both the incidence and case fatality rates increase significantly. Most elderly patients have an underlying condition, such as diabetes, coronary artery disease, smoking, or chronic obstructive sleep disorder. It is not clear whether these conditions are a risk factor for invasive disease, or if they are simply coexisting [5,7].

Hia meningitis cannot be easily distinguishable from other bacterial causes and diagnosing Hia invasive disease in the elderly presents challenges due to the overlapping clinical features with other age-related conditions [8]. Delays in diagnosis are not uncommon, potentially leading to more severe outcomes.

Today there is no strategy to prevent Hia and the Hib conjugate vaccine does not cross-protect against serotype a [9]. The lack of a specific vaccine for Hia compounds the concern for the elderly population. The focus on other serotypes, like Hib, has left a gap in protection against Hia-related diseases. As the global population ages, strategies to address the burden of Hia invasive disease in the elderly become increasingly important. This could include increased surveillance, early diagnosis protocols, and research into potential vaccines targeting Hia [10].

Our patient received a favorable prognosis due to early diagnosis and treatment. This disease can be controlled by timely administration of antibiotics and collection of blood samples. Ceftriaxone should be used for patients with systemic infections such as meningitis or bacteremia. Dexamethasone can serve as an invaluable adjunctive treatment, alleviating cerebral edema associated with inflammation of the meninges while simultaneously decreasing complications such as hearing loss or neurological sequelae [11]. After hospital discharge, patients may require follow-up appointments to monitor their recovery and ensure

**Table 1**
Admission laboratory findings.

| Component | Lab Results | Ref Range & Units |
|---|---|---|
| WBC | 15 | 4.5 - 11.0 K/uL |
| RBC COUNT | 4.46 | 3.70 - 5.50 M/uL |
| HGB | 11.7 | 11.7 - 15.0 g/dL |
| HCT | 38.6 | 34.0 - 47.0 % |
| MCV | 86.7 | 79.0 - 98.0 fL |
| Platelets | 119 | 150 - 450 K/uL |
| BUN | 50 | 6 - 23 mg/dL |
| CREATININE | 1.73 | 0.5 - 1.1 mg/dL |
| SODIUM | 134 | 135 - 145 mmol/L |
| POTASSIUM | 2.9 | 3.5 - 5.2 mmol/L |
| CHLORIDE | 103 | 96 - 108 mmol/L |
| CO2 | 18.0 | 22.0 - 30.0 mmol/L |
| ANION GAP | 13 | 7 - 16 mmoL/L |
| EST GFR | 31 | > 59 ml/min/1.73m2 |

WBC: white blood cells, RBC: red blood cells, HGB: hemoglobin, HCT: hematocrit, MCV: mean corpuscular volume, BUN: blood urea nitrogen, CO2: carbon dioxide, EST GFR: estimated glomerular filtration rate.

**Table 2**
Cerebrospinal Fluid Results.

| Component | CSF results | Ref range & units |
|---|---|---|
| WBC, CSF | 1823 (High) | 0 - 5 /uL |
| RBC, CSF | 390 | /uL |
| NEUTROPHILS, CSF | 75 | % |
| LYMPHOCYTES, CSF | 15 | % |
| MONOCYTOID, CSF | 10 | % |
| COLOR, CSF | Colorless | |
| XANTHOCHROMIA | Negative | |
| APPEARANCE, CSF | Hazy | |
| PROTEIN, CSF | 221.0 | 15.0 - 45.0 mg/dL |
| GLUCOSE, CSF | 7 | 40 - 70 mg/dL |
| Culture, CSF | No growth after 5 days | |

WBC: white blood cells, RBC: red blood cells,

**Table 3**
Blood cultures.

| | |
|---|---|
| Culture | ***Haemophilus influenzae*:** Identification confirmed by MALDI-TOF MS.<br>Method is FDA cleared for clinical testing. BETA LACTAMASE NEGATIVE<br>*Haemophilus influenzae* group A<br>Gram stain: Gram negative bacilli in aerobic bottle after 13 h of incubation. |
| ***Susceptibility*** | *Haemophilus influenzae* |
| Ampicillin | 0.50 Susceptible |
| Ciprofloxacin | 0.094 Susceptible |
| Piperacillin/Tazo | < =2 Susceptible |
| Trimethoprim/ Sulfa | < =0.064 Susceptible |

that the infection has been successfully treated. Neurological sequelae and potential complications may also be assessed during these visits.

It is possible that our patient, who was caring for young children, may have been exposed to Hia and developed invasive disease due to simple upper respiratory infection like sinusitis, otitis, or even nasopharyngeal colonization. In such cases, it can be difficult to pinpoint the source of the infection, especially for elderly patients [12]. Enhanced awareness among healthcare professionals about the changing epidemiology of Hia and its potential to cause severe infections in the elderly is essential for timely recognition and management. Efforts to address Hia global epidemiology must encompass robust surveillance systems, molecular typing methods, and comprehensive data collection [13]. International collaboration is pivotal in understanding the global burden of Hia and devising strategies to mitigate its impact. The absence of vaccination highlights the need for future research to guide potential vaccine development efforts.

## Conclusion

While historically overshadowed by other serotypes like Hib, Hia has gained attention due to its potential to cause significant morbidity and mortality, particularly in certain populations. Hia meningitis is uncommon and remains a notable concern among elderly patients marked by increased severity, complications, and mortality rates. Emerging research sheds light on the evolving epidemiology and increasing incidence of Hia, underscoring the need for better epidemiological surveillance and tailored preventive strategies. As part of ongoing research, the emergence and clinical significance of Hia invasive diseases continue to be explored, guiding public health efforts and potential vaccine development.

## Ethics approval and consent to participate

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## CRediT authorship contribution statement

**Anjali Anne Ajit:** Conceptualization, Data curation, Writing – original draft. **Stanley R Yancovitz:** Supervision, Writing – review & editing. **Harika Kalangi:** Conceptualization, Data curation, Writing – original draft. **Bernard Camins:** Supervision, Writing – review & editing.

## Declaration of Competing Interest

The authors declare that they have no competing interests. This manuscript has not been published and is not under consideration for publication elsewhere. Additionally, all authors have approved this paper's contents and agreed to the journal's submission policies.

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### *Institutional Review Board Statement*

Not applicable.

### *Informed Consent Statement*

Informed consent was obtained from the patient involved in the study.

## Data availability

Because this manuscript is a case report there are no datasets, which could be freely available to use supporting the conclusions of this article.

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