Case Report

Non-typeable Haemophilus influenza ventriculitis, a case report and literature review

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ABSTRACT

Introduction: and importance: Haemophilus influenza severe presentations have decreased dramatically after the Hib vaccination was introduced. However, due to the emergence of Multi-drug resistance organisms, severe presentations like meningitis and ventriculitis may occur.

Case presentation: Here, we have described a rarely reported case of non-typeable Haemophilus influenza ventriculitis in a previously healthy patient. MRI of the head with contrast was suggestive of tiny foci of diffusion restriction in occipital horns of bilateral ventricles with minimal intraventricular pus formation. The diagnosis was confirmed based on blood culture results and MRI findings as the patient refused to have a lumbar puncture procedure for CSF analysis. The patient was treated with intravenous antibiotics and showed a good response.

Clinical discussion: In the post-HiB immunization era, we have seen a decline in invasive diseases caused by Type B Haemophilus influenza. However, non-typeable Haemophilus influenza is now on the rise. Central nervous system infection due to non-typable Haemophilus influenza is infrequent as this organism is predominantly a respiratory mucosal pathogen resulting in acute and chronic respiratory tract infections. Multi-drug resistance of non-typeable Haemophilus influenzae is also becoming a cause of concern.

Conclusion: Ventriculitis secondary to non-typeable beta-lactamase non-producing, ampicillin-resistant (BLNAR) Haemophilus influenza is rare, and more such cases need to be reported within the adult population to avoid under-recognition.

1. Introduction

Haemophilus influenza is a common respiratory pathogen that is a gram-negative coccobacillus. It can be classified broadly based on its capsular polysaccharide composition into six different serotypes (a-f) and non-capsulated strains [1,2]. The most commonly reported presentations of Haemophilus influenza include involvement of the upper and lower respiratory tracts such as otitis media, sinusitis, and pneumonia. Severe manifestations could have meningitis, epiglottitis, septic arthritis, and bacteremia [2]. With the routine use of the HiB vaccine in national immunization programs worldwide, invasive disease due to Haemophilus influenza type B has reduced significantly [3]. However, non-typeable Haemophilus influenza has become a cause of concern, especially with the emergence of multdrug resistance to commonly used antibiotics [3,4].

In our case, we would like to describe a very rarely reported clinical presentation of Beta-Lactamase non-producing, ampicillin-resistant (BLNAR) non-typeable Haemophilus influenza in a previously healthy adult patient.

2. Case presentation

A previously healthy 21-year-old Turkish gentleman presented with acute onset of severe vomiting, diarrhea, abdominal pain, fever, and headache of 1-day duration. The patient reported having 20 episodes of greenish vomiting and dull epigastric pain radiating to the back that was not relieved by the vomiting and was associated with low-grade fever and loose stools without blood or mucus. There were no chills or rigors. The patient also had a pulsatile frontal headache for one day. On systemic review, the patient complained of having fatigue, generalized body aches, nasal congestion, and dry cough with no sputum production for a 1-day duration.

The patient has no significant past medical or surgical history but had a 10-pack year smoking history. He had a recent travel to Turkey 3 months back but had no exposure to birds, animals, or toxic fumes. Upon presentation, he was febrile (38.5°C), normotensive (109/54 mm of Hg),...
not tachypneic (20 breaths per minute), not tachycardiac (71 beats per minute), and maintained saturation on room air. He was conscious, alert, and oriented to time, place, and person. The patient had diffuse tenderness on deep palpation in the epigastic and umbilical areas. No rebound tenderness was present. Neurological examination was negative for meningeal signs, and the Glasgow coma scale (GCS) was 15/15. The rest of the examination was Unremarkable.

A working diagnosis of acute gastroenteritis was considered, and the patient was started on intravenous (IV) fluids, paracetamol, metoclopramide, ondansetron, and IV ciprofloxacin. Initial investigations showed neutrophilic leukocytosis (14.5 x10^3/μL) and elevated CRP (111.1 mg/L). Real-time reverse transcription-polymerase chain reaction (rRT-PCR) for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) was negative. Other laboratory investigations were Unremarkable. Sepsis workup, stool culture, and Clostridium difficile toxin were sent, which were negative (Table 1). Ultrasound abdomen was done to rule out acute cholecystitis and was Unremarkable.

Despite treatment, the patient continued spiked fever and vomited multiple times over the next two days, with worsening headache and back pain. Physical examination revealed neck stiffness and photophobia. A lumbar puncture was planned to rule out meningitis, but the patient firmly refused. His antibiotic was changed to IV ceftriaxone 2 g twice daily, and a new set of blood cultures, a viral panel, and a repeat COVID-19 rRT-PCR were sent. Human rhinovirus/enterovirus was positive from a nasal smear (Table 2). Magnetic resonance imaging of the head with contrast showed foci of diffusion restriction in the occipital horns of both lateral ventricles with a high signal on fluid-attenuated inversion recovery (FLAIR). The ventricular system was dilated without midline shift or mass effect. There was mucosal thickening of left ethmoidal air cells, left frontal and maxillary sinuses. These features were in keeping with ventriculitis and minimal intraventricular pus formation (Fig. 1).

The MDT concurred on a working diagnosis of ventriculitis secondary to non-typeable Hemophilus influenzae and recommended IV Ceftriaxone for 3–4 weeks in addition to performing repeat blood cultures. With the use of IV ceftriaxone patient became afebrile and his symptoms, including headache and vomiting, resolved. A repeated blood culture on day seven following treatment showed no growth. On day ten since admission, the Patient requested discharge against medical advice after acknowledging the risks. The initial plan was to switch the Patient to oral antibiotics on discharge as he refused to receive any further IV antibiotics. As per ID team recommendations, because oral antibiotics would not play any significant role in his case and the Patient firmly refused IV antibiotics, no antibiotics were prescribed upon discharge. He then traveled to his home country and was well before travel.

### 3. Discussion

Our case describes a previously healthy gentleman who developed ventriculitis secondary to non-typeable beta-lactamase non-producing, ampicillin-resistant (BLNAR) Haemophilus influenzae. Our literature search performed on 30th January 2022 showed that only one similar case has been reported by Holt et al. in which they described a case of a 46-year-old female with sickle cell disease who developed ventriculitis as a result of non-typeable Haemophilus influenzae [5]. Our case is unique in that our Patient did not have any comorbidities.

We have observed that invasive non-typeable Haemophilus influenzae is a better-explored topic within the pediatric age group. Bacteremia with pneumonia has been the most frequently reported presentation within this age group [6–8]. However, a case series conducted by Antony et al. revealed meningitis as a more prevalent cause of significant morbidity and mortality in previously healthy children under one year of age with no comorbidities [9]. We believe that more such cases must be reported within the adult population to determine the incidence, prevalence, and disease burden of neurological complications due to invasive non-typeable Haemophilus influenzae.

Despite being a common respiratory pathogen, non-typeable Hae-mophilus influenzae can reach the central nervous system by crossing the blood-brain barrier through the invasion of the choroid plexus cells, causing neurological complications like meningitis and ventriculitis [10]. Ventriculitis typically appears on MRI imaging as ventricular debris that is hyperintense to CSF on T1-weighted images and hypointense to CSF on T2-weighted images. Homogenous enhancement of the ependymal lining can also be seen with contrast imaging [11]. In our Patient, the diagnostic studies, in addition to a blood culture growth, allowed us to determine that ventriculitis likely developed due to Haemophilus influenzae.

The emergence of multidrug-resistant strains poses a challenge to effectively treating invasive non-typeable Haemophilus influenzae.

### Table 1

| Table 1 |  |
| --- | --- |
| **WBC** | 14.5 μL (normal 4–10) |
| **HGB** | 15.0 gm/dL (normal 13–17) |
| **Platelet** | 163 x10^3/μL (normal 150,000–400,000) |
| **Absolute neutrophil count** | H 12.1 x10^3/μL (normal 2–7) |
| **Lymphocyte auto #** | 1.0 x10^3/μL (normal 1.0–3.0) |
| **Monocyte auto #** | H 1.2 x10^3/μL (normal 0.2–1.0) |
| **Eosinophil auto #** | 0.0 x10^3/μL (normal 0.0–0.5) |
| **Basophil auto #** | 0.0 x10^3/μL (normal 0.0–0.1) |
| **Blood culture aerobic and anaerobic sent day 1 of admission** | No Growth |
| **CRP** | H 111.1 mg/L (normal 0.5–1.0) |
| **Lactic acid** | 1.2 mmol/L (normal 0.5–2.2) |
| **Procalcitonin** | 0.08 ng/mL |
| **Stool culture** | No Salmonella and no Shigella isolated |
| **Clostridium difficile toxin** | Not detected |
| **Prothrombin time** | H 18.1 seconds (normal 9.4–12.5) |
| **INR** | 1.5 |
| **APTT** | 36.0 seconds (normal 25.1–36.5) |
| **UREA** | 5.2 mmol/L (normal 2.5–7.8) |
| **Creatinin** | 80 μmol/L (normal 62–106) |
| **SODIUM** | 134 mmol/L (normal 133–146) |
| **Potassium** | 3.9 mmol/L (normal 3.5–5.3) |
| **Chloride** | 107 mmol/L (normal 95–108) |
| **Bicarbonate** | 24 mmol/L (normal 22–29) |
| **Bilirubin T** | 10 μmol/L (normal 0–21) |
| **Total protein** | 65 g/L (normal 60–80) |
| **Albumin** | 30 g/L (normal 35–50) |
| **Alkaline phosphatase** | 84 U/L (normal 40–129) |
| **ALT** | 91 U/L (normal 0–41) |
| **AST** | 130 U/L (normal 0–40) |

### Table 2

| Table 2 |  |
| --- | --- |
| **Rapid malaria test** | Negative |
| **Adenovirus PCR** | Negative |
| **Influenza Virus A and B PCR** | Negative |
| **Coronavirus NL63 PCR, Coronavirus 229E PCR** | Negative |
| **Coronavirus HKU PCR** | Negative |
| **Parainfluenza virus 1, 2, 3, 4 PCR** | Negative |
| **hMVPC PCR** | Negative |
| **Human Bocavirus PCR** | Negative |
| **Mycoplasma Pneumoniae PCR** | Negative |
| **Respiratory Syncytial Virus PCR(RSV) PCR** | Negative |
| **Human Rhino/Entero Virus** | Positive |
| **RSV A and B Virus** | Negative |
| **Bordetella pertussis** | Negative |
| **Chlamydia pneumonia** | Negative |
| **Legionella pneumophilia** | Negative |
| **MERS Coronavirus** | Negative |
| **COVID-19 PCR** | Negative |
| **Bordetella parapertussis** | Negative |
| **Blood culture Aerobic Sent on Day 3 of admission** | Haemophilus influenzae, not Type B |
| **Blood culture anaerobic Day 3 of admission** | Beta-lactamase negative, ampicillin resistant (BLNAR) strains of Haemophilus influenzae | No growth |
Ampicillin was the primary empirical drug of choice for treating most respiratory tract infections and for confirmed Haemophilus influenza infections. The first reported resistance to Ampicillin in Haemophilus influenza was recorded in 1974. Since then, multiple global studies have shown increased incidence of resistant strains [4,12]. The strain cultured from our Patient was found resistant to Ampicillin, Moxifloxacin, and Trimethoprim/Sulfamethoxazole.

Our case study had certain limitations. Firstly, we could not perform a lumbar puncture for cerebrospinal fluid analysis for our Patient, as he rejected the procedure after fully understanding the risks and benefits. Therefore, we could not determine the cause of ventriculitis early on within his hospital course. Secondly, our Patient only completed ten days of IV Ceftriaxone and did not complete an entire course of IV antibiotics treatment as the infectious disease team recommended for 3–4 weeks due to refusal. Hence, we cannot determine in this case if the Patient was appropriately treated or not. We are also unable to explore if oral antibiotics could have any role in the possible effective treatment of his case.

The work has been reported in line with the SCARE 2020 criteria [13].

4. Conclusion

To our knowledge, ventriculitis secondary to non-typeable BLNAR Haemophilus influenzae is a poorly explored topic. From various studies conducted around the world, it can be noted that the epidemiology of invasive infection due to Haemophilus influenza is altering. More evidence needs to be gathered for the adult population to determine how neurological complications by invasive non-typeable BLNAR Haemophilus influenzae infections affect the incidence, prevalence, and disease burden within the adult age group in the HiB post-immunization era.

Ethical approval

The case report was approved by Hamad Medical Corporation Medical Research Centre.

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Author contribution

Asiya aqeel thakur identified the case, reviewed the literature, and wrote the manuscript. ELMustafa Abdalla is the corresponding author who helped in manuscript writing, doing a review for literature.

Leena Saeed, Yara Abouazab, and Sulafa K.Khalil, helped in identifying the case, reviewing the literature, and doing the final review and approval for the manuscript.

Registration of research studies

Not required.

Guarantor

ELMustafa Abdalla.

Consent

Written informed consent was obtained from the patient for publication of this case report and the accompanying image. A copy of the written consent is available for review by the Editor-in-Chief upon request.

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Provenance and peer review

Not commissioned, externally peer reviewed.

Research registration

N/A.

Declaration of competing interest

The authors have no competing of interest to declare.

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Appendix A. Supplementary data

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