



Haemophilus influenza Meningitis in a Woman Recently Initiated on Rituximab



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Introduction

- Bacterial meningitis carries an incidence of 1.38 per 100,000 person years, with an average mortality as high as 14.3%.¹
- The incidence of meningitis caused by *Haemophilus influenzae* continues to decline 20 years after the introduction of Hib vaccine, and is recently estimated to be as rare as .012/100,000 person years.¹⁻³
- The mortality associated with *Haemophilus influenzae* meningitis is estimated to be 7%.³
- Rheumatoid arthritis refractory to traditional disease-modifying antirheumatic drugs (DMARDs) is often treated with immunologic agents including monoclonal antibodies such as rituximab.⁴
- Immunologic agents significantly increase the risk of serious infection, particularly in the first 6 months of treatment initiation.^{5,6}
- There are currently 95 FDA approved monoclonal antibodies, 66 of which have been approved in the last 5 years.⁷

Figure 1. FDA Approved Monoclonal Antibodies⁷



Case Description

History

- 66 year-old Caucasian female with chief complaint of fever and altered mental status.
- On-going chronic bilateral otitis media for eight weeks, being managed by her ENT specialist with oral antibiotics and ofloxacin ear drops.
- Acute worsening of symptoms over the last two days including fever, altered mental status, decreased PO intake, and purulent drainage from the right ear prompted ED visit sent from primary care physician office.
- PMH of rheumatoid arthritis, hypertension, hyperlipidemia, osteoporosis, osteoarthritis of the knee
- Recently started on rituximab immunotherapy two months prior to presentation as well as daily prednisone.
- Surgical history of left knee arthroplasty, bilateral carpal tunnel release
- Social and Family History unremarkable.
- ROS limited due to patient's altered mental status

Physical Exam

- Vitals: Temp: 102.7°F, BP 143/86 mmHg, HR 98 bpm, RR 18 bpm
- Toxic appearance, pale, obtunded but responsive to verbal stimuli
- Purulent drainage from the right external auditory canal, right tympanic membrane bulging and inflamed with small central perforation
- Left tympanic membrane erythematous and bulging
- Passive flexion of the neck elicits obvious discomfort and grimace from the patient, nuchal rigidity
- Heart with regular rate and rhythm
- Lungs clear to auscultation
- Abdominal exam benign
- Examination of the lower extremities revealed reflexive flexion of the hips and knees

Patient management/ Hospital Course

- The patient was started on IV vancomycin, cefepime, and ampicillin, and admitted to the ICU for continued antibiotic therapy pending blood and CSF cultures.
- Culture and sensitivities of cerebrospinal fluid returned sterile, however blood cultures x2 grew *Haemophilus influenzae* with sensitivity to ceftriaxone.
- Patient improved slowly with narrowed antibiotic therapy.
- Complications included: development of oral candidiasis treated with nystatin solution, fluconazole, and lidocaine swishes; and herpes labialis treated with valcyclovir.
- Patient was discharged after 8 days of therapy with ceftriaxone with PICC in place for an additional 7 days of therapy.
- Specimen cultures of right ear purulence grew MRSA, for which patient was also discharged on trimethoprim/sulfamethoxazole 10 day course.
- The patient remained in a skilled nursing facility for administration of IV therapy and recovery for 13 days before being discharged to home.

Discussion

- Computed tomography (CT) of the head is often performed to rule out mass lesion prior to lumbar puncture (LP) due to concern of resulting brainstem herniation in the setting of increased intra-cranial pressure (ICP). However, this practice can delay diagnosis and initiation of crucial antibiotic therapy. Therefore, guidelines suggest CT of the head can be avoided in the absence of the following negative predictive factors for increased ICP:⁸
 - Immunocompromised state
 - History of previous central nervous system disease
 - New onset seizure
 - Papilledema
 - Glasgow Coma Score < 11
 - Focal neurological deficit
- Even in instances that LP is delayed, antibiotic therapy should still be initiated as soon as possible following blood culture collection. This may cause negative CSF gram stain and culture, however a diagnosis may still be made based on clinical criteria and other CSF analysis.⁸

Conclusion

- Haemophilus influenza* is an exceedingly rare cause of bacterial meningitis in adults, and always warrants causal investigation when diagnosed.
- Immunologic therapies such as rituximab carry immunocompromising qualities that significantly increase the risk for severe infection, particularly following initiation of therapy.
- Due to the growing number immunologic therapies, it is increasingly important to familiarize ourselves with these agents and thoroughly review patients' medications for monoclonal antibodies in order to properly risk stratify for infection.

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Case Description- Diagnostic Results

CBC

18.2 12.2 275
39.7

BMP

128 88 10 157
4.0 25 0.6

Lactic Acid: 2.0 mmol/L

CT non-contrast of the head:

- no mass lesion
- bilateral mastoiditis
- bilateral otitis media
- right sided otitis externa

Table 1. Cerebrospinal Fluid Analysis

Protein	319
Glucose	2
Microscope	Many neutrophils, RBCs, Round Cells
Cell Count #1	WBC: 12,480 RBC: 8,000
Cell Count #2	WBC: 11,367 RBC: 15,000