CASE 40-2019: A 26-YEAR-OLD RETURNING TRAVELER WITH HEADACHE

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Chief Complaint

- A 26-year-old women was evaluated in the emergency room for the worst headache of the patients life.
PATIENT HISTORY
Patient History

- History of migraines.
- The patient had had varicella virus infection in childhood.
- She was originally from South America but had immigrated to the United States more than 15 years prior to this case.
- Married and living with her Husband in a suburban region of new England.
- She had visited Canada and Mexico the year before presentation but reported no other travel in the preceding 3 years.
- She drank alcohol in moderation and did not smoke tobacco or use illicit drugs.
- Healthy Family.
iClicker Question 1

1. Which of the following best describes the most common symptoms/signs of a migraine?
   a) An intense headache typically experienced on one side of the head, accompanied by nausea, vomiting, and sensitivity to light.
   b) A mild headache experienced across the forehead, accompanied by fever.
   c) A severe headache located behind the nose and between the eyes.
   d) A mild headache located behind one eye, accompanied by tearing and a red eye.
HISTORY OF CURRENT ILLNESS
History of Current Illness

- 3 weeks before
- 8 days before
- 5 days before
- 1 day before
3 Weeks Before Admission

- Traveled to Europe for vacation.
- Visited a mountainous region and stayed in a cabin at 3400m altitude.
- She had seen evidence of rodents around the mountain cabin where she stayed while traveling in Europe.
- Her head was struck in a low-velocity sledding accident.
- This resulted in a headache that lasted several hours and resolved spontaneously.
- Patient also had mild chills, and a cough, attributed to the cold weather.
Eight Days Before Admission

- Severe headache, described as the worst headache of her life.
- Developed suddenly while eating dinner.
- Located in the bitemporal regions and the occiput, was associated with fatigue, nausea, and vomiting.
- This headache was different from her normal migraines. It was not abated with either acetaminophen or naproxen.
Five Days Before Admission

- Experienced neck stiffness and decreased range of motion the neck.
- Patient was evaluated locally in an emergency department.
- Received a diagnosis of recurrent migraine.
- Intravenous fluid and oral nonsteroidal anti-inflammatory drugs were administered.
- Patient returned to the United States early due to persistent headache.
One Day Before Admission

- Patient arrived in Boston and was taken to an emergency department at another hospital.
- Reported ongoing severe headaches.
- Reported sensitivity to light and noise.
- Patient also reported intermittent fever, chills, and night sweats, as well as constipation that lasted several days.
iClicker Question 2

2. Which of the following could lead to her described history of current illness and symptoms reported prior to being admitted to Mass General?

a) A migraine experienced due to her history of migraines
b) A viral infection
c) Concussion
d) All of the above
PRESENTATION UPON ADMISSION

Ariel Myint
Presentation Upon Admission

- The morning of:
  - *Ongoing severe headaches*
  - *Nausea*
  - *Vomiting*

- No weight loss, sore throat, shortness of breath, cough, chest pain, dysuria, rash, or mucocutaneous ulcers.
3. What do symptoms of headaches and vomiting *usually* signify?
   a) Cancer
   b) Gastrointestinal Infection
   c) Migraines
   d) Acid-Reflux
VITALS
Vitals

- **Temperature:** 36.4°C
- **Pulse:** 91 beats per minute
- **Blood Pressure:** 133/78 mm Hg
- **Respiratory Rate:** 16 breaths per minute
- **Oxygen Saturation:** 100%

Additionally:
- *Full range of motion in neck*
- *Flexion elicited mild pain in posterior cervical region*
- *No oropharyngeal ulcers or rashes*
- *Remainder of examination normal*
LABS AND IMAGING
- Levels of electrolytes were normal
- Results of renal-function tests were normal
- Blood levels of calcium, phosphorus, magnesium, and thyrotropin were normal
- Blood tests for antinuclear antibodies were negative
- Tests for HIV-1 and HIV-2 were negative
- Test for herpes simplex virus (HSV) negative
- Lumbar puncture test revealed abundant mononuclear cells and no organisms.
- Turbidity was moderate.
- Reactive lymphocytes were 4.
iClicker Question 4

4. What does a change in the turbidity of spinal fluid mean?
   a) A decrease in white blood cell count
   b) A decrease in red blood cell count
   c) A decrease in protein levels
   d) An increase in protein levels
Figure 1. CT Angiography of the Head and Neck.

CT angiography of the head and neck reveals no intracranial hemorrhage, infarction, or mass lesion; arterial and venous vasculature appear normal, with no stenosis. The upper jugular lymph nodes (Panel A, arrow), left submandibular lymph nodes (Panel B, arrow), and right spinal accessory lymph nodes (Panel C, arrow) are mildly prominent.
DIFFERENTIAL DIAGNOSIS

Manisha Reddy
Symptoms so far:

- “Worst headache of her life
  - Progressive and unresponsive to medications
- Fever, chills, night sweats, neck stiffness
- CSF studies consistent with meningitis, but no clinical symptoms
Differential Diagnosis - Headache and Meningitis

- Performed a lumbar puncture
  - Revealed abnormal CSF findings consistent with meningitis
    - CSF = Cerebrospinal Fluid, which is a clear fluid that surrounds the brain and spinal cord
- Course of action: determine if patient presented treatable causes of meningitis, such as bacterial or HSV infection
  - Delay in treatment for these possible causes would severely worsen outcomes
Differential Diagnosis - Bacterial Meningitis

- If bacterial meningitis was the cause:
  - Possible symptoms: headache, fever, neck stiffness, and altered mental status
    - Bacterial meningitis patients present with 2/4 of these symptoms
    - Our Patient had ¾ of the symptoms

- Most bacterial meningitis patients also display a predominance of lymphocytic cells in CSF or also neutrophilic pleocytosis
  - lymphocytic cells = white blood cells
  - neutrophilic pleocytosis = increased quantity of neutrophils
    - Patient did NOT have this present in their CSF
    - diagnosis of bacterial meningitis is unlikely
I-Clicker #5

What are neutrophils and what are their function within the immune system?

A. *WBC that work within the adaptive immune system and create antibodies against the foreign invader*

B. *They are agranulocytes that assist B-cells produce antibodies*

C. *Granulocytes that perform chemotaxis towards the foreign invader and perform phagocytosis*

D. *An antigen presenting cell that helps B and T cells identify the foreign invader*
Differential Diagnosis - HSV Encephalitis

- HSV infection can cause both meningitis and encephalitis
  - *Encephalitis is fatal however, and presents with symptoms similar to bacterial meningitis*

- Symptoms: headache, fever, focal neurologic signs
  - *Also frontotemporal signs: behavior changes, amnesia, aphasia, seizures, and hemi-paresis.*
  - *MRI will usually signal hyperintensity in the orbitofrontal and temporal lobes.*

- Findings in patient:
  - *MRI did not display above characteristics and a specific HSV nucleic acid test was negative*
  - *diagnosis of HSV infection unlikely*
Differential Diagnosis – Other Causes

- Viral Infection
  - *Enteroviruses are most present in the summer/fall and are spread from person to person, none of which applied*
  - *Patient also had high protein level and low glucose level, which is atypical for a viral infection*

- Varicella Zoster Virus: but patients CSF abnormalities are atypical for VZV

- Primary HIV virus
  - *Immunosuppressants make a patient even more vulnerable*
  - *But patient screened negative for HIV antibodies and antigens*
How would a HIV diagnosis endanger the patients condition?

A. *The medicine taken for HIV increases risk of infection*

B. *The CD4+ cell deficiency caused by HIV decreases the body’s ability to fight other infections*

C. *The presence of a reverse transcriptase in a retrovirus increases transcription of other viral proteins*

D. *The decrease in antibody production by B cells decrease immune response against infections*
Differential Diagnosis – Other Causes

- **Arboviruses (via anthropod vectors)**
  - *Patient is at risk because she lives in north east and traveled to Europe.*
  - *More prevalent in summer season and elevated lymphocyte count in CSF is atypical*

- **Tuberculous meningitis**
  - *Neurological Symptoms: confusion, lethargy, and cranial-nerve deficits*

- **Fungal Infections**
  - *Patient traveled to Mexico and Canada in the previous year, so higher risk of infection*
  - *All fungal infection tests were negative*

- **Non-Infectious causes**
  - *No history of cancer or other inflammatory diseases*
Differential Diagnosis - Mumps

- The patient's CSF results are atypical of most viral meningitis
  - *CSF result: profound lymphocytic pleocytosis, high protein and low glucose level*
- Mumps and lymphocytic choriomeningitis virus were still viable diagnosis
- Mumps diagnosis:
  - *Patient was probably vaccinated against mumps*
  - *Highly infectious with incubation period of 15-24 days*
  - *Can be diagnosed with CSF nucleic acid testing*
  - *However, physician did NOT believe this was the cause*
Differential Diagnosis - Lymphocytic choriomeningitis virus infection

- Rodent borne arenavirus
  - *Most common in winter*
  - *Incubation period of 1-2 weeks*
  - *Biphasic illness with flu like syndrome*
  - *Can be diagnosed with detection of LCMV nucleic acid*

- Patient fit all of this criteria so the physician treated accordingly
  - *However, the results were not obtained until after the patients discharge*
Final Diagnosis: **Lymphocytic choriomeningitis virus infection**

- CSF sample was sent to the CDC to measure LCMV-immunoglobins through an ELISA
  - *Tested positive, but only received after treatment*
- Diagnosis was harder because there are many causes of meningitis
Which part of the LCMV immunoglobulins would bind to the antigen in the ELISA?

A. Heavy Chain
B. Light Chain
C. The Constant region of the heavy and light chains
D. The variable region of the heavy and light chains
TREATMENT
Treatment

- Symptom oriented care for patients with LCMV infection
  - *No specific course of treatment*
- Patient recovered within a week
RESOLUTION

Chandni Mehta
Vancomycin and ceftriaxone treatment was discontinued
Acyclovir treatment discontinued
Ampicillin treatment discontinued after bacterial culture remained negative after 1 week
What are common side effects of the antibiotic vancomycin?
- A. Bladder Pain
- B. Decreased urine
- C. Dry mouth
- D. All of the above
- E. None of the above
Resolution

- Patient’s headaches abated over the course of 1 week during hospitalization and were treated symptomatically
- Patient remained afebrile with normal vital signs
- Nuchal rigidity resolved
- Discharged after 1 week
Update

- After patient’s discharge, received positive test results for LCMV
- CSF protein level decreased considerably after lumbar puncture
- Headache and fatigue was resolved 3 weeks after discharge
CLINICAL RELEVANCE
Clinical Relevance

- Headaches are very common and clinicians should watch out for any “red flags” that warrant a closer analysis
  - Patient’s progression and severity of the headache, lack of response to treatment and systemic symptoms
Which of the following conditions does not usually result in a secondary headache?

- A. brain aneurysm
- B. Acute sinusitis
- C. Venous thrombosis
- D. Arterial tears
- E. Kidney stones
Clinical Relevance

- LCMV is rodent borne
- House mice are natural reservoirs of LCMV
  - Found in 5% of all house mice in United States
IClicker Number 10

Other than LCMV, which of the following is a common rodent borne disease?
- A. Hantavirus
- B. Cholera
- C. Campylobacteriosis
- D. Listeriosis
- E. Lyme Disease
Clinical Relevance

- Viral nucleic acids may not be detected in CSF after 2 weeks after the onset of symptoms
References

- DOI: 10.1056/NEJMcp1904042
- https://www.cdc.gov/headsup/basics/concussion_symptoms.html
- https://www.cdc.gov/chickenpox/hcp/index.html