39-Year-Old Woman With Headache and Fever

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A 39-year-old woman was transferred to our facility from an outside hospital for neurosurgical management of a right parasellar mass found on computed tomography of the head. Her symptoms had started 2 days before transfer to our facility with a worsening daily headache. The headache was located in the right frontotemporal region and associated with nausea and vomiting. She described the headache as a continuous ache with intermittent throbbing but no associated aura, photophobia, lacrimation, rhinorrhea, or jaw pain. For several days before the onset of symptoms, she had intermittent fever with a maximum temperature of 39.0°C (reference range, 36.0°C-38.0°C), rigors, generalized malaise, light-headedness, and myalgias. She did not have diplopia, blurry vision, dysarthria, paresthesias, productive cough, wheezing, dyspnea, urinary urgency or frequency, dysuria, abdominal pain, loose stools, or any incontinence. A central line had not been placed at the outside facility.

The patient's medical history was notable for untreated hypertension, Bell palsy, and anemia. She was a native of the Ivory Coast and had traveled to Togo and Ghana before arriving in the United States to visit her son 3 months previously. She had no pets, did not consume undercooked meats, and did not take any medications.

On admission, vital signs were notable for a temperature of 37.6°C, a regular pulse rate of 86 beats/min, blood pressure of 152/89 mm Hg, respiratory rate of 16 breaths/min, and normal oxygen saturation while breathing ambient air. Physical examination findings were notable for a mildly erythematous oropharynx and scleral icterus; there was no lymphadenopathy or neck stiffness, and Kernig and Brudzinski signs were absent. Laboratory studies yielded the following notable findings (reference ranges provided parenthetically): white blood cell count of 8.7×10^9/L ($3.5\text{-}10.5 \times 10^9$/L) with a normal differentiation and platelet count of 83×10^9/L ($150\text{-}450 \times 10^9$/L). The total bilirubin level was 1.3 mg/dL (≤1.2 mg/dL) with a conjugated fraction of 0.3 mg/dL (0.0-0.3 mg/dL). Results of an electrolyte panel and liver function studies were otherwise normal. The patient underwent chest radiography, which revealed no consolidations. Urinalysis results were normal. Testing for serum β-human chorionic gonadotropin was negative.

Magnetic resonance imaging of the brain revealed a 6-mm left ophthalmic internal carotid artery aneurysm and a possible cavernous sinus meningioma on the right. On hospital day 2, the patient was scheduled for endovascular treament of the aneurysm, but the development of a fever (temperature, 39.4°C) prompted us to cancel the procedure.

1. Which *one* of the following is the *most likely* explanation for this patient's fever?

a. Lower respiratory tract infection
b. Urinary tract infection
c. Central line–associated infection
d. Tropical illness
e. Liver abscess

Lower respiratory tract infection is unlikely because the patient did not have respiratory symptoms and no abnormalities were noted on chest radiography. She had no signs and symptoms of a urinary tract infection and no history of central line placement. Because the patient is from West Africa, she is at risk of acquiring a tropical illness, which is the most likely diagnosis. Tropical illnesses encountered in West Africa include Ebola, typhoid or enteric fever, yellow fever, dengue fever, malaria, schistosomiasis, and chikungunya. In a patient with liver abscess, fever is typically accompanied by abdominal pain and elevated levels on liver function tests. The patient did not have this presentation.

Further infectious work-up including urine culture, throat culture, rapid *Streptococcus* test, influenza polymerase chain reaction (PCR), QuantiFERON-TB Gold tuberculosis test, and serologies for dengue virus, *Toxoplasma*, *Cryptococcus* antigen, *Histoplasma*, *Coccidioides*, and human immunodeficiency virus yielded negative

See end of article for correct answers to questions.

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results. Blood culture results were also negative. In the hospital, the patient's fever was treated with acetaminophen.

2. At this time, which *one* of the following is the *best* next step?

a. PCR for Ebola
b. Test for yellow fever–specific IgM
c. Thick and thin blood smears for malaria
d. Test for dengue-specific IgM
e. Test for chikungunya-specific IgM

Ebola is included in the differential diagnosis given that the patient is from West Africa. Ebola is a viral illness spread from person to person via contact with contaminated blood or bodily fluids up to 21 days after exposure. Symptoms include fever, headache, myalgias, vomiting, abdominal pain, diarrhea, and, in some cases, hemorrhage.[1] Our patient has been away from home for 3 months. To date, there have been no cases of Ebola in the Ivory Coast, although it shares a border with Guinea and Liberia where there has been an outbreak. Therefore, she is not likely to have Ebola and will not benefit from PCR testing of the blood. There have been outbreaks of yellow fever in the Ivory Coast, and because of this, yellow fever vaccine is recommended for travelers to this country. Illness begins 3 to 6 days after a bite from an infected mosquito. Symptoms include fever, myalgias, headache, photophobia, nausea, and vomiting. Following symptom remission, some patients have progression to a toxic phase that manifests with organ dysfunction and hemorrhage.[2] Our patient has been away from the endemic region for 90 days, much longer than the incubation period for yellow fever, and is unlikely to have this disease. Conversely, malaria can manifest months or even years after initial exposure, especially if one was previously exposed and developed partial immunity or received prophylaxis. Thick and thin blood smear for malaria is the criterion standard for diagnosis and is the most appropriate step at this time.[3] The thick film concentrates the parasites and increases diagnostic sensitivity. Nonimmune individuals may be symptomatic at very low parasite densities that initially may be undetectable by blood smear. In such cases, the smear should be repeated every 12 to 24 hours for 3 sets.

Dengue fever, also known as "break-bone fever," is a mosquito-borne viral illness associated with urban environments and manifests with fever, severe headache with retro-orbital pain, and severe myalgias and arthralgias, The incubation period is several days.[4] Given that the patient has been out of the endemic area for a longer period of time, it is unlikely that she has dengue fever. Chikungunya is another mosquito-borne illness included in the differential diagnosis. Similar to dengue fever, it is associated with urban environments; the incubation period is a few days, and the illness is characterized by sudden onset of fever, rash, and severe joint pain.[5] Our patient is unlikely to have chikungunya because she has been out of the endemic area for longer than just a few days.

A blood parasite smear revealed parasitemia with 0.5% of cells infected with *Plasmodium* that was confirmed by PCR as *Plasmodium falciparum*.

3. Which *one* of the following is the *best* treatment option for a patient who did not take malaria prophylaxis?

a. Chloroquine
b. Atovaquone-proguanil
c. Artesunate
d. Intravenous quinidine gluconate plus doxycycline
e. Exchange transfusion

The treatment choice depends on the malaria species, the clinical status of the patient, and the drug susceptibility of the infecting parasites as determined by the geographic area where the infection was acquired and the previous use of antimalarial medicines.[6] The initial decision is whether the patient has *P falciparum* malaria or malaria due to *Plasmodium vivax*, *Plasmodium ovale*, *Plasmodium malariae*, or *Plasmodium knowlesi*. *Plasmodium falciparum* and *P knowlesi* infections can cause rapidly progressive severe illness or death, whereas the other species are less likely to have severe manifestations. Also, *P vivax* and *P ovale* infections require treatment for the hypnozoite forms that remain dormant in the liver and can cause relapsing infection.

Subsequent treatment decisions are based on classification of the disease as severe (ie, having end-organ damage) or uncomplicated. Uncomplicated disease is treated with oral antimalarial medications, and severe disease is treated with intravenous antimalarials. Our patient had no evidence of end-organ damage including

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