An Atypical Presentation of Malaria in a 19-year-old Woman

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Background

Malaria presents with a constellation of findings – fever, being the hallmark of the disease. Other non-specific symptoms include fatigue, headache, myalgias, nausea, vomiting and diarrhea. In the United States, there were 2,078 confirmed cases of malaria in 2016. Of these, 1,729 originated from Africa. The most common vectors of disease were *Plasmodium falciparum* (68.2%) and *Plasmodium vivax* (12.1%). From 2000 to 2014, there were over 22,000 cases of malaria resulting in hospital costs exceeding $176 million in the United States. Fatal complications of malaria include cerebral malaria, renal failure, acute respiratory distress syndrome, and disseminated intravascular coagulation. Splenic rupture is another major cause of death in those diagnosed with malaria and often remains undiagnosed until autopsy. Complications are preventable with timely diagnosis and treatment.

Figure 1. Proportion of malaria cases due to *Plasmodium falciparum* in Nigeria according to the World Health Organization's 2015 World Malaria Report.

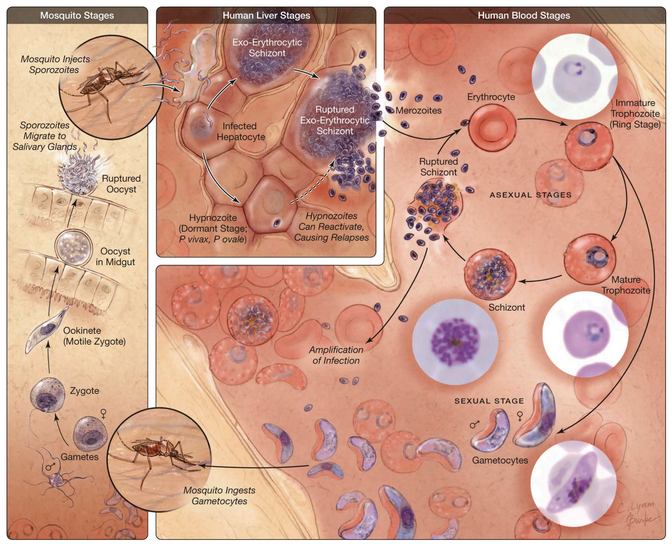

Figure 2. The life cycle of *Plasmodium* species is demonstrated. *Plasmodium vivax* and *Plasmodium ovale* are unique from *Plasmodium falciparum* in that they can have a dormant phase in the liver as hypnozoites.

Clinical Case

A 19-year-old woman with no past medical history presented to the emergency department with severe occipital headache radiating to her neck for 3 days. Associated symptoms included photophobia, subjective fevers, chills, rigors, and fatigue. She immigrated to the United States from Nigeria one year ago and her vaccination status was unknown. Her travel to the U.S. was the first time she had traveled outside of Nigeria.

Patient was admitted for suspicion of meningitis and started on empiric antimicrobial meningitis treatment.

On presentation, her temperature was 101° Fahrenheit, heart rate 121 beats per minute, blood pressure was 124/70 mmHg, and oxygen saturation was 97% on room air. Her body mass index was 21 kg/m2. On physical exam, the patient had no nuchal rigidity, no cervical lymphadenopathy, no cardiac murmurs, and had normoactive bowel sounds with left lower quadrant abdominal tenderness. Initial laboratory findings were significant for WBC 3.2 x103/uL, hemoglobin 10.9 g/dL, platelets 832 x103/uL, potassium 3.5 mEq/L, phosphorus 1.7 mg/dL, prothrombin time 26.2 sec, INR 1.1, ESR 43 mm/hr, CRP 138 mg/L, procalcitonin 5.15 ng/mL, HIV nonreactive, COVID PCR negative. Chest x-ray and abdominal x-ray were unremarkable. Computed tomography of the head showed no evidence of acute infarction or intracranial hemorrhage. Blood cultures showed no growth and urine cultures were significant for mixed flora. Malaria smear was positive for *Plasmodium vivax/ovale* with 0.4% parasitemia. The rapid malaria test, BinaxNOW (Abbott), was positive for *P. vivax/ovale/malariae*. The patient had a normal G6PD protein and no sickle cell trait. Lumbar puncture was attempted but was unsuccessful.

The patient was treated with atovaquone-proguanil 250mg/100mg for 4 days. On day 3 of treatment, patient's symptoms began to resolve. By day 4 of treatment, repeat BinaxNOW was negative. Patient was discharged 7 days after admission with improvement of symptoms. PCR confirmatory tests were sent but quantity was not sufficient to result. Patient was lost to follow-up after discharge from the hospital and the two-week course of treatment for eradication of the liver stage was not completed.

Conclusions

We describe an atypical presentation of malaria, in which a 19-year-old female presents with symptoms of meningitis more than one year after emigrating from a malaria-endemic region. Malaria is endemic in Nigeria; however, the majority of cases of malaria are caused by *P. falciparum*. Finding the malaria smear and BinaxNOW positive for non-*falciparum* species was therefore unexpected, especially since the patient has no other travel history.

P. ovale and *P. vivax* are transferred from infected vectors, mosquitoes, to human hosts as sporozoites through bites. The sporozoites infect and mature in the liver for around 9 days. Merozoites are then released from the liver and infect red blood cells and form immature trophozoites in the cells. These immature trophozoites can mature and release more merozoites or become gametocytes that are later ingested by mosquitos. The parasites in the red blood cells primarily cause the clinical presentation of malaria. *P. ovale* and *P. vivax*, are unique from *P. falciparum* in that they can become dormant in the liver as hypnozoites. This can delay the proliferation of the parasite in the liver for months, which can lead to relapses of malaria weeks or years after the primary attack.

There is a form of *P. vivax* that is also known to have a long-latency period of nine months from inoculation or a two-week time interval between inoculation and primary attack followed by a relapse interval of around nine months. Moreover, cases of latent *P. ovale* infection have been demonstrated with delayed primary attacks when the patients were being treated with anti-malarial medication before and after initial exposure. However, this patient's presentation occurred around one year after her last probable exposure to malaria and she had no known history of treatment or prophylaxis of malaria.

In unusual cases, timely identification of disease through comprehensive travel history, proper molecular testing, and awareness of epidemiology of *Plasmodium* species is essential for appropriate pharmacologic management and avoidance of fatal complications and relapses.

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