



Case report

An atypical presentation of malaria in a 19-year-old woman

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ABSTRACT

We describe an atypical presentation of malaria in a 19-year-old female who emigrated from Nigeria to the United States one year prior to presentation. Her primary complaint was fever and occipital headache radiating down to the neck. Rapid antigen testing was positive for *Plasmodium vivax/ovale* and microscopy demonstrated the same. She received treatment with atovaquone-proguanil with improvement in symptoms but was lost to outpatient follow up. This case is unusual in several aspects: the 12-month latency in disease manifestation after her last epidemiologic exposure and the recovery of *P. vivax/ovale* which is uncommon in Nigeria. Appropriate identification of travel history, clinical presentation and disease epidemiology are necessary to guide pharmacologic treatment.

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Background

Malaria presents with a constellation of findings – fever, being the hallmark of the disease, and supplementary non-specific symptoms – fatigue, headache, myalgias, nausea, vomiting and diarrhea. In the United States, there were 2078 confirmed cases of malaria in 2016. Of these, 1729 originated from travel from Africa. The most common vectors of disease were *Plasmodium falciparum* (68.2%) and *Plasmodium vivax* (12.1%) [1]. From 2000–2014, there were over 22,000 cases of malaria resulting in hospital costs exceeding \$176 million in the United States [2]. 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, often remaining undiagnosed until autopsy [3]. The incubation period ranges from 10 days to 30 days depending on the type of *Plasmodia spp.* involved. *Plasmodium vivax* and *P. ovale*, may have a longer incubation period of several months to years between mosquito bite and initial symptoms [9]. Relapses can occur with *P. vivax* and *P. ovale* because they have dormant liver stage parasites that may reactivate. Complications are preventable with timely diagnosis and treatment.

Objective

To describe a rare, delayed presentation of malaria.

Case report

Patient is a 19-year-old woman with no past medical history who presented to the emergency department with severe occipital headache radiating to her neck for 3 days associated with photophobia, subjective fevers, chills, rigors, and fatigue. She was admitted based on suspicion of meningitis and started on empiric meningitis treatment. She immigrated to the United States from Nigeria one year prior and her vaccination status was unknown. Her travel to the US was the first time she had traveled outside of Nigeria.

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 on auscultations, and had normoactive bowel sounds with left lower quadrant abdominal tenderness. Initial laboratory findings were significant for WBC $3.2 \times 10^3/\mu\text{L}$, hemoglobin was 10.9 g/dL, platelets $75 \times 10^3/\mu\text{L}$, potassium 3.5 mEq/L, phosphorus 1.7 mg/dL, prothrombin time 26.2 s, INR 1.1, sedimentation rate 43 mm/hr, c-reactive protein 138 mg/L, procalcitonin 5.15 ng/mL, HIV nonreactive, COVID PCR negative. Chest x-ray and abdominal x-ray were unremarkable. Complete abdominal ultrasound showed no splenomegaly and bilateral hydrosalpinx with left side greater than right side, left ovarian cyst and otherwise 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. Lumbar puncture was attempted but was not successful. Malaria smear was positive for *Plasmodium vivax/ovale* with 0.4% parasitemia. The rapid

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malaria test BinaxNOW (Abbott) was positive for *P. vivax/ovale/malariae*. The patient was treated with atovaquone-proguanil 250 mg/100 mg for 4 days. A repeat BinaxNOW at day 4 was negative. MRI of the brain to evaluate for cerebral edema was not done as it is not standard of care and the patient's symptoms improved early into the treatment course. The patient had a normal G6PD protein and no sickle cell trait. By day 7 the patient was discharged. A polymerase chain reaction (PCR) test was sent prior to discharge to confirm this rare diagnosis before initiation of treatment for eradication of the liver stage. The PCR quantity was later found to be not sufficient to provide speciation and the patient was lost to follow-up after discharge from the hospital.

Discussion

We describe an atypical case in which malaria presents with classic symptoms of meningitis in a patient whose last travel to an endemic country was more than one year ago. The patient emigrated to the United States from Nigeria, a country in which *P. falciparum* causes the overwhelming majority of cases of malaria. While exact estimates are uncertain, CDC reports in Nigeria, *P. falciparum* accounts for greater than 85%, *P. ovale* 5–10% and *P. vivax* is rare [4–6]. The patient's malaria smear showed positivity of *Plasmodium vivax/ovale/malariae*. BinaxNOW, which has been shown to have 99.8% specificity and 92.9% sensitivity in a study done in the US, was positive for malaria protein antigen, representing *P. vivax* or *P. malariae* or *P. ovale*, which was not expected from a patient emigrating from Nigeria [7]. The patient had no known prior travel to regions where *P. ovale* or *P. vivax* is more prevalent.

P. ovale and *P. vivax*, are unique from *P. falciparum* in that they can become dormant in the liver as hypnozoites [9,10]. This can delay parasite proliferation within the liver for many months and lead to relapses of malaria weeks to years later if not treated [8,9]. In the current case, the patient's presentation occurred around 1 year after her last possible exposure with no knowledge of previous treatment. The patient's delayed presentation is rare, but not improbable and highlights need for extensive travel history when patients present with ambiguous symptomology and understanding of the epidemiology of malaria-endemic nations.

While microscopy is the gold standard of diagnosis of malaria, in these unusual cases, parasite nucleic acid detection using PCR is more sensitive and specific than microscopy but can be performed only in reference laboratories. PCR is also useful in detecting mutations associated with drug resistance. In these cases, it may be worthwhile to use PCR testing for confirmation of speciation as *P. vivax* can present with low parasitemia such our patient who had 0.4% parasitemia [11]. One possible reason for low parasitemia level may be that merozoites of *P. vivax* infect reticulocytes unlike other species of malaria which will infect all stages of the red blood cell [8]. Another reason may be that *P. vivax* and *ovale* have been shown to elicit a stronger host response at lower levels of parasitemia compared to *P. falciparum*, explaining why fever is likely to occur earlier in these infections [12].

Treatment for non-falciparum malaria and *Falciparum* malaria are different and appropriate treatment is required to prevent the development of complications. Our decision to use atovaquone-proguanil over an artemisinin combination was in part related to procurement issues which would have delayed initiation of

treatment. Furthermore, the patient showed clinical improvement with our treatment choice. Non-falciparum malaria due to *P. vivax* and *P. ovale* require additional treatment to eradicate the hypnozoites [13]. In this case before initiating prophylactic treatment, testing with PCR was sent in order to confirm this rare case of *Plasmodium vivax/ovale*. Unfortunately, the patient was lost to follow up in the outpatient setting before prophylactic treatment was initiated. Timely identification of disease through comprehensive travel history, proper molecular testing, and awareness of epidemiology of *Plasmodium spp.* is essential for appropriate pharmacologic management and avoidance of fatal complications.

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Consent

The patient has provided verbal and written consent for publication. No images were used.

CRediT authorship contribution statement

Radhika Malhotra: Writing – original draft (main contributor), Writing – review & editing. **Anjella Manoharan:** Writing – original draft. **Amesika Nyaku:** Writing – review & editing. **Dorothy Castro:** Writing – review & editing, Supervision.

Declaration of competing interest

None.

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