Plasmodium falciparum malaria occurring 8 years after leaving an endemic area

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Abstract

A 29-year-old patient who was born in Angola developed \textit{Plasmodium falciparum} malaria 8 years after leaving Africa. She had not returned to a malaria-endemic area, and there were no apparent risks of local or nosocomial acquisition of malaria in Canada. She recovered after treatment with oral quinine sulfate and doxycycline.

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1. Introduction

Malaria remains a leading cause of global morbidity and mortality. More than 1 million deaths may be attributed to malaria each year, and more than 3 billion people live in malarial endemic regions (Newman et al., 2004; Snow et al., 2005). Although it is not endemic to the United States, Canada, or Europe, malaria still represents a significant but preventable imported disease. In the United States, 1528 cases of malaria were reported in 2005, resulting in 7 deaths (Thwing et al., 2007). In Canada, about 400 cases are reported annually, associated with 1 or 2 deaths each year (Kain et al., 2001; Suh et al., 2004). Disease in North America and Europe generally occurs in travelers to endemic areas, including those returning to their home countries believing themselves to be immune (Kain et al., 2001; Newman et al., 2004). Thus, the timely diagnosis and treatment of malaria remains relevant in developed nations, especially as international travel continues to grow.

In humans, 4 species of plasmodia are associated with malaria: \textit{Plasmodium falciparum}, \textit{Plasmodium vivax}, \textit{Plasmodium ovale}, and \textit{Plasmodium malariae}. Infection by \textit{P. falciparum}, which is the predominant cause of malaria in Africa, accounts for most cases of severe disease and almost all malaria-related deaths. The incubation period for malaria due to \textit{P. falciparum} is typically less than 1 month, and most patients present with onset of symptoms within 1 or 2 months of exposure (Jelinek et al., 1994; Svenson et al., 1995). In the United States, 98% of patients with \textit{P. falciparum} malaria presented within 3 months of departure from a malaria-endemic area (Schwartz et al., 2003). Therefore, the diagnosis may be missed or delayed in patients who present with malaria more than 1 year after leaving an endemic area. In this article, we describe a patient who developed \textit{P. falciparum} malaria 8 years after leaving Angola, her country of birth. No other source of her infection was identified.

A previously healthy 29-year-old woman was admitted to hospital in Toronto, Ontario, in May 2007 with a 3-day history of general malaise, fever, chills, anorexia, nausea, vomiting, and watery stools. She did not have melena, rectal bleeding, or hematemia, and there were no respiratory or urinary symptoms. She was not taking any medications. There had not been any recent travel, and she was unaware of any sick contacts. There was no history of intravenous drug use, and she lived in an urban area of Toronto, not near the airport. The patient had immigrated to Canada from Angola in 1999 and had not traveled outside Canada since 2002, when she had visited family in Portugal. While still living in Angola, she had been treated for malaria and had made a
good recovery. She had received a blood transfusion in Angola in 1997 while she was giving birth to her 1st child; this had been her only transfusion of blood products.

On admission to hospital, she was alert and oriented with fever (38.5 °C), blood pressure of 115/75 mm Hg without a postural change, and tachycardia (114 beats/min). Her respiratory rate was 26/min, and she had an oxygen saturation of 97% while breathing room air. There was no rash, scleral icterus, or lymphadenopathy. The lungs were clear, and cardiac examination revealed normal heart sounds without murmurs. There was mild discomfort on deep palpation of the epigastrium, but there were no abdominal masses or organomegaly. Neurologic and musculoskeletal examinations were normal.

The initial laboratory investigations are summarized in Table 1. Urinalysis revealed 1+ hemoglobinuria and proteinuria. Microscopic urine examination revealed 2 to 5 erythrocytes and 0 to 1 leukocytes per high-power field, with no bacteria, crystals, or casts. The chest x-ray was normal, and the electrocardiogram showed sinus tachycardia. Examination of the peripheral blood film showed spherocytes, but no schistocytes. There were numerous red blood cells with malarial infestation, including multiple ring forms (Fig. 1). The level of parasitemia was 5.4%. Malaria due to P. falciparum was diagnosed, and this was later confirmed by a polymerase chain reaction assay (Farcas et al., 2006).

As soon as the blood film results became available, treatment was started with oral quinine sulfate (600 mg 3 times per day) and doxycycline (100 mg twice a day) for a total of 7 days. Within 48 h of starting treatment, she became afebrile, and her gastrointestinal symptoms resolved. Parasitemia peaked at 6% 24 h after presentation, and by day 4 of treatment, no malarial parasites were seen. However, her hemoglobin dropped to a low of 68 g/L on the day after admission. She was transfused with 2 U of packed red blood cells, and on discharge from hospital, her hemoglobin was 89 g/L. Her platelets recovered to 370 × 10⁹/L, and her renal function normalized with rehydration. Blood and urine cultures yielded no growth. Stool samples were negative for bacterial and viral enteric pathogens, and for ova and parasites. At a follow-up visit 3 weeks after discharge from hospital, she appeared to be clinically well and reported no further episodes of fever, chills, or gastrointestinal symptoms.

Although the patient’s clinical presentation and laboratory findings were consistent with malaria, this diagnosis was not initially considered because there had been no travel to a malaria-endemic area for at least 8 years, and there was no reason to consider local or nosocomial acquisition of malaria (Brook et al., 1994; Mungai et al., 2001). A diagnosis of thrombotic thrombocytopenic purpura was initially considered because of the presence of fever, renal impairment, thrombocytopenia, and hemolytic anemia. It was for this reason that an urgent examination of the

<table>
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<td>Results of the initial laboratory investigations</td>
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<td>Laboratory test (normal values)</td>
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<td>Hemoglobin (115–165 g/L)</td>
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<td>Leukocyte count (4.0–11.0 × 10⁹/L)</td>
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<tr>
<td>Platelet count (150–400 × 10⁹/L)</td>
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<td>Serum glucose, random (4.0–8.0 mmol/L)</td>
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<td>Serum creatinine (44–106 µmol/L)</td>
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<td>Serum bilirubin (&lt;20.0 µmol/L)</td>
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<td>Serum aspartate aminotransferase (&lt;31 IU/L)</td>
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<td>Serum alanine aminotransferase (&lt;31 IU/L)</td>
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<td>Serum alkaline phosphatase (40–120 IU/L)</td>
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<td>Serum lactate dehydrogenase (100–250 IU/L)</td>
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<td>Serum haptoglobin (0.3–2.0 g/L)</td>
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<td>HCG screen</td>
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HCG = human chorionic gonadotrophin.

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Fig. 1. The diagnosis of P. falciparum malaria was made by the examination of a thin peripheral blood film initially ordered to rule out the presence of schistocytes in possible thrombotic thrombocytopenic purpura (panel A—Wright’s stain). Thick and thin peripheral blood smears, stained with Giemsa stain (panel B—thin smear, higher magnification), remain the standard for routine clinical diagnosis. They allow for both species identification and quantification by assessing the percentage of erythrocytes infected on the film. The blood film derived from our patient contained morphologic features that were diagnostic of P. falciparum, namely, the presence of multiple ring forms per erythrocyte (black arrows), thin ring forms with double chromatin dots (arrow heads), and rings that were found in the periphery of the red cells (appliqué) (blue arrows) and the preservation of red-cell size and color.
peripheral blood film was requested, and this subsequently established the correct diagnosis.

Late recrudescence of *P. falciparum* malaria, though extremely uncommon, has been reported previously. *P. falciparum* malaria was diagnosed in a pregnant woman 4 years after her last stay in an endemic area (Giubbia et al., 2005). The delayed presentation was attributed to the pregnancy, impairing her preexisting immune equilibrium and acting as a trigger. However, there are also a few reports of nonpregnant adults developing malaria due to *P. falciparum* 4 or more years after leaving an endemic region (Eloy et al., 1998; Kyrönseppä et al., 1989). It is thought that preexisting partial immunity from repeated prior exposures may account for prolonged asymptomatic infection of malaria due to *P. falciparum*. This has been described after transfusion-associated malaria; the longest documented interval between prior exposure to malaria and the donation of blood products that transmitted *P. falciparum* infection is 13 years (Besson et al., 1976). We believe that our patient was likely infected while still in Angola, and that the infection remained latent for at least 8 years, possibly because of partial immunity (Bouchaud et al., 2005).


Kevin Kain for performing the malaria polymerase chain reaction assay.

References


