Adult respiratory distress syndrome complicating *Plasmodium falciparum* malaria

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In people who do not have clinical immunity to malaria, infection with the malaria parasite could lead to severe complications. We describe a patient who had acute and severe lung injury from malaria. A 37-year-old woman had a 24-hour history of generalized weakness and chills 2 days after returning from Nigeria. She had received mefloquine as prophylaxis, but the patient did not take the medication. On admission, a thick blood smear revealed severe *Plasmodium falciparum* parasitemia. She was given doxycycline and quinine, but as her parasitemia resolved, dyspnea and hypoxemia developed and she consequently required placement of an endotracheal tube. Chest radiography results showed bilateral and diffuse infiltrate. This report shows that patients with *P falciparum* malaria should be monitored closely and transferred to an intensive care unit for additional management if respiratory distress develops. Physicians caring for patients who have recently traveled to malaria-endemic areas need to anticipate the possible development of malaria with all of its complications, including acute lung injury. (Heart Lung® 2000;29:294-7.)

Malaria is a major cause of morbidity and mortality in the tropics. Death from malaria is mainly attributed to *Plasmodium falciparum*, 1 of 4 malaria parasites (*P falciparum, P vivax, P ovale,* and *P malariae*). People in all continents are potentially at risk for malaria. Increased world travel, neglected travel advice, and the increasing resistance of *P falciparum* and *P vivax* to prophylactic medicines may contribute to the transmission of malaria to countries where it had been eradicated.[1] In people who do not have clinical immunity to malaria, infection with the parasite combined with delayed diagnosis and treatment could lead to severe complications. The clinical effects in adults include acute renal failure, anemia, jaundice, hepatosplenomegaly, and impaired pulmonary function.[2] We describe a patient with acute and severe lung injury from malaria.

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CASE REPORT

A 37-year-old woman had a 24-hour history of generalized weakness, headache, chills, nausea, vomiting, and one episode of diarrhea 2 days after returning from a trip to Nigeria, West Africa. Four days before coming to the hospital, she had similar symptoms and was treated for malaria with chloroquine (intramuscular) and hydration at a hospital in Nigeria. Before traveling she had received mefloquine as prophylaxis, but the patient did not take the medication. She had been to Nigeria several times before and apparently had never taken prophylactic medication.

Her medical history was significant for migraine headaches and asthma. She was not taking any medications, she had no allergies, and she neither smoked nor used alcohol. Her vital signs on admission were a temperature of 40°C (104°F), pulse of 86 beats/min, respiratory rate of 18/min, and blood pressure of 92/50 mm Hg. The results of the rest of the physical examination were unremarkable.

Basic metabolic panel results and blood count on admission are shown in Table I. Her renal function was normal, and the liver function test revealed a normal prothrombin time of 13.5 seconds, an albumin level of 3.1 g/dL (normal range:

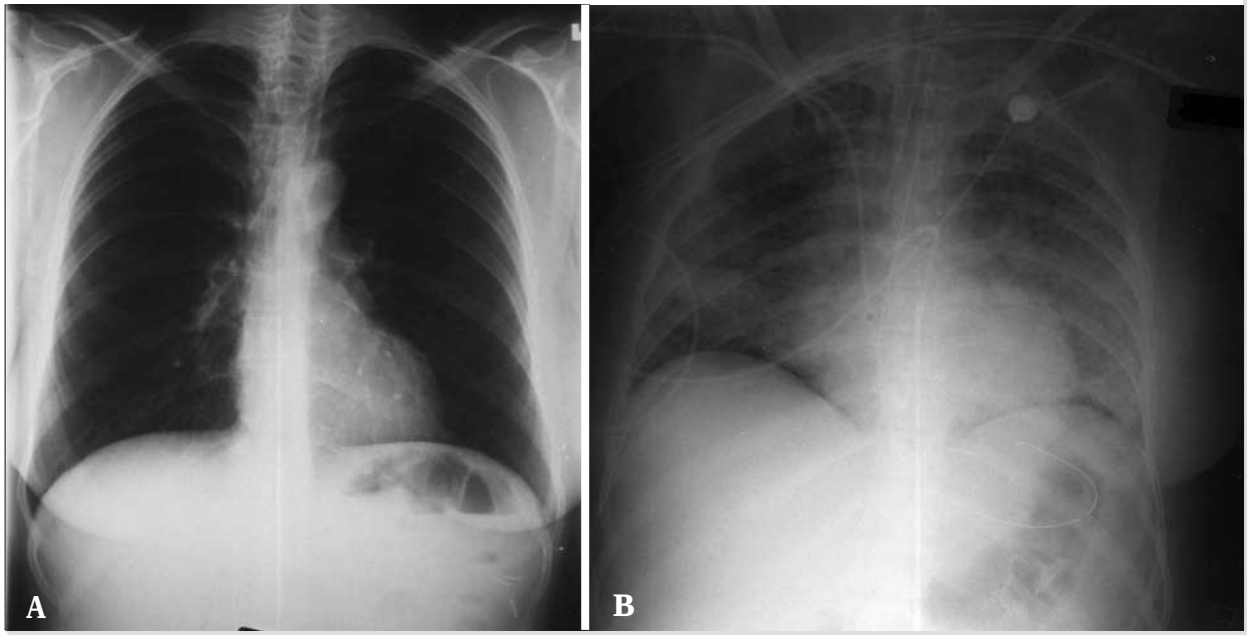

Fig 1 Chest radiographs on admission to the hospital **(A)** and when diffuse, bilateral airspace infiltrates developed **(B)**.

3.5 to 5.0 g/dL), and a total bilirubin of 4.3 mg/dL (0.2 to 1.2 mg/dL). Urinalysis test results showed 2+ protein, 1+ bacteria, and trace bilirubin. A thick blood smear was obtained, and it revealed more than 500 malaria parasites per 1000 red blood cells (RBCs), with predominantly blue ring forms; no mature forms were noted. Blood cultures showed no growth. No ova or parasites were noted in the stool, and her chest radiography result was normal (Fig 1, *A*).

It was determined that the source of the patient's infection was *P falciparum*, and the initial treatment included hydration, intravenous doxycycline 100 mg twice a day, and oral quinine 300 mg 3 times a day. Over the next 2 days of treatment, the patient continued to have fevers (maximum threshold, 39.6°C [103°F]), tinnitus developed, and she had some difficulty hearing and mild scleral icterus. As her parasite load decreased (2 parasites/1000 RBCs with some more mature forms but no Schwartz or Schüffner stippling), anemia (hemoglobin = 8.7 g/dL) and thrombocytopenia (platelet count 70,000) developed. She received a transfusion of 2 units of packed RBCs.

On the third admission day, the patient became extremely short of breath. Pulse oximetry results were 77% with room air and this increased to 90% with 50% O_2 on double nebulizer. Blood gas measurements with room air showed pH 7.46, $Paco_2$ 35 mm Hg, Pao_2 49 mm Hg, O_2 saturation 90%, and bicarbonate 24 mEq/L. Chest auscultation revealed diffuse, dry crackles throughout both lung fields, and a chest radiograph showed bilateral bibasilar infiltrate. Ventilation-perfusion scan done at the time was read as low probability for pulmonary embolus. The patient was given cefuroxime for a presumptive pneumonia. Workup for disseminated intravascular coagulation was negative. She was subsequently transferred to the intensive care unit (ICU) because of hypoxemia.

She had increasing shortness of breath and tachypneia and required placement of an endotracheal tube and mechanical ventilation. A chest radiograph taken at that time showed diffuse bilateral airspace disease (Fig 1, *B*). Her arterial blood gas on pressure support 30 cm H_2O, positive end-expiratory pressure of 5 cm H_2O, and fraction of inspired oxygen of 100%, was pH 7.44, $Paco_2$ 37 mm Hg, Pao_2 113 mm Hg, O_2 saturation 99%. She was treated aggressively with ventilatory and supplemental oxygen support, inhalers (albuterol 4 to 6 puffs every 3 hours and ipratropium bromide 4 to 6 puffs every 3 hours), and her hemodynamic status was monitored via a pulmonary artery catheter (cardiac index 4.21 L/min/m^2, pulmonary artery wedge pressure 13 mm Hg).

While in the ICU, she received 2 extra units of packed RBCs because of persistent anemia. Hypoglycemia developed, with blood glucose level as low as 46 g/L. The patient gradually improved over

Table I
Basic metabolic panel and blood count of the patient on admission

Basic metabolic panel		Blood count	
Sodium	129 mEq/L	Hemoglobin	11.2 g/dL
Potassium	3.2 mEq/L	Hematocrit	33%
Chloride	94 mEq/L	White blood cell count	3.1×10^9/L
Bicarbonate	24 mEq/L	Neutrophils	59%
Glucose	133 g/L	Bands	28%
AST	63 IU/L	Lymphocytes	3%
ALT	99 IU/L	Monocytes	7%
ALP	105 IU/L	Eosinophils	1%
LDH	507 IU/L	Active lymphocytes	2%

ALT, Alanine aminotransferase; *ALP,* alkaline phosphatase; *AST,* aspartate aminotransferase; *LDH,* lactate dehydrogenase.

the next few days and eventually underwent extubation on day 7 in the ICU. Blood gas values of pH 7.43, $Paco_2$ 50 mm Hg, Pao_2 123 mm Hg, O_2 saturation 99% were obtained with the patient receiving 2 L supplemental oxygen. The patient's condition continued to improve, and she was discharged having spent 16 days in the hospital.

DISCUSSION

More than 7 million Americans travel every year to countries where malaria transmission occurs, and hundreds become infected with *P falciparum*, the malaria species responsible for nearly all malaria deaths.[3] Falciparum malaria may be accompanied by severe complications including cerebral malaria, severe anemia, hypoglycemia, renal failure, shock state, and respiratory distress syndrome. It is common, in adults, for more than one of these complications to occur in combination during the same illness.[2] In this report we present a young woman who had severe Falciparum malaria with several complications.

Adult respiratory distress syndrome (ARDS) is a rare but severe, and often fatal, manifestation of Falciparum malaria in adults.[2] It mostly occurs in patients who initially have cerebral malaria or in elderly patients and is often complicated by concomitant bacteremia.[2] This was not the case in the patient described. An interesting aspect of this patient's case was that as her parasitemia resolved with treatment, marked dyspnea, hypoxemia, and diffuse lung infiltrate developed.

The management of ARDS in Falciparum malaria is difficult. It consists of starting intravenous antimalarial drugs at standard doses, intubation, and ventilating the patient's lungs early by use of high concentrations of oxygen. Anemia should be treated with blood transfusion, but it is imperative to avoid fluid overload.

The pathogenesis of severe Falciparum malaria has been outlined by Urquhart.[4] It starts when inoculated malarial sporozoites invade liver cells and develop into schizonts, which then release merozoites into the bloodstream. Merozoites invade RBCs, degrade their contents, and grow to become trophozoites and, subsequently, multinucleated schizonts. Falciparum malaria produces its clinical effects by sequestration and destruction of parasitized RBCs in the capillaries and venules of the spleen, brain, lungs, liver, and bone marrow. The clinical effects from these events include anemia, jaundice, reduced level of consciousness, renal failure, hepatosplenomegaly, and disseminated intravascular coagulation.[2]

An erythrocyte rosette forms when infected red cells containing ring stages of the parasite, which cannot deform in the usual way, become lodged in the pulmonary vasculature.[4] The development of an inflammatory response to these parasites leads to the release of mediators including interleukin (IL)-1, IL-6, IL-8, platelet activating factor, tumor necrosis factor, and interferon-γ.[5] The inflammatory process leads to the release of toxic substances by macrophages and neutrophils, which then leads to alveolar and endothelial damage and capillary leakage. Fluid overload and hypoalbuminemia could exacerbate the capillary leak.

Falciparum malaria is a medical emergency. Travelers to malaria-endemic areas should be advised strongly to use malaria prophylaxis. Patients with Falciparum malaria should be monitored closely with respect to their level of consciousness and for signs of respiratory distress. Such patients should be sent to an ICU for addi-

tional management. Physicians caring for patients who have recently traveled to malaria-endemic areas need to anticipate the possible development of malaria with all of its complications, including ARDS.

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