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Malaria retinopathy and cerebellitis in a 9-year-old boy in the United States

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Abstract

Malarial retinopathy is characterized by retinal whitening, vessel change, and hemorrhages usually associated with a white center. We present the case of a 9-year-old boy who presented with a systemic *Plasmodium falciparum* infection, hemorrhagic cerebellitis and malarial retinopathy characterized by “fire flare” hemorrhages (scleral icterus with subconjunctival hemorrhages), Roth spot-like hemorrhages, and subhyaloid hemorrhage. To our knowledge, this is the first reported case of hemorrhagic cerebellitis secondary to *P. falciparum* infection in the United States.

Case Report

A 9-year-old African American boy presented to the emergency room at Children’s Memorial Hermann Hospital, Houston, Texas, with complaints of lethargy, nausea, abdominal pain, tachypnea, a blood pressure of 98/38 mm Hg, and bilateral “fire flare hemorrhages”—a combination of icteric sclera with overlying patchy subconjunctival hemorrhage. Blood smear analysis was positive for *Plasmodium falciparum*. Two weeks prior he had returned from 2 months of travel in Tanzania, a country known as an endemic region of *P. falciparum* malaria.^{1, 2} He subsequently developed hypovolemic shock, respiratory distress and was intubated for airway protection. Peripheral blood analysis showed thrombocytopenia, severe microcytic hypochromic anemia, and leukocytosis. Liver function tests and coagulation profiles were also abnormal. *P. falciparum* parasitemia testing revealed a parasite load of 20%-22%. Continuous intravenous infusion of quinidine at 0.0125 mg/kg/min and clindamycin at 5 mg/kg every 8 hours was initiated. Three days after admission, magnetic resonance imaging of the head showed diffuse cerebellar swelling with

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an edematous cerebellar cortex accompanied by several small hemorrhages, indicating hemorrhagic cerebellitis (Figure 1).

The following day, retinal hemorrhages with whitening in the center were noted bilaterally, in addition to a subhyaloid hemorrhage in the macula in the left eye (Figure 2). The patient was examined again 12 days after initial evaluation. Visual acuity was 20/25 in the right eye and 20/70 in the left eye. The retinal hemorrhages were improving, but the subhyaloid hemorrhage in the left eye remained, partially obstructing the fovea. The subconjunctival hemorrhages had resolved.

Discussion

The Global Burden of Diseases, Injuries, and Risk Factors Study estimated that in 2010, over 710,000 children under the age of 10 died from malaria.³ The pathogenesis of cerebral malaria appears to result from the sequestration of parasitized erythrocytes in the microvasculature of the central nervous system, leading to blockage of blood supply and tissue hypoxia.⁴ Studies have shown that hemorrhage in the small vessels of the cerebellum often occurs first because of a higher vascularity and lower blood flow rate compared to the cerebral cortex. For this reason, cerebellar pathology presents before cerebral signs such as confusion, delirium, personality change, or paresis.⁵ Although acute cerebellitis following viral infections is well known in the United States, to our knowledge, our patient is the first reported case of hemorrhagic cerebellitis secondary to *P. falciparum* infection in the United States.

Retinal examination plays a unique role in the diagnosis of a patient with suspected cerebral malaria⁶ and offers valuable insight into the degree of sequestration in the microvasculature and the prognosis of the disease^{7,8}; the presence of retinal hemorrhages in a child with cerebral malaria has been shown to be associated with increased disease severity. Taylor and colleagues⁹ found that on autopsy of a group of children with suspected cerebral malaria, 74% of patients (17/23) with cerebral malaria displayed retinal hemorrhages prior to death. By contrast, in those children that did not have cerebral malaria, none (0/7) had retinal hemorrhages. Beare and colleagues⁸ reported that retinopathy was present in 61% of children (170/278) with cerebral malaria. They also noted a trend of increasing fatal outcome with the number of retinal hemorrhages: 12% of patients (10/85) with 1-5 retinal hemorrhages had fatal outcomes compared to 21% (6/28) with 6-20 hemorrhages, 58% (7/12) with 21-50 hemorrhages, and 75% (3/4) with >50 hemorrhages ($P < 0.001$).

With increasing globalization, physicians should be equipped to assess patients with suspected cerebral malaria infection. Although not all patients with subconjunctival hemorrhages and abnormal liver function tests need to be evaluated for retinal hemorrhages, an ocular examination may help elucidate cases of cerebral involvement in patients with malaria. The retinal examination can also be a valuable tool in the confirmation of the diagnosis of cerebral malaria and assist the physician in providing a prognosis.^{7,8} In endemic areas, an ocular examination should be performed in patients with fevers, abnormal liver function tests, and concern for malaria. As Beare and colleagues⁶⁻⁸ discussed in their series of papers, the severity of the retinopathy is strongly related to the overall morbidity

and mortality of the patient. It is important for the physician to recognize early signs of retinopathy as related to cerebellar inflammation and treat the patient as quickly as possible.

Literature Search

PubMed was searched using the following terms: Plasmodium falciparum, retina, retina malaria, malaria hemorrhagic cerebellitis, malaria cerebellitis, cerebral malaria hemorrhagic, and Plasmodium falciparum *cerebellitis*.

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FIG 1.
A, Sagittal T1-weighted magnetic resonance image demonstrating diffuse cerebellar edema.
B, Axial T2-weighted cut with several hemorrhages noted in the cerebellum (B, indicated by arrow).

FIG 2. Fundus photographs displaying Roth spots in the right eye (A) and Roth spots in the left eye (B) with a macular subhyaloid hemorrhage.