A patient with bilateral midbrain syndrome due to *Plasmodium falciparum* infection - a rare presentation

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Abstract

Cerebral malaria is a serious complication of *Plasmodium falciparum* infection with a high mortality rate, usually present with diffuse cerebral involvement and rarely with focal neurologic deficit. Here we report a case of a young adult without any risk factors for stroke who presented with quadriparesis and was diagnosed to have bilateral midbrain stroke-like syndrome due to *Plasmodium falciparum* malaria. This is an unusual presentation of *Plasmodium falciparum* malaria. In tropical countries like India, all patients who present with fever and neurologic deficit should be tested for malaria.

INTRODUCTION

Malaria is a common parasitic disease caused by a protozoan from the genus Plasmodium. It is the most important parasitic disease in the world. *P. falciparum* infects around 234 million people worldwide with 2.5 million death per year. Here we present a case presenting with quadriparesis due to bilateral midbrain stroke-like syndrome as a result of *P. falciparum* infection, which is a very atypical presentation of cerebral malaria.

CASE REPORT

A 26-year-old male patient presented with headache, high rise temperature, altered sensorium and weakness of all four limbs developed over two days. Fever was intermittent, associated with headache, chills and rigor. There was no history of head trauma, seizure, alcohol or illicit drug intake. The patient was non-diabetic and non-hypertensive. Patient’s relative gave a history of his inability to move the right side of the body initially, gradually involving all four limbs over two days. Bladder was involved with acute retention of urine following which he was catheterized.

On examination, the patient was drowsy but arousable. He was disoriented to time, place and person. General examination revealed raised temperature and mild pallor. Blood pressure was 120/84 mmHg, pulse was 100/minute and regular in rhythm. Nervous system examination revealed no neck rigidity or Kernig’s sign. The cranial nerve examination revealed bilateral complete ptosis, pupil was mid dilated in left eye and fully dilated in right eye. Both eyes were down and out and not reacting to light. Ophthalmoscopic examination was normal. There was decreased sweating in the left half of the face. Other cranial nerve examinations were normal. Motor system examination revealed upper motor neuron type quadriparesis, right more than left. Sensory impairment in all modalities was present in both sides. Plantar reflex was bilaterally extensor with loss of all other reflexes. Cerebellar sign and gait could not be examined due to weakness. The patient was diagnosed to have bilateral midbrain (left more than right) involvement, also with left Horner’s syndrome. Cardiovascular, respiratory, gastrointestinal and reticulo-endothelial systems examination were normal.

Laboratory investigations revealed no abnormality except mild anemia (hemoglobin 12.50gm%). Peripheral smear showed mature schizonts and gametocyte form of *Plasmodium falciparum* malaria (Figure 1) with marked parasitaemia (30%). Blood antigen test using *P. falciparum*-specific histidin-rich protein (PfHRP2) was positive. Blood sugar was low (45mg/dl). Blood biochemistry workup including serum urea, creatinine, ammonia, electrolytes was normal. Serum HBsAg and anti HCV markers were negative. Liver function test and lipid profile were normal. Blood for dengue antibody, HIV (I & II) and leptospira antibody tests were negative. Blood and urine culture revealed no growth. Electrocardiogram, chest x-ray, ultrasonogram of abdomen, echocardiography were normal.

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CT of brain showed bilateral acute infarction of midbrain, left more than right (Figure 2). Cerebrospinal fluid (CSF) examination showed no abnormality. MR imaging of brain (DWI sequence) showed bilateral midbrain infarction, left more than right (Figure 3). MR angiography, MR venography of brain and carotid Doppler studies were normal. Blood for Rheumatoid factor, antinuclear factor, antineutrophil cytoplasmic antibody (ANCA), anticardiolipin antibody, homocysteine, lipoprotein-α (Lpa) were normal. A diagnosis of bilateral midbrain syndrome due to cerebral malaria (*P. falciparum* infection) was made.

He was treated with intravenous artesunate (2.4mg/kg) stat followed by doses at 12 and 24 hours, then once daily for 5 days. Following which, oral artemether-lumefantrine combination (1.5/9mg/kg twice daily) was started and continued for three days. Supportive therapy and oral aspirin (75mg/day for three months) were also given. His fever subsided and consciousness level improved. However, there were residual neurological deficits of weakness, pupillary changes including Horner’s syndrome when he was discharged at the 11th day of admission. On follow up after 6 months, he has recovered fully without any neurological deficit.

**DISCUSSION**

Malaria is a major health problem in tropics like in India. More than 300-500 million people globally are affected each year, 25% in Southeast Asia and 70% in Africa. Among Southeast region, 75% reported cases are from India. Cerebral malaria is the most serious complication of *P. falciparum* infection.
infection with high mortality specially in children and pregnant women.

Cerebral malaria usually presents with diffuse encephalopathy, convulsion to coma along with other systemic complications. Focal neurologic signs are infrequent. The manifestations include ataxia, hemiplegia, aphasia, cortical blindness and extra pyramidal syndrome. Our patient predominantly presented with focal neurologic deficit as stroke-like bilateral midbrain syndrome. Altered sensorium in our patient was probably due to involvement of reticular activating system as well as diffuse encephalopathy. Our patient was a young adult without any risk factors for stroke, such as hypertension, diabetes mellitus, dyslipidemia, smoking, sedentary lifestyle, previous history of stroke or any cardiac ailments. It was thus likely that the posterior circulation stroke was due to \textit{P. falciparum} malaria. This was supported by the midbrain syndrome occurring in the same time as fever and headache and improved dramatically with antimalarial treatment. Ischaemic stroke involving posterior circulation presenting as bilateral midbrain syndrome is a rare presentation of cerebral malaria. To the best of our knowledge, our case represents the first reported association of cerebral malaria with bilateral midbrain infarction in the English literature.

The pathophysiology of cerebral malaria is largely unknown. Parasitized erythrocytes express high molecular transmembrane protein \textit{P. falciparum} erythrocyte membrane protein 1 (PfEMP1), which can bind to CD36 receptors in different organs except brain vessels which lack CD36 receptor and intercellular adhesion molecule 1 (ICAM 1) on brain endothelium, chondroitin sulfate B in the placenta. However, cytoadherence of parasitized erythrocytes in the microcirculation of capillaries and post-capillary venules of brain parenchyma may be enhanced by intercellular adhesion molecule 1 (ICAM 1) which is over expressed on brain endothelium by inflammatory cytokines like TNF-\(\alpha\), IL-1, IL-6 and IL-18 and presence of CD36 receptor on platelets which can bridge parasitized red cells and vascular endothelial cells in brain parenchyma. In cerebral malaria, red cell deformability is also reduced. These rigid erythrocytes along with auto agglutinated red cells further compromise microcirculation. All these factors may play a pathogenic role for formation of small vessels stroke as in our case (MR angiography brain was normal, which excluded large vessels stroke).

Regarding management, our patient was treated initially with intravenous artesuanate followed by oral artesunate combination therapy (ACT) when the patient regained consciousness. Aspirin was also given for three months.

In conclusion, our patient suggests that in the tropical countries where malaria is endemic, every patient who presents with fever and stroke like neurologic symptoms should be tested for malaria.

**DISCLOSURE**

Conflict of interest: None

**REFERENCES**