Magnetic Resonance Features of Cerebral Malaria

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Background: Cerebral malaria is a major health hazard, with a high incidence of mortality. The disease is endemic in many developing countries, but with a greater increase in tourism, occasional cases may be detected in countries where the disease is not prevalent. Early diagnosis and evaluation of cerebral involvement in malaria utilizing modern imaging modalities have an impact on the treatment and clinical outcome.

Purpose: To evaluate the magnetic resonance (MR) features of patients with cerebral malaria presenting with altered sensorium.

Material and Methods: We present the findings in three patients with cerebral malaria presenting with altered sensorium. MR imaging using a 1.5-Tesla unit was carried out. The sequences performed were 5-mm-thick T1-weighted, T2-weighted, fluid-attenuated inversion-recovery (FLAIR), and T2-weighted gradient-echo axial sequences, and sagittal and coronal FLAIR. Diffusion-weighted imaging was performed with $b$ values of 0 and 1000 s/mm$^2$, and apparent diffusion coefficient (ADC) maps were obtained.

Results: Focal hyperintensities in the bilateral periventricular white matter, corpus callosum, occipital subcortex, and bilateral thalami were noticed on T2-weighted and FLAIR sequences. The lesions were more marked in the splenium of the corpus callosum. No enhancement on postcontrast T1-weighted MR images was observed. There was no evidence of restricted diffusion on the diffusion-weighted sequence and ADC map.

Conclusion: MR is a sensitive imaging modality, with a role in the assessment of cerebral lesions in malaria. Focal white matter and corpus callosal lesions without any restricted diffusion were the key findings in our patients.

Key words: Cerebral malaria; MR; Plasmodium falciparum

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Malaria is a major public health problem in developing countries. Cerebral involvement occurs in 2% of patients infected with Plasmodium falciparum (1,2). Affected patients present with various nonspecific neurologic manifestations. Modern imaging techniques are increasingly being utilized for the clinical evaluation of altered sensorium. Magnetic resonance (MR) study is infrequently performed in cases of cerebral malaria, and there are only a few reports describing the diffusion-weighted imaging in clinical or experimental malaria (3, 4). We report the MR findings of cerebral malaria with altered sensorium in three patients.

Material and Methods

A total of 51 patients with malaria were admitted for management at our tertiary-care hospital between July 2006 and December 2006. Forty-one patients had complicated malaria. Among the patients with complications, acute renal failure was observed in 25 patients, hepatic failure in 17, disseminated intravascular coagulation in six, acute respiratory distress syndrome in three, and hypoglycemia in two. A total of 21 patients presented with altered sensorium. Headache was a presenting feature in four, six had seizures, and neck rigidity was present in two patients. All patients with...
complicated malaria except one had *Plasmodium falciparum* on peripheral smear examination (one patient had *Plasmodium vivax* on peripheral smear). Cerebral imaging was performed in 14 patients: computed tomography (CT) of the head in nine and MR of the brain in five. Three (two males and one female) of the patients had abnormalities on MR. Peripheral blood smear examination in all three cases revealed the presence of *Plasmodium falciparum* gametocytes. Cerebrospinal fluid study showed no cells and a normal protein level. The clinical details of the study cases were as follows.

Case 1: A 30-year-old man was evaluated for loss of consciousness after a 10-day history of high-grade fever and headache. Neurological examination revealed a Glasgow coma score of 6 and exaggerated deep tendon reflexes. He had acute renal failure, acute respiratory distress syndrome, and deranged liver function tests at the time of presentation. Serum creatinine was 707.2 μmol/l, and blood urea was 46.4 mmol/l.

Case 2: A 28-year-old man presented with altered sensorium and seizures following a 13-day history of high-grade fever with chills and rigors. There were no meningeal signs. He had deranged liver and renal function tests.

Case 3: A 22-year-old woman presented with fever, chills, acute mental status change, and involuntary movements. She had a few episodes of generalized tonic clonic seizures prior to deterioration in mental status. Physical examination revealed exaggerated deep tendon reflexes and no meningeal signs.

MR examinations were performed on a 1.5-Tesla unit. The sequences performed were 5-mm-thick T1-weighted, T2-weighted, fluid-attenuated inversion-recovery (FLAIR), and T2-weighted gradient echo axial sequences with sagittal and coronal FLAIR. Diffusion-weighted imaging was performed with *b* values of 0 and 1000 s/mm², and apparent diffusion coefficient (ADC) maps were obtained.

**Results**

**Imaging findings**

Case 1: MR imaging performed 24 hours after the onset of neurological symptoms showed focal hyperintensities in the bilateral periventricular white matter and corpus callosum on T2-weighted (Figs. 1A and B) and FLAIR (Fig. 1C) sequences. The lesions were more marked in the splenium of the corpus callosum. No evidence of restricted diffusion was seen on the diffusion-weighted sequence and ADC map. The patient had near-complete recovery from the illness except for deficit in the memory after 1 week following treatment with intravenous quinine dihydrochloride.

Case 2: MRI revealed a focus of hyperintensity in the left occipital subcortical region on T2-weighted and FLAIR sequences (Fig. 2), likely to be subcortical infarct. No evidence of hemorrhage was noted on the T2-weighted gradient-echo sequence. Diffusion was not restricted on the diffusion-weighted sequence and ADC map. The patient improved clinically and regained consciousness after intravenous antimalarial treatment.

Case 3: MRI showed symmetrical hyperintensity involving the bilateral thalami on T2-weighted (Fig. 3A) and FLAIR (Fig. 3B) sequences, without any evidence of hemorrhage on the T2-weighted

Fig. 1. Axial (A, B) and sagittal FLAIR (C) images show focal areas of hyperintensity in the periventricular white matter and corpus callosum.
gradient sequence. No enhancement on postcontrast T1-weighted MR images was observed, and no restriction of diffusion was seen on diffusion-weighted imaging (Figs. 3C and D).

No follow-up imaging was performed in these patients.

Discussion

Cerebral malaria has a high incidence of mortality. Even with appropriate treatment and intensive care, 15–25% of patients die (5, 6). Therefore, early diagnosis and treatment may affect the clinical outcome. Although all three of our cases were adults, children are affected far more frequently than adults in endemic areas. Affected patients may present with nonspecific neurological signs such as behavioral changes, transient extrapyramidal signs, and isolated cerebellar ataxia. The symptoms can progress to altered sensorium followed by seizures.

Two mechanisms for the pathogenesis of neurological symptoms have been described: 1) blockage of capillaries by the infected red blood cells and 2) potential cerebral toxicity by cytokines (1, 7). Cytokine release may result from nonspecific immune inflammatory response and endothelial activation (7, 8). The above two factors can lead to vascular engorgement and vasodilatation with reduction of cerebral blood flow and edema. Observations on histological examination include sequestration of infected erythrocytes in brain vessels, mainly in cortical and perforating arteries, with perivascular ring-like hemorrhages and white matter necrosis (9, 10).

There are only a few reports of MR imaging in cases of cerebral malaria. LOOAREESUWAN et al.
(11) reported the presence of increased brain volume and brain swelling in patients with cerebral malaria. Other MR findings described in the literature are diffuse cerebral edema (1, 2), focal cortical and subcortical infarcts (12), and focal or diffuse changes in white matter, centrum semiovale (1, 13), and corpus callosum (1). Central pontine myelinolysis (14), myelinolysis in the upper medulla (15), cerebellar syndrome with demyelination, and microinfarcts of the cerebellar hemispheres (2) have also been reported. Similar observations have been documented in experimental cerebral malaria in mice models. An MRI and MRS study in mice revealed structural, vascular, and metabolic cerebral alterations (4). The findings in the experimental study were attributed to the sequestration of cells in small vessels resulting in ischemic lesions along with the synergistic action of proinflammatory cytokines producing deleterious vascular effects. Vascular dysfunctions including blood–brain barrier breakdown, reduced cerebral blood flow, and arterial flow perturbation were observed. In our first case, white matter hyperintensities had characteristics of edema, which may be due to ischemia or toxic injury (1). The cortical infarcts observed in case 2 may be the result of blockage of capillaries by infected erythrocytes (1). To the best of our knowledge, the MR finding of thalamic abnormality, as observed in our case 3, is the first such description, although bilateral thalamic lesions with or without cerebellar involvement on CT have previously been described by Patankar et al., who attributed the changes to cytotoxic edema (2). We did not find any evidence of restricted diffusion on the diffusion-weighted sequence and ADC map, which is contrary to the findings reported by Sakai et al. (3).

In conclusion, MR imaging is a sensitive modality to evaluate the neurological manifestations of cerebral malaria. The findings may include focal white matter and corpus callosal lesions, subcortical infarcts, and symmetrical thalamic abnormality. In this study, diffusion was not restricted on diffusion-weighted imaging in the affected patients.

References