

No Coma, but Expressive Dysphasia with Cerebellar Signs: An Unique Presentation of Cerebral Malaria

Dear Editor,

Malarial infection is not uncommonly complicated by cerebral involvement and poses significant mortality and morbidity especially in children. Similar complications may be seen in the adult population. Cerebral malaria is defined as encephalopathy that presents with impaired consciousness, delirium, and/or seizures. Neurological deficits are commonly seen as sequelae of cerebral malaria rather than as presenting symptoms or signs.

We present here a unique case of cerebral malaria with focal neurological deficits but without alteration in conscious level. Keeping rare presentations of common illnesses in mind, clinicians should consider the possibility of cerebral malaria in a patient with neurological deficits and a history of fever and travel in endemic areas.

Case Presentation

A 56-year-old gentleman presented to us with a 4-day history of fever and sudden onset of slurred speech with difficulty in expressing himself on the day of presentation. Three weeks earlier, he had gone on a 5-day jungle exploration trip in northern Kedah without malaria prophylaxis. The fever was intermittent and was associated with chills and rigors. There was no loss of consciousness or altered behaviour. He had no past medical illness or history of prior hospitalisation. He did not have neurological symptoms prior to presentation or pre-existing neurological illness. He was not on any over-the-counter medication nor did he consume traditional medicines.

On examination, the patient was febrile with expressive dysphasia and left cerebellar signs with dysmetria, and dysdiadochokinesia. Neurological examination was otherwise normal. Mini mental state examination could not be performed due to his expressive dysphasia. Systemic examination revealed no significant findings, such as irregular pulse, carotid bruit and cardiac murmur. Because of a high clinical suspicion, a peripheral blood film was requested and this confirmed the presence of *Plasmodium falciparum* with a parasite count of 6634 parasites per milliliter of blood.

Initial investigations revealed that he had normochromic normocytic anaemia with haemoglobin 8.8 g/dL, leukocyte count $5.6 \times 10^9/L$ and platelet count $266 \times 10^9/L$. There

was also renal impairment with urea of 21.2 mmol/L and creatinine 174 $\mu\text{mol/L}$, which was later corrected with hydration. Corrected calcium was 2.3 mmol/L. Coagulation profile showed PT 11.5s, aPTT 21.0s and INR of 1.1. Bilirubin and alanine transaminase were 19 $\mu\text{mol/L}$ and 63 U/L respectively. The random blood sugar was 6.0 mmol/L. The cerebrospinal fluid analysis revealed a normal cell count, protein level of 250 mg/L and a glucose level of 4.4 mmol/L. The cerebrospinal fluid was negative for herpes simplex viral polymerase chain reaction, cryptococcal antigen, and Indian ink. The blood, urine and cerebrospinal fluid cultures were also negative. Computed tomography and magnetic resonance imaging of the brain were normal. Autoimmune studies and leptospira serology were not performed. There were no dyslipidaemia or dysglycaemia. Echocardiogram was normal.

The patient was given intravenous quinine, which was subsequently changed to quinine and doxycycline oral therapy. With the initiation of therapy, the dysphasia, dysmetria, and dysdiadochokinesia, improved gradually. On day 10 of presentation, blood film revealed no more malaria parasites. Upon discharge on day 13, there was some residual expressive dysphasia, but no dysmetria and dysdiadochokinesia. When the patient returned again to the outpatient clinic a month later, he had made a full recovery with normal speech and cerebellar function.

Discussion

The presentation of the patient is unique in that no coma was observed. Instead, focal neurological signs were the presenting complaint, and recovery was achieved with anti-malarial therapy. Although the patient was not coma as was expected according to the strict definition of a cerebral malaria, the presence of *Plasmodium falciparum* with neurological symptoms, makes the diagnosis most likely. All patients with *P. falciparum* malaria with neurological manifestations of any degree should be treated as cases of cerebral malaria.¹

There are sporadic case reports on cerebral malaria associated with focal neurological deficits as presenting symptoms. Leopoldino et al² reported a case of cerebral malaria presented with left hemiparesis in 1999. However, the imaging studies revealed findings consistent with an

ischaemic stroke with persistent deficits after complete eradication. Currie et al³ also reported 2 patients with focal neurological deficit at presentation, which was later found to be due to pre-existing neurological disease prior to contracting malaria. However in our patient there were no signs and symptoms of any preexisting neurological disease. Idro et al⁴ and Sattar et al⁵ have documented cases of focal neurological deficits with cerebral malaria without pre-existing neurological diseases. This suggests that there may be a separate mechanism which causes the neurological damage seen in cerebral malaria.

As the parasite stays only in the blood vessels, the question of how the infection causes neuronal dysfunction needs to be considered. Blood brain barrier dysfunction has been proposed to explain the observed phenomenon. Adam et al⁶ in 2002, suggested that binding of infected erythrocyte to Inter-Cellular Adhesion Molecule 1 (ICAM-1) on the cerebrovascular endothelium induces complex intracellular signaling cascade events, which affect the cytoskeletal-cell junction, causing alterations in the blood brain barrier. Localised increase in blood brain barrier permeability may cause localised increase in cytokines and inflammatory mediators that may disrupt neuronal function and predispose a patient to neurological deficit and seizures.⁶⁻⁸

The presence of expressive dysphasia and left cerebellar signs imply the involvement of the Broca's area and the left cerebellar hemisphere respectively. Simultaneous involvement of these 2 very distant intracranial sites are obviously a result of occlusion of 2 different vessels and activation of inflammatory process at 2 distinct sites. The pathological process may be postulated to be occlusions of small vessels feeding these areas by "rosette" of infected erythrocytes or their "sticky" schizon causing micro-inflammatory or localised inflammation rather than an overt large inflammatory area with oedema or infarct would will be evident in a brain imaging study.

Recovery following anti-malarial therapy may indicate underlying ischaemia rather than established infarcts similar to the pathogenesis of transient ischaemic attacks (TIA). An alternative explanation is resolution of the inflammation in the affected areas as the parasites are eradicated. The latter postulation is much more plausible as recovery occurred over a period of days. Ischaemia would have been more likely to progress to infarcts, resulting in established permanent neurological damage if not reversed within 24 hours.

Conclusion

This case depicts the importance of cerebral malaria as a differential diagnosis of a pyrexial patient with neurological deficits in tropical countries. A simple blood film for malaria parasites had initiated the proper therapy and spared the

patient from possible morbidity and mortality. This case also illustrates the unique neurological manifestations of cerebral malaria, which improved with quinine therapy.

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