CASE REPORT

Cerebral Malaria Due to Plasmodium Vivax: An Unexpected Presentation

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ABSTRACT

Cerebral malaria (CM) is a severe encephalopathy typically caused by Plasmodium falciparum (*P. falciparum*), presenting with altered consciousness, confusion, psychomotor agitation, and/or seizures. Diagnostic criteria require the laboratory confirmation of *P. falciparum* infection, alongside the systematic exclusion of alternative etiologies for encephalopathy. However, rare cases implicating Plasmodium vivax (*P. vivax*) as the causative agent have been reported.

Pakistan is endemic for *P. vivax*, generally considered a benign cause of malaria, and encephalopathy is almost never encountered in clinical practice. This study presents a rare case of CM in a 16-year-old boy caused solely by *P. vivax*, confirmed on thick and thin peripheral smears showing rings and trophozoites. The patient was started on intravenous artesunate, to which he responded well, and was discharged on primaquine for radical cure. This case highlights the need for clinical vigilance, timely intervention, and recognition of *P. vivax* as a potential cause of CM, particularly in endemic regions.

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Introduction

Malaria is endemic in the developing world and is caused by various forms of Plasmodium, of which Plasmodium vivax *(P. vivax)* and Plasmodium falciparum (*P. falciparum)* are the most prevalent. According to the World Health Organization (WHO), the disease burden of *P. falciparum* is 9.87%, and that of *P. vivax* is 7.94%. [(1)(2)].

Malaria has many severe complications, including cerebral malaria (CM) considered to be a neurological complication of *P. falciparum* malaria, manifesting as altered consciousness, confusion, psychomotor agitation, and/or seizures.

CM syndrome affects multiple organs and presents with pyrexia, lethargy, headache, myalgia, loss of appetite, and confusion, followed by unconsciousness. Coma, seizures, and brainstem signs are the cardinal features of CM. [(3)] Reports suggest that neurological observations are more common in the pediatric age group. Blood dyscrasias, retinopathy, blood gas, and electrolyte abnormalities are also reported. [(4)]

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CM must be suspected in any patient with a fever with altered consciousness residing in or recently traveled to a malaria-endemic area within the last 3 months. However, it typically presents 1 to 3 weeks after exposure. A thick, Giemsa-stained blood smear is used to confirm the diagnosis. Three negative peripheral blood smears 8 to 12 hours apart rule out the diagnosis. A thin smear is used to identify the species of Plasmodium and quantify parasitemia. [5] Rapid testing kits can be useful when smears are negative, but they do not quantify parasitemia, and they have low sensitivity and specificity if the parasite load is limited. Polymerase chain reaction tests have better sensitivity as compared to smears, but are costly and do not provide estimates of parasite load. [6] A lumbar puncture can exclude other neurological diseases like meningitis and encephalitis.

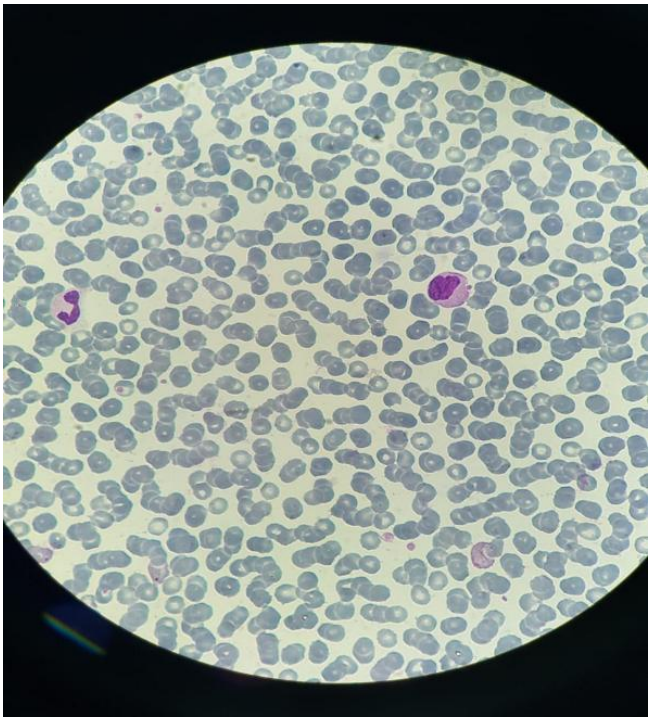


Figure 1: Rings and trophozoites of Plasmodium vivax can be seen.

CM must be managed in the highest available care unit with timely administration of intravenous antimalarial drugs. Complications of CM, such as seizures, hypoglycemia, and high fever, should be averted or recognized and managed swiftly. Fluid, electrolyte, and acid-base imbalances must be corrected. Proficient nursing care of the comatose patient is essential. Supportive therapy should be refrained from unless safety and efficacy have been demonstrated. [7]

According to WHO, CM is manifested by seizures followed by coma for an hour, *p. falciparum* parasitemia is confirmed by peripheral smear, and no other cause of seizure or unconsciousness is identified. [6] A confirmed *P. falciparum* infection is a prerequisite for diagnosis, provided that other potential causes of encephalopathy have been ruled out. [8]

Until recently, *P. vivax* was widely considered a benign cause of malaria. [9][10] However, rare case reports have highlighted its potential to cause CM, a seldom-recognized complication. This case adds to the limited literature from malaria-endemic regions like Pakistan, where *P. vivax* is not typically associated with severe neurological outcomes, underscoring the importance of considering *P. vivax* as a differential diagnosis in patients presenting with unexplained encephalopathy, even when *P. falciparum* malaria has been ruled out. This report adds to the growing body of evidence that *P. vivax* alone can lead to severe cerebral manifestations, prompting a re-evaluation of diagnostic and treatment protocols.

Table 1. Table showing tests performed on the subject to exclude other causes.

Test name	Sampl	Test	Result
P. vivax	Blood	Smear ICT	Rings & trophozoites seen Positive
P. falciparum	Blood	Smear ICT	Not seen Negative
Dengue NSI antigen	Serum	ELISA	Negative
LFT RFT	Serum Serum		Normal Normal
Full Blood Count	Serum		Hb:13.5 g/dl TLC 11300 /cmm Platelets:116000/ cmm
Random Blood Sugar	Serum		78.3 mg/dl
Serum Calcium Serum Magnesium	Serum Serum		9.79 mg/dl 1.74 mg/dl
Serum Electrolytes	Serum		Normal
CSF-RE	CSF		Colorless Cell count 4/cmm Proteins 30mg/dl Glucose 84mg/dl
CT scan of brain	–		Normal
MRI with MRV	–		Normal
Electroencephalogram	–		Normal

Case presentation

A 16-year-old male from Pakistan, with no previously known medical conditions, having high-grade fever and headache for the past 3 days, presented to the Emergency Department of the Khyber Teaching Hospital with recurrent generalized tonic convulsions followed by unconsciousness for 2 hours. He was treated as a case of status epilepticus. On initial assessment, his vital signs were stable, but he was confused. Signs of meningeal irritation were positive, but the rest of the neurological examination was unremarkable. No hepatosplenomegaly was

appreciated on abdominal examination, and cardiovascular and respiratory examinations were also normal.

A full blood count revealed thrombocytopenia. All other investigations, including LFTs, RFTs, serum electrolytes, random blood sugar, serum calcium, dengue serology, and serum magnesium, were normal. A lumbar puncture was performed, revealing normal cerebrospinal fluid opening pressure and routine examination. Magnetic Resonance Imaging and Electroencephalogram were done and were consistent with features of encephalopathy (Figure 2,3). Investigations are presented in Table 1.

CM was suspected, and thick and thin smears for malarial parasite were done on two occasions, demonstrating trophozoites and rings of *P. vivax* shown in Fig. 1. ICT was performed, which was also positive for *P. vivax*. Hence, a diagnosis of CM secondary to *P. vivax* was made, and the patient started on an IV Artesunate regimen to which he responded. Upon completion of the regimen, he was discharged on Primaquine tablets for a radical cure of *P. vivax* malaria once G6PD deficiency was ruled out.

Discussion

CM is traditionally synonymous with *P. falciparum*, owing to its well-documented cytoadherence properties that allow trapping of parasitized erythrocytes in the cerebral microvasculature. In contrast, *P. vivax* has long been considered a benign species due to its low levels of parasitemia and limited reticulocyte infection. However, recent studies suggest that *P. vivax* is also capable of causing severe malaria, including cerebral complications, though through less well-understood mechanisms. [11][12]

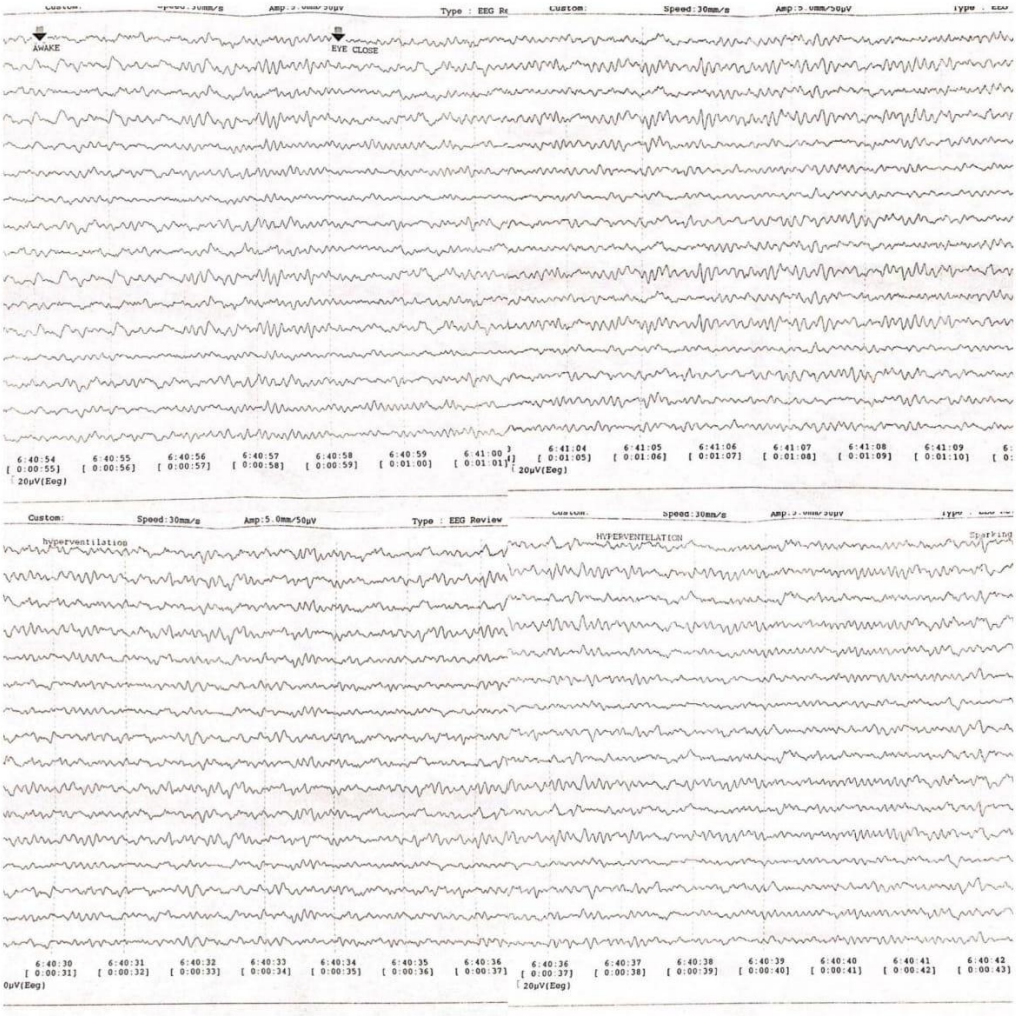


Figure 2: EEG of the patient showing normal findings

P. vivax is hypothesized to cause CM through various mechanisms, including an augmented inflammatory response, endothelial activation, and compromise of the blood-brain barrier due to

proinflammatory cytokines such as tumor necrosis factor alpha (TNF- α) and interferon gamma (IFN-γ). A high WBC count was observed in the studied patient, suggestive of inflammation. [13]

While reviewing the literature, forty-five cases of CM caused by *P. vivax* were found, mostly from India and Pakistan (67%). Around four cases were found in non-endemic regions, including the United States, Italy, and Africa. [14][15]

A recent case series from Ethiopia also reported neurological involvement in *P. vivax* mono-infections, supporting broader geographical relevance of this complication. Interestingly, some of these cases occurred in adults with no comorbidities or prior malaria episodes, as seen in the studied patient. [8]

The present patient, a previously healthy adolescent from an endemic region, developed rapidly progressive encephalopathy and seizures, with laboratory confirmation of *P. vivax* mono-infection. This aligns with recent reports highlighting that even in the absence of co-infection or comorbidities, *P. vivax* can result in life-threatening cerebral complications. Recognition of this possibility is vital for early diagnosis and appropriate antimalarial therapy, particularly in areas where *P. vivax* remains the dominant species.

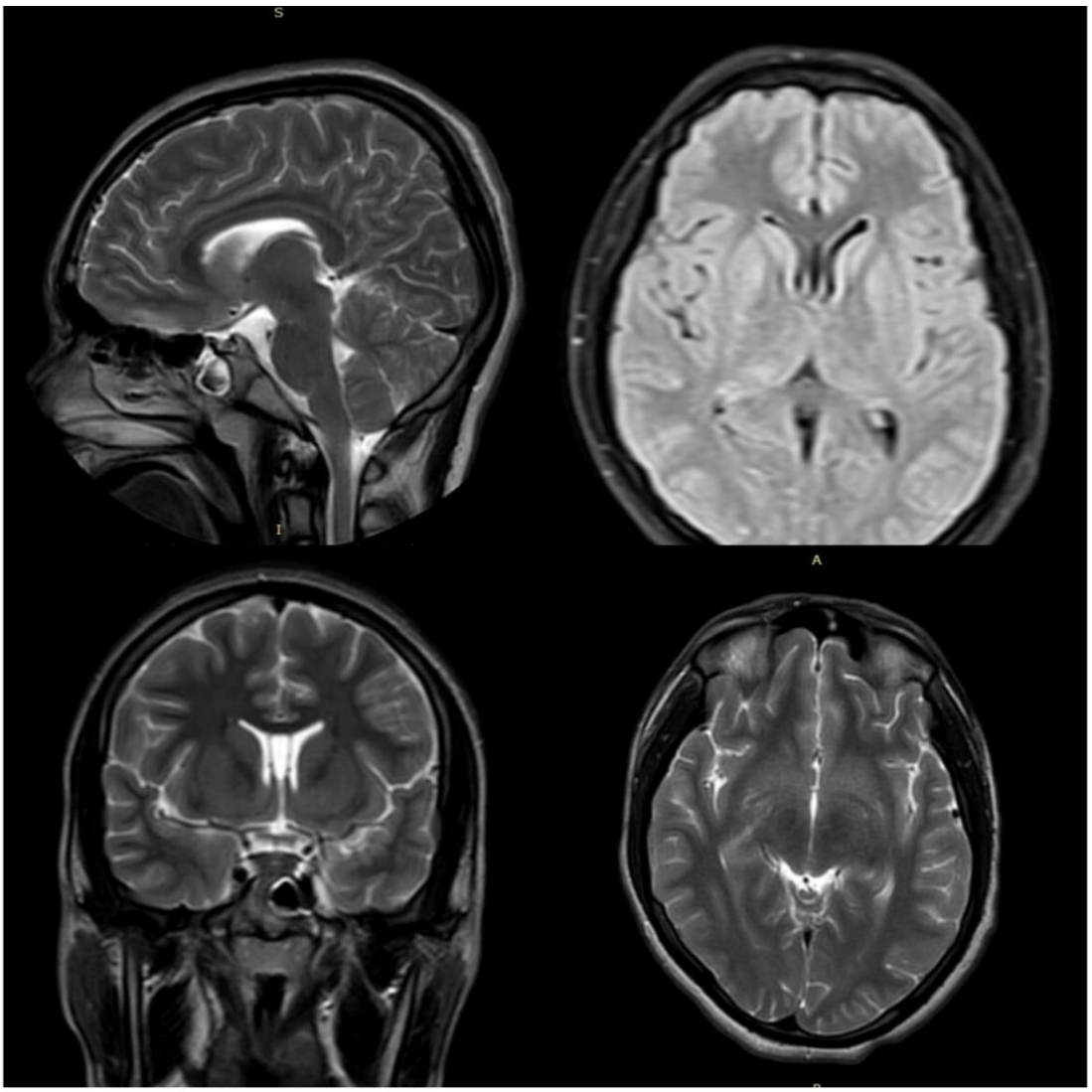


Figure 3: MRI of the patient showing normal findings

In Conclusion

This case reports a rare instance of CM caused by *P. vivax* in a 16-year-old boy from Pakistan. While typically linked to *P. falciparum*, *P. vivax* can also lead to life-threatening neurological complications. This case highlights the need to recognize *P. vivax* as a potential cause of CM, particularly in endemic regions. Early diagnosis and prompt, species-specific treatment are critical for patient recovery. In summary, CM must be suspected in a patient with neurological manifestations in endemic as well as non-endemic areas, even without a history of malaria progression.

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Author's Contribution:

M Hassaan Shah, Conceptualization of the case report, clinical data collection, and preparation of the initial manuscript draft.

Muhammad Osama, Literature review, interpretation of clinical findings, manuscript drafting, and critical revision.

Farid Ullah, Collection of clinical records and investigation results, and revision of the case presentation.

Imran Ullah, Clinical supervision, interpretation of diagnostic findings and management, and critical revision of the manuscript.

Abdul Basit, Literature review, preparation of the discussion, and manuscript revision.

Iman Hameed, Organization of clinical data, preparation of the case timeline, and manuscript revision.

Waheed Ullah, Interpretation of investigation results and revision of the clinical description and discussion.

Farhan Shahzad, Preparation of figures and legends, reference verification, and manuscript revision.

Conflict of Interest:

There was no conflict of interest.

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