# Case reports on atypical presentation of *Plasmodium falciparum* malaria in pediatric patients

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#### Abstract

Variable atypical symptoms are commonly observed in malaria caused by *Plasmodium falciparum* especially in endemic tropical nations such as India. Nystagmus is observed following involvement of the cerebellum especially during the postrecovery phase. While psychotic features such as severe agitation, hallucination, paranoia may be the early symptoms of falciparum malaria among pediatric patients, urticaria with or without fever can be the initial manifestation of the disease. As the morbidity and mortality of severe malaria are very high in India, these atypical presentations should be considered during diagnosis. We believe our report on atypical cases of falciparum malaria will sensitize doctors and health personnel about rare presentations in children and help in early diagnosis and management to reduce the severity and death toll due to the disease.

Key words: Nystagmus, Plasmodium falciparum, psychosis, urticaria

# INTRODUCTION

*Plasmodium falciparum* is one of the major causes of mortality among children in rural India. States such as Odisha have high childhood mortality due to *P. falciparum* positive malaria often occurring in various forms. Lack of awareness of atypical manifestation leads to delay in diagnosis and early management often leading to death. Upsurge of unusual features are due to development of immunity, increased resistance and injudicious use of antimalarial drugs. We present here three cases of falciparum malaria with unusual and atypical symptoms.

## **CASE REPORTS**

#### Case 1

A 15-month-old male child was admitted with the chief complains of high-grade fever for 7 days followed by altered sensorium for 1 day. On examination, child was febrile and unconscious. The child had uneventful perinatal history, no developmental delay, and no history of seizure. Blood pressure was 80/60 mmHg. Respiratory and heart rate were within normal limits. He had severe pallor. On systemic examination, he had hepatosplenomegaly with liver being around 4 cm palpable. Spleen was enlarged

and measured to be 3 cm. All other systems were examined to be normal. Blantyre scoring showed 4/10. Blood investigations showed Hb was 5.8 mg/dl; total leucocyte count 12,400/cumm, and total platelet count 65,000/cumm. Other blood investigations were within normal limits. MPICT (antigen test) was positive and peripheral smear showed multiple rings of *P. falciparum*. Final diagnosis of cerebral malaria was made. Patient was treated using intravenous (IV) artesunate followed by ACT according to WHO guidelines. On follow-up fever decreased and sensorium improved, but on day 4 of the treatment child developed bilateral nystagmus with rapid component towards the right side. Child had no gait abnormality. Cerebrospinal fluid study and contrastenhanced computed tomography were normal. After ruling out all other causes of nystagmus, it was diagnosed as an early complication of cerebellar involvement due to severe malaria. The child was followed-up and found nystagmus relieved with MPICT negative.

#### Case 2

A 6-year-male child was admitted with the chief complain of high-grade fever for 4 days with abnormal behavior and occasional vomiting. He was highly irritable, agitated, with abnormal talks. He had no history of hematemesis, melena, bladder bowel abnormality, abnormal movement or altered sensorium. He had neither relevant history nor any drug history. He had mild pallor and icterus. All vitals signs were normal except for mild tachycardia. On abdominal examination, liver was around 6 cm palpable. Spleen was around 4 cm. On neurological examination, child was highly irritable and agitated. No other abnormality found. Respiratory and cardiologic examinations were uneventful. Blood investigation suggested Hb was 7.2 mg/dl while other complete blood count (CBC) parameters were normal. Peripheral smears suggested P. falciparum rings. MPICT showed presence of P. falciparum antigen. Liver function tests were mildly raised. Patient coming from an endemic region with high-grade fever, antigenic positivity, and the absence of other risk factors for psychosis confirmed diagnosis of malaria with psychosis. Child was treated by IV artesunate with sedatives (IV lorazepam). On day 4, the fever decreased and behavior was completely normal.

#### Case 3

A 11-year-old child was presented to pediatric outpatients department with severe crampy and episodic abdominal pain with urticarial rash over face and abdomen and generalized malaise and lethargy. He had no history of recent fever, seizure, conjunctivitis, abnormal vomiting, and bowel bladder anomaly. He had no previous history of similar abnormality. On examination, child was conscious with mild pallor. All vitals were stable. On systemic examination mild splenomegaly was evident. All other systemic examinations were within the clinical range. The child was worked up for allergic disorder. CBC were normal except Hb 6.4 mg/dl and mp slide was negative. Urological examination and abdomen ultrasonography were normal. He was treated using antihistaminic and antispasmodics (injection cyclopam, injection ranitidine, and oral cetirizine tablet). On day 2 of admission the child had high-grade fever with episodic pain in abdomen and urticaria. As a child was from an endemic region of P. falciparum, MPICT (antigen) was performed. MPICT was positive along with repeat slide showed P. falciparum rings. IV artesunate was initiated according to WHO protocol along with antihistamines and antispasmodics (injection cyclopam -10 mg/dose T.D.S, injection ranitidine -1 ml IV BD, and oral cetirizine -5 mg BD). Urticaria in a malaria endemic patient nonresponsive to antihistamine drugs is an indication of underlying malaria and should be managed accordingly.

## DISCUSSIONS

*Plasmodium falciparum* is a major cause of mortality in pediatric age group.<sup>[1]</sup> Although Orissa state has about 3.6% of the total population of the country, it accounts

for 47% of *P. falciparum* cases and 34% of all reported deaths due to malaria.<sup>[1]</sup> Classic symptoms of severe malaria caused by *P. falciparum* among pediatric patients include high-grade fever, sweating, jaundice, vomiting, nausea, and pallor. According to WHO criteria impaired consciousness, prostration, respiratory distress, multiple seizures, jaundice, hemoglobinuria, abnormal bleeding, severe anemia, circulatory collapse and pulmonary edema are features of severe malaria.<sup>[2]</sup> However in endemic areas *P. falciparum* can present very abnormally in children. The unusual features are due to development of immunity, indiscriminate use and increasing resistance of antimalarial drugs.<sup>[3]</sup>

Cerebellar syndromes after recovery of severe malaria are previously reported.<sup>[4]</sup> Cerebellar involvement in *P. falciparum* malaria can occur during the acute stage of fever as sequelae of cerebral malaria among survivors or as a side effect of drugs, which is evident as delayed cerebellar ataxia.<sup>[5]</sup> However, isolated nystagmus in children after severe malaria is very rarely reported<sup>[5]</sup> although ataxia and tremor are commonly observed. The cerebellar symptoms are due to injury to Purkinje cells as a consequence to hyperpyrexia, anemia, hypoglycemia and persistent seizures eventually leading to hemorrhages, small infarction, and the microglial infiltration in Purkinje cells of the cerebellum.<sup>[4,5]</sup>

Another atypical complication observed is acute psychosis indicative of cerebral malaria. Paranoid, agitation, manic symptoms are observed in the acute stage although it can present as confusional state, severe agitation, delirium, delusion, hallucination and transient amnesia in children.<sup>[4,6]</sup> Nevertheless these features generally disappear after treatment but can be observed in few patients following chloroquine use. Very rarely psychotic features may be the first manifestation in malaria<sup>[7]</sup> with persistent abnormality.<sup>[8]</sup> Cerebral malaria can disrupt neuropsychological integration during critical developmental periods resulting in several developmental delays.<sup>[8]</sup>

Urticaria as a symptom of falciparum malaria is rare. It is due to immunological factors, increase vascular permeability and capillary-dilatation due to cell mediators such as histamine, serotonin, heparin, and proteoglycans.<sup>[9]</sup> As observed in our case, rarely (1.35-25.6% incidence rate) urticaria may also be present without fever as the primary manifestation.<sup>[10]</sup> Although the deposition of IGE in endothelial cells cause itching followed by urticaria, however this generally subsides after 12-48 h of antimalarial management.<sup>[10]</sup>

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