

Original Research Article

Unusual manifestations of malaria in children

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ABSTRACT

Background: Till recently, vivax malaria was being regarded as a “benign” disease. *Falciparum* malaria is known to be a serious illness with life threatening complications as cerebral malaria, jaundice, acute kidney injury, metabolic acidosis and bleeding diatheses. Recently, some other atypical presentations are also being noted which have hardly been discussed previously. The present report highlights the various unusual presentations of malaria in children.

Methods: The study design was hospital based prospective observational study conducted over one year. Children between the ages of 1 month to 18 years admitted with a diagnosis of malaria confirmed by peripheral blood smear examination and/or rapid diagnostic test having unusual manifestations were studied. Patients with dengue fever, enteric fever, viral hepatitis, or any other concomitant infection were excluded. The various unusual manifestations of malaria, disease course and outcome were analysed.

Results: 58 (27.1%) out of 214 patients studied were found to have atypical manifestations. The unusual features observed were ARDS in vivax malaria (n=11), fulminant hepatic failure (n=5), post malaria neurological syndrome (n=3), stroke (n=3), bilateral optic neuritis (n=1), abducens nerve palsy (n=1), autoimmune haemolytic anemia (n=1), nephrotic syndrome (n=1), splenic infarction (n=2), acute abdomen (n=2), hemiplegia (n=2), psychomotor agitation (n=7), sepsis (n=5), shock (n=3), disseminated intravascular coagulation (n=3) and urticaria (n=2). Six children with vivax presented in deep coma.

Conclusions: Clinicians in endemic areas should be aware of unusual and varied presentations of malaria; failure of recognition of which may lead to delayed diagnosis resulting in increased mortality.

Keywords: Malaria, Unusual presentations, Recognition, Mortality

INTRODUCTION

Malaria continues to be an important cause of morbidity and mortality in the tropics.

Classical symptoms of malaria with paroxysms of fever are not seen quite often. A significant number of patients of malaria in endemic areas may present with unusual manifestations that mimic other illnesses. Recently, some atypical/unusual complications of malaria are being reported, lack of awareness of which may often lead to misdiagnosis or delayed diagnosis resulting in increased mortality.¹

Till recently, vivax malaria was being regarded as a “benign” disease. On the contrary, in the recent years, a few serious complications have been reported.² In our study, besides these, we encountered some other unusual complications in children which also merit attention. *Falciparum* malaria is known to be a serious illness with life threatening complications commonly seen as cerebral malaria, jaundice, acute kidney injury, metabolic acidosis, haemoglobinuria and bleeding diatheses.³ In the recent years, apart from these, some other atypical presentations are also being noted, which have hardly been discussed previously.⁴ The present report highlights the various unusual

presentations of malaria in children admitted to a tertiary care hospital in North India.

METHODS

The study design was hospital based prospective observational study. Children between the ages of 1 month to 18 years admitted between November 2018 to October 2019 at children’s hospital, medical college Kanpur with a diagnosis of malaria confirmed by peripheral blood smear examination and/or rapid immunochromatographic assay (rapid diagnostic test) and having unusual manifestations were studied prospectively. Approval for the study was obtained from the institutional ethics committee (approval number 85/EC/19). Patients with dengue fever, enteric fever, viral hepatitis, or any other concomitant infection were excluded from the study.

Sample size was calculated using the formula= z^2pq/l^2 ($z=3.98$, p (peak prevalence)=10%, $q=90$, $l=10$), minimum sample size was estimated to be 36. Detailed history was taken, thorough clinical examination, relevant investigations were done to rule out other similar illnesses and disease course and outcome was analysed. Data were collected and analysed using SPSS version 22.0. Categorical variables were expressed as frequencies and percentages.

RESULTS

Out of 214 malaria patients who presented to our hospital, 109 patients had vivax malaria, 71 had *falciparum* malaria, while 34 patients were of mixed malaria infection. 58 patients (27.1%) were found to have unusual manifestations (Tables 1 and 2). Age of patients ranged from 2 years to 17 years (mean age=9.1 years). Fever was not a prominent feature in many patients.

Five patients presented with features simulating fulminant hepatic failure with fever, jaundice, coagulopathy and grade 4 encephalopathy. They were initially diagnosed as viral hepatitis; one of them had been referred to higher centre for liver transplantation. They were later found patients of malaria. Viral markers

for hepatitis were negative. 2 of them showed dramatic response to parenteral artesunate therapy with regain of consciousness within 72 hours; the rest died due to massive hematemesis.

Two patients of mixed malaria infection had unusual manifestations. One of them had fulminant hepatic failure and died. The other presented with acute abdomen and recovered following antimalarial treatment.

We found a significant number of patients of vivax malaria presenting with acute respiratory distress syndrome (ARDS) with acute onset of severe dyspnoea and refractory hypoxemia rapidly progressing to respiratory failure requiring ventilatory support. Chest radiography showed bilateral pulmonary infiltrates. Patients with malarial ARDS had been misdiagnosed and treated as pneumonia or congestive cardiac failure. Children with ARDS had a high mortality (54.5%) despite assisted ventilation.

A 7-year-old boy presented with sudden onset marked loss of vision in both eyes without alteration of consciousness one week after recovery from *P. vivax* infection. Fundus examination revealed bilateral disc oedema suggestive of optic neuritis; cerebrospinal fluid examination and neuroimaging of brain was normal.

A 12-year-old girl developed neuropsychiatric symptoms such as visual hallucinations, decreased verbal output, encephalopathy resembling acute disseminated encephalomyelitis (ADEM), urinary incontinence and schizophrenia like symptoms following recovery from *falciparum* malaria which persisted for about two weeks. MRI brain and CSF examinations were normal. She was found to have post-malaria neurological syndrome.

Severe agitation, irritability, delirium, irrelevant talk and abnormal behaviour simulating acute psychosis was also, observed. Two patients who presented with fever and acute hemiparesis and were admitted for evaluation of acute stroke, were later found to have underlying malarial aetiology. MRI brain in one of the patients showed infarct in frontoparietal cortex and internal capsule suggesting ischemic stroke of middle cerebral artery territory.

Table 1: Unusual presentations seen with vivax malaria in children and their outcome.

Presentation	No.	Percentage (%)	Discharge	Mortality
Fulminant hepatic failure	2	5	1	1
ARDS	11	31	5	6
Splenic infarction	2	5	2	-
Bilateral optic neuritis	1	3	1	-
Unilateral abducens nerve palsy	1	3	1	-
Isolated hemiplegia	2	5	2	-
Autoimmune hemolytic anemia	1	3	1	-
Sepsis like presentation	5	14	4	1
Unexplained shock	3	7	2	1
Coma (Glasgow coma score <8)	6	17	5	1
Disseminated intravascular coagulation	3	7	-	3
Total	37	100	24	13

Table 2: Unusual presentations seen with *falciparum* malaria in children and their outcome.

Presentation	No.	Percentage (%)	Discharge	Mortality
Fulminant hepatic failure	2	11	1	1
Post malaria neurological syndrome	3	16	3	-
Psychomotor agitation	7	36	7	-
Stroke like presentation	3	16	2	1
Nephrotic syndrome	1	5	1	-
Acute abdomen	1	5	1	-
Urticaria	2	11	2	-
Total	19	100	17	2

Decompensated shock without any evidence of bleeding was also found. They were initially suspected to be patients of dengue; however, dengue serology was negative. Schizonts of *P. vivax* were seen on slide microscopy.

DISCUSSION

Malaria can have varied and unusual presentations in children that may mimic other illnesses and often lead to difficulty in diagnosis.

Although jaundice and deranged liver function tests in malaria is common; presentation mimicking fulminant hepatic failure is rare.⁵ This has important therapeutic and prognostic implications. Fever, disproportionate anemia, hepatomegaly, mild elevation of transaminases and response to artemisinin therapy favour malarial aetiology.⁶ Physicians in endemic areas should be aware of this unusual presentation as the prognosis is better when the underlying etiology is malaria.

ARDS was hitherto considered to be common in adults and unusual in children with malaria.^{7,8} In our study, we found a significant number of patients of *P. vivax* malaria with ARDS, which has been described to be rare. Recent studies have shown that pulmonary involvement in pediatric malaria is increasingly being recognized.⁸ Malaria should always be suspected as a cause of acute lung injury/ARDS in endemic areas. Failure of recognition of this entity often leads to delay in diagnosis and increased mortality. Acute onset of dyspnoea and refractory hypoxemia in a child with malaria should alert clinician to possibility of ARDS.

Malaria being a common problem in tropical countries even rarest complication or sequel is important to be recognized. PMNS is a rare self-limiting entity of new neurological and/or psychiatric manifestations occurring within two months of recovery from severe malaria following a symptom free period.⁹ Till date, very few cases have been reported in pediatric patients.^{9,10} Awareness and recognition of this rare manifestation is important since this condition may present a diagnostic dilemma for clinicians in endemic areas who may seek unnecessary psychiatric referrals and treatment. It may manifest as an encephalopathy

resembling ADEM, from which it needs to be differentiated.^{9,10}

Cerebral malaria is described as diffuse symmetric encephalopathy.⁷ A stroke like presentation and focal neurologic signs such as cranial nerve palsies are unusual. However, in patients presenting with fever and features of acute stroke, the possibility of cerebral malaria should also be considered. Psychiatric features described above are rare manifestation of cerebral malaria that may be misdiagnosed as functional psychoses.¹¹ Various neurological manifestations have been described with *falciparum* malaria. We also observed unusual neurological manifestations such as optic neuritis and abducens nerve palsy in association with *P. vivax* malaria which have rarely been described previously.¹²

Nephrotic syndrome secondary to *P. falciparum* infection as seen in our study has rarely been documented.¹³ Malaria induced splenic infarction is unusual and rare complication.¹⁴ Physicians should be aware that severe pain in left hypochondrium in a patient with malaria could be due to splenic infarction and should not be overlooked.

Severe anemia is known to occur with vivax malaria but autoimmune hemolysis in association with malaria is rare. Clinicians should consider immune mediated destruction of red cells if a patient with malaria develops severe anemia or hemolysis after treatment.

Limitations

Our study has some limitations. Important limitations include the fact that all of the described syndromes can have other causes and that parasitaemia can be incidental, not representing the cause of the illness. Many syndromes resolve spontaneously and a recovery cannot be assumed to be due to antimalarial drugs administered. Information on the prevalence of asymptomatic parasitaemia (quantitated for density) in the age-matched local population would be helpful towards knowing the likely contribution of malaria to each illness.

CONCLUSION

Malaria may present with unusual and varied presentations in pediatric patients which often lead to

difficulty in diagnosis and may confound the clinicians. Lack of awareness of such presentations may result in diagnosis being missed causing increased morbidity and mortality. Classical symptoms of malaria may not always be present; hence clinicians in endemic areas should maintain a high index of suspicion and also consider unusual presentations while making diagnosis. A step further to the existing knowledge that *P. vivax* malaria is not a benign illness, some other unusual complications are being recognized and unfolded as a result of critical evaluation of such patients.

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