

CASE OF THE MONTH

An Unusual Sequelae of Uncomplicated Vivax Malaria

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Albeit malaria is a common health problem in many parts of the world, the entity of post-malaria neurological syndrome (PMNS) is not well recognized. This is a rare entity of neurological and psychiatric manifestations described in patients with falciparum malaria which usually develops within 2 months of recovery from the illness. It has been reported in 1.2/ 1000 falciparum malaria cases, more commonly in those with severe disease. We report case of a 62-yrs-old male presenting with recurrent generalized seizures following adequately treated vivax malaria. Relevant investigations were done to rule out other differentials. The patient recovered completely reiterating the self-limiting course of PMNS. Occurrence of PMNS following uncomplicated vivax malaria is peculiar in this report.

Case Report

A 62-year-old male, resident of an endemic zone for malaria in India, presented to the emergency services of our hospital with complaints of recurrent episodes of generalized tonic-clonic seizures (GTCS) for 3 days. A detailed history revealed that he was apparently well 1 month back, when he developed high grade fever associated with chills and rigors. He was admitted to a local hospital where evaluation revealed *Plasmodium vivax* (ring forms) in the peripheral smear. He was treated with appropriate dosages of chloroquine and primaquine as per the national guidelines. The clinical features and laboratory investigations didn't reveal any features of severe malaria (Table 1). The fever subsided within 2 days and he was discharged after being afebrile for 24 hours. One day after discharge, he was found lying unconscious with frothing from mouth. He was readmitted for evaluation in the same hospital. On examination, he had no fever or focal neurological deficits. A rapid malaria antigen card test was positive for *Plasmodium vivax* but peripheral smear did not reveal malaria parasites. He was again given a course of antimalarials (proguanil, arteether and primaquine) along with anti-epileptics. He was discharged with no in-hospital recurrence of seizures, but the relatives noticed change in his behaviour in form of decreased verbal

output and difficulty in recognizing relatives. After 2 weeks, he had multiple witnessed episodes of GTCS and was brought to the emergency of our hospital. There was no history of any head injury, prior comorbidities, addictions, any chronic medication intake or similar episodes in the past.

On examination, his blood pressure was 120/78 mmHg in supine position, heart rate was 88/min, regular, respiratory rate was 22/min and SpO₂ 95% on room air. Limited neurological examination was possible as he was in post-ictal state. There was no neck stiffness, pupils were normal size reacting to light, plantars were flexor and there were no apparent focal neurological deficits. Rest of the systemic examination was within normal limits.

Urgent investigations to rule out metabolic causes of seizures including serum electrolytes (Na 139 mEq/L, K 4 mEq/L), blood glucose (182 mg/dL), calcium (8.9 mg/dL) and urine toxicology screen were normal. The routine hematological, liver and kidney functions profile was essentially normal (Table 1). Malaria rapid antigen based card test and a peripheral smear were negative. Contrast enhanced computed

tomography (CECT) of brain was normal. On lumbar puncture, clear cerebrospinal fluid (CSF) was obtained which on examination revealed cell count of 2 cells/cmm, sugar of 62 mg/dl (corresponding blood sugar – 98 mg/dl), protein of 60 mg/dl, no organisms on Gram stain and ZN stain and HSV, CMV PCR were negative (Table 2). Electroencephalogram (EEG) brain showed diffuse slowing of waves with right frontal lobe focus of discharge. Magnetic resonance imaging (MRI) brain was normal (Figure 1).

Post infectious encephalomyelitis, drug resistant cerebral malaria and metabolic encephalopathies were kept as differentials on presentation, but initial blood investigations and CSF analysis were not supportive for same, hence a possibility of PMNS was considered. The patient was discharged after 10 days in hemodynamically stable condition on four oral antiepileptics drugs. No fresh episodes of seizures have occurred and the antiepileptics have been tapered off and the patient is doing well at 3 months follow up.

Discussion

Our patient had uncomplicated vivax malaria followed by PMNS and although had difficult to control seizures, he recovered completely.

PMNS is a rare entity of neurological and/ or psychiatric manifestations occurring within 2 months after recovery from an episode of malaria, usually in severe forms of disease caused by *Plasmodium falciparum*. It was first described from Vietnam in 1996, wherein 22 cases of PMNS were reported with incidence of 1-2 per 1000 (CI, 0.7 to 1.8 per 1000) and relative risk for developing the disease after severe versus uncomplicated falciparum malaria was 299¹. Subsequently, few

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Table 1: Hematological and biochemical profile

	At first hospitalisation	At admission to our hospital	At discharge
Hemoglobin (g/dL)	11.2	12.6	11.7
TLC (/mm ³)	6200	11000	7700
Platelet counts (/mm ³)	213	223	216
DLC	N59 L32 M7 E2	N64 L31 E2	N67 L24 M7
Urea (mg/dL)	39	14	26
Creatinine (mg/dL)	1.2	0.8	0.4
Calcium (mg/dL)	8.0	7.9	7.8
Phosphate (mg/dL)	2.7	2.6	2.6
Uric acid (mg/dL)	NA	2.7	1.2
Sodium (mEq/L)	132	139	138
Potassium (mEq/L)	3.8	4.0	4.2
Bilirubin (mg/dL)	0.8	0.3	0.2
T. Protein (g/dL)	6	5.9	6.2
Albumin (g/dL)	3.5	3.5	3.7
Globulin (g/dL)	2.5	3.5	2.0
SGOT(IU/L)	38	22	16
SGPT(IU/L)	26	22	38
ALP (IU/L)	210	217	114
Prothrombin time sec	NA	12.1	11.2

TLC/DLC-Total/Differential Leucocyte Count, AST – Aspartate transaminase, ALT – Alanine transaminase

cases have been reported mainly from African continent, and all being preceded by *Plasmodium falciparum* infection²⁻⁷. Other neurological features described after successful treatment of malaria include delayed onset cerebellar ataxia (DCA) and acute disseminated encephalomyelitis (ADEM)⁸⁻¹⁰.

Our patient developed PMNS following uncomplicated vivax malaria which, to the best of our knowledge, is first such case in literature. *Plasmodium falciparum* was ruled out as a rapid card test was negative for same and initial peripheral smear was suggestive of presence of ring forms of *Plasmodium vivax*. The pathophysiology of PMNS is poorly understood and various proposed mechanisms include sequestration of parasitized erythrocytes, immunological phenomenon, co-infections and drugs (mefloquine)¹. Lately, various complications of severe malaria classically described in falciparum malaria are being increasingly recognized in vivax malaria¹¹. The pathophysiology of severe vivax malaria is not completely understood. Similarly, PMNS in uncomplicated vivax malaria in our patient, throws up interesting questions regarding the underlying pathophysiology.

A wide range of manifestations have been described in PMNS including acute psychosis, generalized seizures, tremors, speech disturbances, visual/

auditory hallucinations and ataxia^{1,2}. Acute confusional episodes/ psychosis is the most common reported feature followed by generalized seizures, which were reported in 36% of patients in the largest series described from Vietnam¹. The reported median duration of occurrence of PMNS is 4 days with a range of 6hrs- 60 days. Our patient had seizures 1 day after completion of therapy for malaria. Cerebrospinal fluid findings are variable, elevated proteins and a lymphocytic pleocytosis have been reported^{1,2}. EEG findings are consistent with encephalopathy and MRI findings reported are nonspecific.

PMNS usually lasts 1-14 days although it has been reported to last up to 57 days^{1,2,12}. It recovers completely without any sequelae with symptomatic treatment, although anecdotal use of steroids has also been reported in severe symptoms⁷. Our patient recovered completely although he required multiple anti-epileptics to control the seizures.

Conclusion

Post malarial neurological syndrome is a neglected complication of malaria and high index of suspicion is needed to diagnose the same. Though more commonly seen with falciparum malaria, it may also be seen in vivax malaria. It is self-limited with good prognosis but sometimes can have a little prolonged course as seen in

Table 2: CSF analysis

Total count/Differential count	2 cells/ml (L100%)
Sugar/Protein (Blood Sugar) mg/dl	62 / 60 (98 mg/dl)
Gram stain/Bacterial culture	Negative / Sterile
Fungal stain / culture	Negative / Sterile
Acid fast stain / Gene xpert	Negative
HSV /CMV PCR	Negative
Cytology	No atypical cells seen

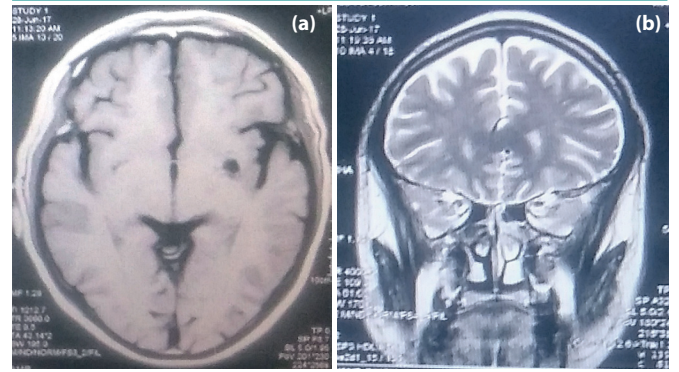


Fig. 1: Normal MRI brain at admission (a) T1 weighted image, axial section, (b) T2 weighed image, coronal section

our patient. A difficult to diagnose condition may be an uncommon manifestation of a common disease rather a rare disease.

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