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Case Report

Two unusual neuro-psychiatric manifestations of malaria in a tertiary care hospital: a review of literature

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ABSTRACT

Malaria, a highly prevalent parasitic disease in tropical country, have some atypical neuro-psychiatric manifestations seen in both vivax and falciparum malaria. We are reporting two cases of unusual neuro-psychiatric manifestations of malaria admitted in our hospital, one with intralobar haemorrhage and other with atypical psychiatric features. The rarity of the presentation has been highlighted with possible pathogenesis discussed after literature review.

Keywords: Vivax, Falciparum, Neuro-psychiatric manifestations

INTRODUCTION

Malaria is one of the most common infectious disease affecting all ages globally. Among the four species of malaria, falciparum is the most dangerous, since it causes multisystem failure. Several neurological complications are associated with severe complicated falciparum malaria, which is rarer than other forms of malaria. Common neurological manifestations are acute febrile convulsion and cerebral malaria which is a fatal disease can present as hemiplegia, convulsion, disorientation, delirium, coma and death. Cerebral falciparum malaria presenting as intra lobar haemorrhage is an uncommon presentation, not yet reported.

Acute psychiatric manifestations in the form of delusion, hallucination and aggressive behaviour during the course of illness in vivax malaria are very rarely noted in adult. After through literature review we are reporting these two rare atypical clinical manifestations of malaria with probable pathogenesis.

CASE REPORT

Case 1

A 28 years male farmer non diabetic, non-hypertensive, non-smoker admitted with high grade intermittent spiky fever associated with chills and rigor for last 5 days. Along with he had a complain of severe holocranial headache with few episodes of vomiting for last 3 days. For last 1 day he developed gradual deterioration in level of consciousness. There was no history of joint pain, rash, cough, burning sensation in micturation, weakness of limbs, visual blurring, bleeding from any sites. Past history, drug history, family history and personal history were absolutely non-contributory.

On examination patient had a Glasgow Coma Scale (GCS) was E3V2M3, febrile with normal vitals. There were no neurological deficits with absent meningeal sign. Ophthalmoscope examination showed mild blurring of temporal margin of both disc without any retinal haemorrhage. Other systemic examinations were normal.

Non Contrast Computer Tomography (NCCT) study of brain revealed large left temporal-parietal lobe haemorrhage, perilesional oedema and mid line shift. Blood thick and thin smear showed trophozoites of plasmodium falciparum with positive antigen test. Other investigations revealed haemoglobin was 13 gm/dl with normal total, differential count and platelet count. Liver and renal function studies showed a urea of 18 mg/dl, a creatinine of 0.9 mg/dl with normal bilirubin, total protein and liver enzymes. Coagulation profile shows normal clotting time, bleeding time, prothrombin time, partial thromboplastin time and normal platelet function and count.

He was treated with intravenous artesunate and anti-oedema measures as per protocol. The patient's symptoms improved, fever subsided, sensorium improved. Repeat NCCT brain decreasing midline shift, oedema with decreased haemorrhage size. At that time Magnetic Resonance Angiography (MRA) done to rule out any aneurysm which showed normal cerebral vascular angiogram. Patient discharged after 7 days with primaquine 45 mg one dose and followed up in for next 3 months without.

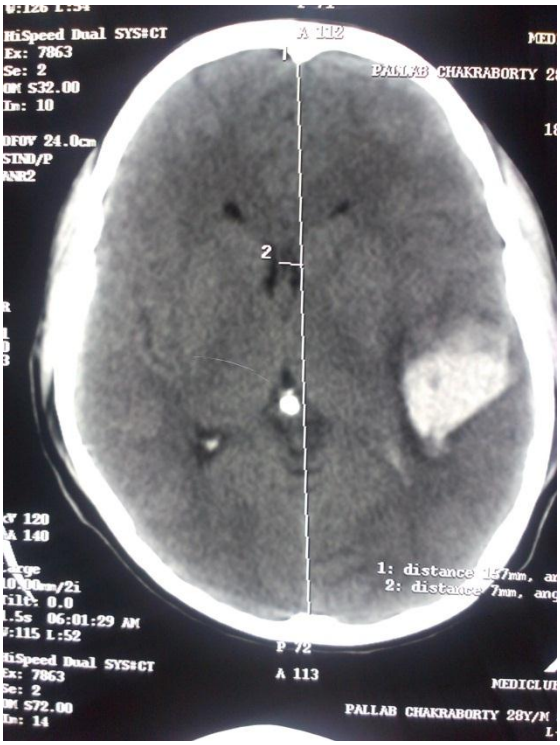

Figure 1: Non contrast computer tomography study of brain.

Case 2

A 26 years male non diabetic, non-hypertensive, non-smoker admitted with history of high grade intermittent fever measuring about 104°F associated with chills and rigor for last 4 days. Fever was not associated with cough, burning micturation, joint pain, rash, headache, vomiting, altered sensorium, seizure. She consulted with local physician and was prescribed with oral amoxicillin and clavalunic acid and investigated for malaria slides, blood count and routine urine examination which were largely non-contributory. There was no other significant history related to past illness, drug intake or familial illness.

On clinical examination except having mild pallor, vitals were stable with normal general survey. Systemic examination was non-significant. Her investigations showed haemoglobin was 9.8 gm/dl, total count of 8800/mm^3 with normal differential count and platelet count. NS1 antigen, IgM, IgG dengue were negative. Ultrasonography, chest skiagram and doppler were non-contributory. Other routine investigations were largely non-contributory and treated conservatively.

On next day, patient developed acute onset behavioural disturbance in the form of irrelevant talk, visual hallucination, and aggressive behaviour. Psychiatric consultation was acute onset delusion, but she continued to display same symptoms for next day too. Patient was reassessed and neurological examination did not reveal any neurological deficits with absent meningeal sign, flexor planter response, normal deep tendon jerks, normal ocular movement. Patient was investigated, having normal contrast enhanced computer tomography of brain.

Patient was treated with intravenous artesunate (2.4 mg/kg) stat and repeated after 12 hours on two occasion followed by oral artesunate combination therapy and primaquine given for 14 days thereafter. Intramuscular haloperidol given as needed. Patient showed dramatic improvement following second dose of artesunate and discharged 3 days later.

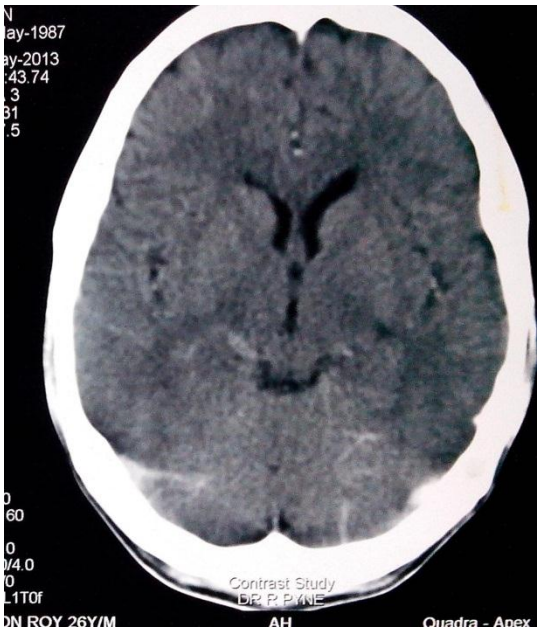

Figure 2: Normal contrast enhanced computer tomography of brain.

DISCUSSION

Central nervous system malaria occurs around 2% of patients of falciparum malaria.[1] It is usually manifested by deep coma; convulsion (may be subtle - only detected by electroencephalography). Convulsion is commonly observed in children.[2] Localisation signs are not common. Neuro-ophthalmological signs like internuclear ophthalmoplegia, ocular bobbing, vertical nystagmus, 6th cranial nerve palsy are common. Papilledema is rare. Conjunctiva, cornea, pupils are usually normal including reflexes. Motor system examination reveals upper motor neuron signs. The histological examination shows widespread cerebral vasculopathy due to sequestration of parasitized erythrocytes in vascular endothelium with increase endothelial permeability, perivascular infiltrations, cerebral oedema, and necrosis of vascular wall, petechial haemorrhages, ring haemorrhages, intravascular microthrombosis, perivascular demyelination and gliosis.[3,4]

Immunohistochemical and electron microscopy studies have shown parasite derived proteins that are present on parasitized erythrocytes facilitates adherence of erythrocytes to capillary endothelium through a glycoprotein i.e. plasmodium falciparum erythrocyte membrane protein (PfEmP)-I, leading to diffuse cerebral endothelial cell damage and necrosis.[5-7]

Rosette formation due to agglutination of normal erythrocytes around the parasitized erythrocytes aggravates venular obstruction and diffuse cerebral anoxia and induction of local mediators such as nitric oxide and Tumour Necrosis Factor (TNF) alpha are responsible for coma of cerebral malaria. Though various cerebral symptoms are explained some features like intra cerebral haemorrhage without coagulopathy like DIC not well established.

In our patient intra-cerebral (lobar) haemorrhage without features of coagulopathy and other organ dysfunction or anatomical variation of cerebral vasculature is very rare and not yet reported till now.

Psychosis is a rare atypical manifestation of malaria, which can be due to hyperpyrexia, cerebral malaria, due to antimalarial drugs like mefloquine or chloroquine or due to as a manifestation of Post Malaria Neurological Syndrome (PMNS). Associated disease like meningo-encephalitis or typhoid fever may mimic malaria induced psychosis.

In our patient as there was no history of previous antimalarial drug intake, so drug like chloroquine or mefloquine induced psychosis could be easily ruled in our case which is extremely rare as was noted by Thapa et al.[8] Post Malaria Neurological Syndrome (PMNS) is defined as the acute onset of confusion, epileptic seizures, or any other neurological or psychiatric sign occurring with a latency of several days to weeks (generally within 2 months) after an episode of successfully treated P. falciparum malaria.[9] Schnorf et al. divided PMNS into three types ranging from mild localised cerebellar encephalopathy, diffuse but not severe encephalopathy and severe generalised encephalopathy simulating acute disseminated encephalomyelitis.[10] PMNS was certainly not a differential diagnosis in this case. Other mimicars of malaria induced psychosis were ruled out with relevant investigations like cerebrospinal fluid examination and serum IgM typhi Dot.

Pathogenesis of psychosis in vivax malaria is less understood and precise documentation is scanty in these respects.[11,12] Malarial psychosis could develop due to encephalopathy in patients with cerebral malaria. In the acute stages, it manifests as paranoid and manic syndromes, depression being the late sequel.[13] As the patient did not had any past history of psychosis and also did not have psychosis at the onset of hyperpyrexia the exact cause for psychosis in our case was unclear, she did not have psychosis at the onset of hyperpyrexia. The psychosis in our patient was probably induced by Plasmodium vivax malaria, which corroborates with other research studies and a rare entity.[14,15]

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