Case Report

Post malaria neurological syndrome in a Cameroonian child after a *Plasmodium falciparum* malaria infection

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Abstract: Post malaria neurological syndrome (PMNS) is a rare neurological complication occurring after malaria treatment, and manifests by neuropsychiatric symptoms. We report the first reported case in a Cameroonian child who presented with this syndrome, following severe *Plasmodium falciparum* malaria. The outcome was favorable.

Keywords: *Plasmodium falciparum*; post-malaria neurological syndrome (PMNS); child; Cameroon

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Introduction

Falciparum malaria is a leading cause of ill health, neuro-disability and death in tropical countries, with cerebral malaria being the most severe neurological manifestation of severe malaria (1). Amongst the neurologic complications of severe malaria is the post malaria neurological syndrome (PMNS) which can occur in patients recovering from falciparum malaria.

We report a case of a Cameroonian child who developed the PMNS, after being treated for severe *Plasmodium falciparum* malaria. It is important that clinicians treating patients with malaria know and recognize this syndrome, else patients who develop this syndrome might be referred to psychiatric centers unnecessarily.

This is the first published case in a child in the Cameroonian context, and merits its recognition and awareness by all clinicians managing patients with malaria especially in malaria endemic zones.

Case presentation

A 7 years old female child, referred from a health centre for management of fever and seizures associated with impaired consciousness.

From the history, she had fever with diarrhoea 10 days before, and consulted in a health centre where she was treated for malaria with arthemeter-lumefantrine. Following this treatment there was slight improvement. A few days after, she had an episode of generalized tonic-clonic seizures, and was taken to another health center where diazepam was administered intra-rectally.

Following this treatment, two more generalized tonic-clonic seizures occurred and this motivated her referral to our hospital.

In the past history, we noted she was not sleeping under a mosquito net, had never been hospitalised, and her vaccinations were complete for her age.

On admission she was ill looking, asthenic and unconscious with a Glasgow coma score of 10/15. Her vital signs were: temperature 38 ℃, respiratory rate of 22/min, heart rate of 121/min, and a weight of 21 kg. There were no signs of meningeal irritation. The rest of the physical and neurological examinations were normal.

The diagnosis of meningitis was made based on the

seizures in a febrile context. Severe malaria was also considered a differential diagnosis with seizures and coma (Glasgow score 10/15) as criteria of severity.

A lumbar tap for cyto-bacteriological analysis of the cerebrospinal fluid, rapid diagnostic test for malaria, thick blood smear and a full blood count were requested.

Analysis of the cerebrospinal fluid showed: leucocytes: 0; red blood cells: 0; culture: sterile; rapid diagnostic test—positive for *Plasmodium falciparum*, thick blood smear: 200 trophozoites of *Plasmodium falciparum*; full blood count—leucocytes: 13,780/mm^3, red blood cells: 4,840,000/mm^3, hemoglobin: 12 g/dL, platelets: 250,000/mm^3.

Meningitis was thus excluded and the diagnosis of severe malaria retained. The patient was then placed on: artesunate 2.4 mg/kg corresponding to 50 mg at H_0, H_{12}, H_{24} and then once daily; paracetamol 15 mg/kg equivalent to 300 mg every 6 hours; phenobarbital 10 mg/kg loading dose and 5 mg/kg after 24 hours and every 24 hours intravenously. A nasogastric tube was placed for feeding.

On this treatment, the evolution was favorable. The fever dropped and the patient regained consciousness.

On day 5 of hospitalisation, the patient had a good general state, was conscious with a Glasgow coma score of 15/15, the nasogastric tube was removed and oral feeding began progressively. Phenobarbital had been stopped on the second day as there were no more convulsions.

On day 6 of hospitalisation, the child developed some behavioural disorders; exaggerated fear of imaginary people she said she was seeing (visual hallucinations), a state of confusion, voicing out incomprehensible words, and fleeing from everybody who came close to her. These behavioural disorders were intermittent and occurred when she was awake, during the day and at night. Physical examination revealed no abnormalities. A control thick blood smear was performed and was negative.

Artesunate was stopped since she was able to eat and take oral medications. We relayed with dihydroartesunate-piperaquine phosphate syrup.

These behavioural disorders started regressing as from day 8, and completely regressed on the 9th day and she was then discharged.

She was brought back for a control, one week after and she was fine and showed no abnormal findings, and had started going back to school.

Discussion

PMNS is a discrete, transient neurological syndrome seen after recovery from malarial infection. Criteria for inclusion under this syndrome are: recent symptomatic malarial infection with parasites cleared from blood, full recovery of consciousness in cases of cerebral malaria and the development of new neuro psychiatric symptoms within two months of acute illness (2).

This syndrome was first described by Nguyen *et al.*, in Vietnam (2). In a series of 18,124 patients with falciparum malaria 19 adults and 3 children developed the PMNS. In this study PMNS was defined as patients with symptomatic malarial infection (initial blood smear positive for asexual forms of parasite) whose parasites have cleared from the peripheral blood and who have recovered after treatment (and in cerebral cases had recovered consciousness fully), and who developed neuropsychiatric symptoms within 2 months of acute illness.

The overall incidence of PMNS after falciparum malaria was 1.2/1,000 and the relative risk for developing PMNS after severe malaria compared to uncomplicated malaria was 299 (2). This syndrome occurs 300 times more frequently in severe malaria than simple malaria (3,4).

Our case was severe malaria with criteria of severity being coma and seizures according to the Cameroon's National Malaria Control Program (5).

The diagnostic criteria are (2): a recent history from plasmodium malaria; a blood smear negative for parasites at the onset of neuropsychiatric symptoms, and complete recovery without any therapy within 10 days.

Most reported cases of PMNS are in adults (2,3,6-8). In the series reported by Nguyen *et al.* in Vietnam, three were children of 6, 9 and 10 years all recovering from malaria. Our patient was 7 years old and was recovering from severe malaria (2).

In many studies, *Plasmodium falciparum* is incriminated (2,3,6-9). A few cases have been reported with *Plasmodium vivax* infestation (10,11).

This syndrome has also been associated with some antimalarial drugs as atovaquone-proguanil (8), and mefloquine (2). Nguyen *et al.* showed strong association between treatment with mefloquine and the development of PMNS suggesting a role for mefloquine in the aetiology of this syndrome (2).

Nguyen *et al.* noted that 4.4% of patients with severe malaria who received mefloquine after parenteral treatment developed PMNS compared to 0.5% of those who received quinine, with a relative risk of 9.2 (2).

Our patient developed the syndrome following artesunate parenteral treatment for severe malaria, in accordance with

WHO guidelines (12) and Cameroon's National Control Malaria Control Program guidelines (5).

The pathogenesis of PMNS remains unclear. The delay between the onset of *Plasmodium falciparum* infection and PMNS might indicate immunologic damage following the sequestration of parasite infected erythrocytes in brain capillaries (2).

The pathogenesis of PMNS which generally occurs when the patient is recovering from malaria and in the absence of parasitemia might be due to the presence of cytokines (tumor necrosis factor-α, interleukin-2, and interleukin-6), produced during the malaria episode and which may persist after treatment (3,4,6). There is also some evidence of molecular mimicking during which antibodies produced in response to antigens expressed by some *Plasmodium falciparum* strains cross and react in the central nervous system, inducing an inflammatory reaction (6).

The clinical manifestations are generally new neuropsychiatric symptoms such as psychosis or acute psychiatric symptoms or acute confessional episodes, seizures, tremor, hallucinations within 2 months of a malarial infection (2,3,7).

Our patient developed neuropsychiatric symptoms on day 6 of hospitalization when there was total parasite clearance from the blood.

Some authors have classified PMNS in three subtypes: a mild or realized form characterized by isolated cerebella ataxia or postural tremor; a diffuse but moderate encephalopathy form with acute confusion states or epileptic seizures; and a severe corticosteroid responsive encephalopathy causing confusion, focal deficits, generalized myoclonus postural tremor and cerebellar ataxia (11,13).

An important differential diagnosis to exclude is acute disseminated encephalomyelitis (ADEM). ADEM is a monophasic acute demyelinating disorder of the central nervous system, characterized by diffuse neurologic signs and symptoms coupled with evidence of multifocal lesions of demyelination on neuroimaging (14). This often follows viral infections and occasionally bacterial infections or immunization measles or could occur spontaneously (14-17). Its occurrence after malaria infection is uncommon (13,16). In ADEM, electroencephalographic changes are common but non-specific (17); the cerebrospinal fluid may be normal or occasionally increase pressure, lymphocytic pleocytosis or elevation of protein levels (15,17). Neuro imaging is a valuable tool for diagnosis, but computed tomography is often initially normal but changes occur during 5–14 days later, and include multifocal lesions in the sub cortical zone of the white matter; on magnetic resonance imaging, demyelinating lesions are better seen, and can distribute throughout the white matter of the posterior fossa and cerebral hemisphere and sometimes to the cerebellum and brainstem (17). According to Mohsen *et al.*, there are no specific identifiable clinical or radiologic lesions to distinguish PMNS from ADEM (4). Whereas according to Prendki *et al.*, characteristic lesions of ADEM are surrounding demyelination and hypertense lesions depicted by brain MRI (9).

In our patient, neuroimaging was not done as the manifestations occurred at the end of the treatment, and the patient had no other focal neurological signs, and recovery was rapid and complete. ADEM has often been associated with *Plasmodium vivax* infection (13,16); or *Plasmodium falciparum* (18), or both *Plasmodium falciparum* and *Plasmodium vivax* infection (15).

Conclusions

This report indicates that PMNS can occur after severe malaria. Clinicians should be aware of this as a neurological complication of severe malaria, and the fact that it has a spontaneous resolution. Close follow up of malaria patients during and after treatment, will permit early diagnosis and differentiate from other similar neurological disorders.

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Footnote

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at http://dx.doi.org/10.21037/jphe.2016.12.07). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee(s) and with the Helsinki Declaration (as revised in 2013). Informed consent was obtained from the patient for publication of this manuscript and any accompanying images.

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