Acute Demyelinating Encephalomyelitis in a Child Following Malaria

AMIT AGRAWAL AND SHWETA GOYAL

From Department of Pediatrics, Chirayu Medical College & Hospital, Near Bairagarh, Bhopal 462 030, MP, India.

Correspondence to:
Dr Amit Agrawal,
28, Ravidas Nagar, Near Nizamuddin Colony, Indrapuri, Bhopal, MP 462 023, India. agrawaldramit@yahoo.co.in.
Received: January 13, 2012;
Initial review: February 06, 2012;
Accepted: June 25, 2012.

Acute demyelinating encephalomyelitis usually follows viral infections and its occurrence following malarial infection is very uncommon. We report a 12-year-old girl who presented with encephalopathy and generalized convulsions following complete recovery from the *Plasmodium falciparum* infection. Diagnosis of ADEM was made on the basis of brain MRI findings.

Key words: *Acute demyelinating encephalomyelitis, Malaria, Post-malaria neurological syndrome.*

Acute demyelinating encephalomyelitis (ADEM) is a disease of prepubertal children, typically occurring one to three weeks after a clearly identifiable febrile prodromal illness of viral infections and occasionally bacterial infections or immunization [1,2]. Most patients of ADEM recover fully, usually without treatment. Post-malarial ADEM usually occurs after recovery from the severe falciparum malaria and is considered to be an immune-mediated neurological complication [3-8]. However, we could not find any report of ADEM following malaria in children.

CASE REPORT

A 12-year-old female child was admitted with complaints of high-grade fever, generalized tonic-clonic convulsions and altered consciousness. She was admitted three weeks prior also for high grade fever, headache and vomiting for three days and an episode of generalized convulsions and clouding of consciousness on the day of admission. Her laboratory examinations revealed anemia (6.5 mg/dL), mild thrombocytopenia (34000/mm^3) and *Plasmodium falciparum* infection with 13% parasitemia. She was treated with intravenous quinine, doxycline, packed red cell transfusions, along with supportive therapy. On day, 2, patient regained consciousness with no further convulsions. On day 4, there was complete resolution of fever with clearance of parasitemia and she was discharged on day 5. Sixteen days after discharge, patient again developed headache, confusion progressing to clouding of consciousness, and generalized convulsions leading to another hospitalization. On admission, patient was hemodynamically stable with Glasgow coma scale of E3M5V2. There were no meningeal signs, and no cranial nerve palsy. Deep tendon reflexes and superficial reflexes were absent, tone was decreased with positive Babinski's sign. Rest of the systemic examination was normal.

Routine blood investigations including complete blood count, blood sugar, serum electrolytes, and renal and liver function tests were within normal limits except mild elevation in liver enzymes. Repeated blood smears were negative for malarial parasites. CSF examination showed normal sugar (57 mg/dL), protein (11.2 mg/dL), and total cells (5, all lymphocytes). MRI brain revealed asymmetrical hyperintense signals on T2 and Diffusion weighted images (DWI) involving bilateral periventricular white matter, centrum semiovale and genu of corpus callosum. On the basis of MRI findings, diagnosis of ADEM was made and intravenous methylprednisolone therapy was initiated. Patient showed dramatic response to above therapy and on day 3, patient regained consciousness, started moving limbs spontaneously but could not speak. On day 5, she was conscious and oriented, power was normal but motor aphasia was still present. Methylprednisolone was continued for 5 days and then replaced with oral prednisolone. On day 8, speech output started showing improvement and by day 13 of admission, she became neurologically normal and was discharged. Her repeat MRI brain, done after 3 weeks, showed resolution of changes seen in previous MRI. After three months of follow up, patients is normal with no neurological deficits.

DISCUSSION

ADEM has been reported following *P. falciparum* infection in adults [3-7]. Etiology of ADEM following malaria remains unclear but seems to be immunologically mediated, the mechanism supported by latency period between falciparum infection and the onset of ADEM as well as rapid response to steroid therapy [4,7]. Index case also showed improvement after steroid therapy with resolution of MRI changes on repeat imaging study.

Studies have shown plasmodium infection induced suppression of both humoral and cellular immunity, leading to superinfection with other microorganisms [6]. This lag in immunologic improvement might be seen

even after clinical recovery from malaria, predisposing them to the development of ADEM. Most of the patients with ADEM show spontaneous and favourable recovery. In mild cases, symptomatic treatment is usually sufficient, but in severe cases, corticosteroids can help limit brain inflammation. As in our case and case reported by Sharma, *et al*. [4], patients received steroids, while few other cases improved without steroid therapy [5,6]. Signs of recovery can be seen within days, but complete resolution usually takes weeks or months [1,2].

The present case reiterates the importance of post-malarial neurological complications, which one should keep in mind especially after clinical recovery from malaria. A few patients may experience neurological symptoms after complete recovery from falciparum infection, termed as post-malaria neurological syndrome (PMNS). PMNS patients typically have negative blood films at the time of onset, distinguishing it from cerebral malaria, which occurs during parasitemia [8,9]. Overall incidence of PMNS was estimated to be 0.7-1.8 per 1000, with symptoms occurring within 2 months after malarial episode [9].

According to severity of symptoms, Schnorf, *et al*. [10] classified PMNS into three subtypes: (*i*) Mild and localized encephalopathy, characterised by isolated cerebellar ataxia or postural tremor; (*ii*) Diffuse but relatively mild self-limiting encephalopathy causing acute confusion with or without convulsions; and (*iii*) Severe generalized and progressive encephalopathy, characterised by motor aphasia, generalised myoclonus, postural tremor, and cerebellar ataxia, resembling ADEM.

No clear demarcation line can be laid down between PMNS and ADEM due to striking similarities between these two *e.g.* latency period, multifocal neurological deficits, response to steroids, and good prognosis. However, in PMNS, brain MRI can be normal or show non-specific hyperintensity as against the characteristic changes of ADEM that include perivenular inflammation with surrounding demyelinization and diffuse or scattered hyperintensity in the white matter of brain or spinal cord. ADEM also bears clinical and pathological resemblance with multiple sclerosis and initial differentiation can be difficult, but later in the course these two can be distinguished on the basis of clinical course of disease, lack of relapses, and resolution of lesions on repeat MRI [1,2].

Contributors: SG: Acquisition of data, patient management, and literature review; AA: Concept, drafting the article, manuscript review, manuscript editing, revising the article critically for important intellectual content; AA will act as guarantor. Both the authors approved the final manuscript.
Funding: None; *Competing interests*: None stated.

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