CASE REPORT

# Acute Disseminated Encephalomyelitis in A 4-Year-Old Female Treated for Cerebral Malaria: A Case Report

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**ABSTRACT**

Acute disseminated encephalomyelitis (ADEM) is a multifocal demyelinating disease and a rare post-malarial neurologic sequela. It usually follows cerebral malaria few days to weeks after full recovery and there is absence of malaria parasites in the patient's peripheral blood film. It can also follow bacterial and viral illnesses. Malaria is an endemic disease in tropical countries like Nigeria, but with careful literature search, no reported case of ADEM following complicated malaria in Nigerian children was seen. Reported cases of post malaria ADEM from other malaria endemic countries were in older children and young adults.

We report a case of ADEM in a 4year old female who presented to our centre with features of complicated malaria (cerebral malaria and black water fever). She was treated for complicated malaria and recovered fully. Few days' post recovery, she suddenly developed diffuse neurologic symptoms with a CT scan result which suggested ADEM. There was no malaria parasite seen in a repeat peripheral blood film and cerebrospinal fluid analysis showed elevated protein and lymphocytic pleocytosis. With institution of steroid therapy, she recovered remarkably and was discharged home.

This case demonstrates the need for a high index of suspicion, close monitoring and follow up of children treated for cerebral malaria as ADEM is a treatable post malarial complication, which if undetected, can lead to permanent neurologic sequelae.

***Key words:*** *Multifocal demyelinating disease, Neurologic sequelae, Non traumatic encephalopathy, Children.*

## INTRODUCTION

Cerebral malaria is the most common non traumatic encephalopathy in the world.[1] It has a clinical hallmark of coma and it is the most severe neurologic presentation of acute *falciparum* malaria.[1] In a stable transmission area, a prevalence of 14% was reported in children with severe malaria.[2] Amongst all the complications of malaria, cerebral malaria has the highest fatality.[2] Neurologic sequelae has

been reported in up to 13% of survivors of cerebral malaria.[3] These include seizure disorders, cranial nerve deficit, memory impairment, hyperactivity, mono and quadriparesis, cerebellar ataxia, psychosis, pyramidal/extrapyramidal rigidity, hemiplegia and rarely pseudobulbar paralysis.[1,2,3,4,5] Acute disseminated encephalomyelitis (ADEM) is a rare complication of cerebral malaria and has been reported in older children and adults.[6,7,8] Very few cases have been reported in young children.

CASE REPORT

A 4-year-old female patient was admitted with a 4-day history of fever and multiple episodes of convulsion of a day duration. The fever was high grade with rigors. It was followed 3 days later with multiple episodes of generalized tonic-clonic convulsions associated with loss of consciousness. She was injected with anti-tetanus serum by a nurse a day prior to the onset of convulsion following a puncture wound sustained on her right foot sustained two days prior to the onset of the current illness.

General examination revealed a pre-school girl in respiratory distress, febrile with axillary temperature of 38.9ºC, anicteric, moderately pale and weighed 15kg. Pulse rate was 152beats/minute with blood pressure of 110/70mmHg and respiratory rate of 44cycles/minute. She had altered consciousness with a Glasgow Coma Score (GCS) of 9, had generalized tonic-clonic seizures, with no demonstrable cranial nerve abnormalities. She had global hypertonia and no plantar response. There were no signs of meningeal irritation. The liver was palpably enlarged 6cm below the right costal margin, non-tender, firm, smooth surfaced and sharp edged. There was an ulcer on the lateral edge of the plantar surface of the right foot, measuring 4cm by 3cm, with sloping edge and a necrotic base.

Investigation showed Packed Cell Volume(PCV)=21%; Total White Blood Cell(TWBC)= 3,300/$mm^3$ with differential count: Neutrophils= 37%, Lymphocytes= 59.8%, Eosinophils = 0.9%, Monocytes = 2.0%, Basophils = 0.2%; Random Blood Sugar (RBS)= 96mg/dl, Rapid Diagnostic Test(RDT) for Human Immunodeficiency Virus (HIV) I & II screening was non-reactive. RDT for malaria (Histidine Rich Protein2) was reactive; peripheral blood smear showed trophozoites of *Plasmodium falciparum* with a parasite density of 615,333/µl. Blood urea level was 6.2mmol/l while serum creatinine was 102µmol/l. serum electrolytes showed Sodium(Na) = 127mmol/l, Potassium(K) = 3.7mmol/l, Chloride(Cl)= 90mmol/l, Bicarbonate($HCO_3$) = 13mmol/l. Urinalysis revealed the following: appearance = bloody, blood = >3+, bilirubin = >3, urobilinogen = normal, nitrites = negative, ketones = nil, casts = granular++. Cerebro Spinal Fluid (CSF) analysis and clotting profile were normal.

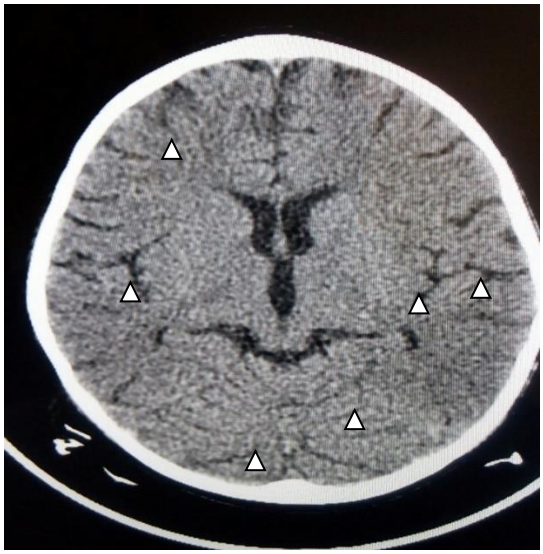
A diagnosis of complicated malaria (cerebral malaria and black water fever) was made. She received 3 doses of intravenous artesunate within the first 24 hours and subsequently 24hourly till she was able to take orally; then a full course of artemisinin-based combination therapy was given amongst other supportive measures.

The patient's GCS gradually improved and she became fully conscious on the 12th day of admission. She was now able to eat, play and interact with her mother.

On the 15th day of hospitalization (3rd day post recovery), she suddenly developed abnormal movement of the left upper limb, difficulty with swallowing and drooling of saliva. She was unable to speak or hear and laughed uncontrollably. Patient's mother also observed that she frequently touched her lower back as though in pain but when the area was pressed, she would laugh.

Examination revealed altered sensorium with a GCS of 12. Notably, the patient laughed when painful stimulus was applied. There was neck stiffness with positive Kerning's and Brundzinski's signs, generalized hypertonia of clasp knife type, brisk deep tendon reflexes, flexor plantar response and sustained ankle clonus. Pupils were sluggishly reactive to light, there was no reaction to visual stimulus and corneal reflex was absent. The eyes were fixed in a left downward gaze, there was no facial asymmetry, no response to sounds, she was unable to swallow and had tonic head turn to the left. Ophthalmologist's review confirmed bilateral sluggish, direct and consensual pupillary reaction to flashlight with normal retinal findings; a diagnosis of bilateral optic neuritis was entertained. A repeat lumbar puncture showed clear CSF, raised CSF protein (177mg/dl) with lymphocytic pleocytosis and normal blood glucose. Repeat peripheral blood smear showed no malaria parasite. Cranial Computed Tomography (CT) with serial pre and post contrast axial images acquired at 2.5mm cuts through the base of the skull, brain to vertex showed cerebral and cerebellar volume loss, with no intraparenchymal lesions (Figure 1). Magnetic Resonance Imaging (MRI) could not be done because the machine was faulty at the time the patient was managed.

**Figure 1.** Cranial CT scan of the patient with arrows showing abnormally prominent cerebral sulci and gyri (evidence of cerebral volume loss) and cerebellar folia (evidence of cerebellar volume loss



A diagnosis of ADEM as a complication to cerebral malaria was made. The patient was treated with intramuscular methylprednisolone. She recovered remarkably after 12 days of steroid therapy and was discharged home on oral steroids. She was followed up weekly in the outpatient clinic and by 3rd week post discharge, all the symptoms had resolved completely. By 6th week follow up visit, mother revealed that she was experiencing learning difficulties but declined a repeat CT scan or MRI due to financial constraints. Thereafter, patient was lost to follow up and all attempts to get them to visit the hospital through several phone calls were abortive.

DISCUSSION

ADEM is a multifocal monophasic demyelinating disease characterized by sudden onset of neurologic dysfunction.[10] It follows viral and bacterial infection, vaccination and rarely plasmodium infection.[10,11,12,13,14] ADEM following *falciparum* malaria occurs as one of the post malarial neurological syndrome (PMNS) which is defined as an acute onset of neurological or neuropsychiatric symptoms in patients who recently recovered from *Plasmodium falciparum* malaria with negative blood films at the time of onset.[10] ADEM has been reported in other malaria endemic countries, but a careful literature search on google scholar, Pubmed and African Journals Online(AJOL) showed no reported case of ADEM in Nigerian children following malaria infection.[3,11,12,14]

Majority of childhood ADEM occur in children younger than 10years with a mean age of 5 to 8years.[15] The index patient was aged 4, and also had negative blood film at the time of the disease manifestation. ADEM following cerebral malaria as a part of post malarial neurologic syndrome has been described.[10] Prevalence of ADEM in children with *falciparum* malaria is unknown, however, prevalence of PMNS is 0.12% and it is most common with cerebral malaria.[10]

ADEM is characterized by class-switched IgG autoantibodies to various myelin proteins supporting antigen-driven immune response.[16] *Plasmodium falciparum* as was identified in our patient has been implicated to cause ADEM either directly or indirectly through reactivation of neurotropic viruses.[11,12] Cytokines (Tumour Necrosis Factor and interleukins 2 and 6) which are elevated in complicated malaria and remains high even after the parasite is cleared have been implicated as there is a higher concentration of these cytokines in serum of patients with PMNS compared to the recovery period.[10]

Typically, ADEM occurs 1-2 days to several weeks after a childhood infectious disease. Features of ADEM include sudden onset of encephalopathy unexplained by the systemic illness; these include altered sensorium, multiple cranial nerve abnormalities, quadriplegia, paraplegia, dystonia, speech defect, mood changes, choreiform movement, nystagmus, urinary incontinence/ retention, aggressive behavior, bilateral optic nerve neuritis and meningisim.[5,13]

CSF protein is raised with lymphocytes predominance. There may be hypo attenuation, gyral enhancement or even a normal cranial CT because CT is insensitive to white matter changes compared to MRI and this may yield false-negative results. Gyral enhancement was found on our patient's cranial CT scan, but MRI could not be done to further identify the white matter changes as the facility's MRI was faulty as at the time the patient was managed.

Also, there is typically a delay between the onset of neurologic symptoms and the appearance of ADEM-associated hypodense subcortical lesions which can show on CT scan as a ring-like enhancement.[17] There is diffuse demyelination on MRI and lesions appear hyperintense in Fluid Attenuated Inversion Recovery [FLAIR and Transverse relaxation Time [T2] weighted MRI which is best for diagnosis.[11,18]

Treatment is with high dose methylprednisolone, tapering off with oral prednisolone over the next few weeks.[13,19] Cases of steroid responsive post malarial ADEM without sequelae have been reported, however few of the patients involved had relapses.[5,11,15,20] Response to treatment is usually prompt and majority of children have total remission within 1 week of starting steroids.[13] There may be a greater impact on the behavior and intelligence of children with an ADEM onset younger than 5years of age.[21]

## CONCLUSION

ADEM is a rare post-malarial neurologic complication which could occur after treatment for cerebral malaria, even in very young children. In a resource poor setting like ours, a high index of suspicion combined with symptomatology, cranial CT scan and CSF analysis can aid in its early diagnosis and treatment. It is therefore very important to follow up patients who were managed for cerebral malaria for at least 8 weeks, looking out for features of ADEM and other PMNS.

## REFERENCES


1. Newton CR, Hein TT, White N. Cerebral malaria. *J Neurol Neurosurg Psychiatry* 2000; 69(4): 433-441.
2. Olarewaju WI, Johnson AW. Malaria in children in Ilorin, Nigeria. *East Afr Med J*2001 Mar; 78(3): 131-134.
3. Oluwayemi IO, Brown BJ, Oyedeji OA and Oluwayemi MA. Neurological sequelae in survivors of cerebral malaria. *Pan Afr Med J* 2013; 15: 88-90.
4. Bajiya HN, Kochar DK. Incidence and outcome of neurological sequelae in survivors of cerebral malaria. *J Asso Phys Ind* 1996; 44:679-681.
5. Mohaptra MK, Sethy G, Mohanty SC. Pseudobulbar paralysis-A sequelae of cerebral malaria. *JAPI* 2004; 52:324-325.
6. Koibuchi T, NakamuraT, Muira T, Endo T, Nakamura H, Takahashi T. Acute disseminated encephalomyelitis following plasmodium vivax malaria. *J Infect Chemother* 2003; 9(3):254-256.
7. Mani S, Mondal SS, Guha G, Gangopadhyay S, Pani A, Das B, *et al*. Acute disseminated encephalomyelitis after mixed malaria infection (P. falciparum and P. vivax) with MRI closely simulating multiple sclerosis. *Neurologist* 2011; 17(5): 276-278.
8. Agrawal A, Goyal S. Acute disseminated encephalomyelitis in a child following malaria. *Indian Pediatr* 2012; 49:922-923.
9. Rachita S, Satyasundar M. Mrutunjaya D, Birakishore R. Acute disseminated encephalomyelitis(ADEM)- a rare complication of falciparum malaria. *Indian J Pediatr* 2013; 80(6):499-501.
10. Menge T, Hemmer B, Nessler S, Wiendi H, Neuhaus O, Hartung HP, *et al.* Acute disseminated encephalomyelitis. *Arch Neurol* 2005;62: 1673-1680.
11. Suresh V, Srinivas PS, Bhagavati A, Ramana Murthy SV. Acute disseminated encephalomyelitis following falciparum malaria. *J Indian Acad Clin Med* 2012, 13(3): 233-235.
12. Mohsen AH, McKendrick ML, Schmis ML, Green ST. Post malarial neurological syndrome: a case of acute disseminated encephalomyelitis? *J Neurol Neurosurg Psychiatry* 2000; 68:388-389.
13. Jayakrishnan MP, Krishnakumar P. Clinical profile of acute disseminated encephalomyelitis in children. *J Pediatr Neurosci* 2010;5(2):111-114.

14. Prendki V, Elziere C, Durand R, Hamdi A, Cohen Y, Onnen I, *et al.* Post malarial neurological syndrome-two cases in patients of African origin. *Am J Trop Med Hyg* 2008; 78:699-701.
15. Anlar B, Basaran C, Kose G, Gaven A, Haspolat S, Yakut A, *et al.* Acute disseminated encephalomyelitis in children: outcome and prognosis. *Neuropediatrics*. 2003;34(4):194-199.
16. Van Haren K, Tomooka BH, Kidd BA, Banwell B, Bar-Or A, Chitnis T, *et al.* Serum auto antibodies to myelin peptides distinguish ADEM from relapsing-remitting multiple sclerosis. *Mult Scler J* 2013; 19(13):1726-1733.
17. Lukes SA, Norman D. Computed tomography in acute disseminated encephalomyelitis. *Ann Neurol* 1983 May; 13(5):567-572.
18. Johnson RT. Post infectious demyelinating diseases. In: Viral infections of the nervous system. Johnson RT (ed). 2nd edition, Lippincott Raven, Philadelphia: 1998;181-210.
19. Hahn JS, Seigler DJ, Enzmann D. Intravenous gammaglobulin therapy in recurrent acute disseminated encephalomyelitis. *Neurology* 1996; 46:1173-1174.
20. Sharma N, Varma S, Bhalla A. Acute disseminated encephalomyelitis after treatment of severe falciparum malaria. *Indian J Med Sci* 2008; 62:69-70.
21. Jacobs RK, Anderson VA, Neale JL, Shield LK, Kornberg AJ. Neuropsychological outcome after acute disseminated encephalomyelitis: impact of age at illness onset. *Pediatr Neurol* 2004 Sep; 31(3): 191-197.