International Journal of Research in Medical Sciences
Yadav V et al. Int J Res Med Sci. 2020 Nov;8(11):4001-4005
www.msjonline.org
pISSN 2320-6071 | eISSN 2320-6012
DOI: https://dx.doi.org/10.18203/2320-6012.ijrms20204893

Original Research Article

MRI brain findings of cerebral malaria in children with acute encephalitis syndrome: a prospective study in 60 patients

Vibha Yadav*, Sharad Thora, Prachi Choudhary

Department of Pediatrics, Mahatma Gandhi Memorial Government Medical College, Indore, Madhya Pradesh, India

Received: 31 August 2020
Accepted: 06 October 2020

***Correspondence:**
Dr. Vibha Yadav,
E-mail: drvibha.yadav28@gmail.com

ABSTRACT

Background: Acute encephalitis syndrome (AES) is defined as a person of any age group, at any time of the year with the acute onset of fever and change in mental sensorium (including confusion, disorientation, coma or inability to talk) and/or new onset of convulsions (excluding febrile seizures). Encephalitis is a inflammation of brain tissue which presents as a diffuse and/or a focal neuropsychological dysfunction and inflammation of adjacent meningitis. Objectives were to determine clinicoepidemiological profile in AES with special to reference cerebral malaria and to study various MRI findings in patients of AES especially in cerebral malaria.
Methods: A prospective study of all cases of fever with unconsciousness or altered sensorium with or without convulsions admitted in PICU of MYH and CNBC Indore. Inclusion criteria was all those children who were previously neurologically normal, of age 1-14 years, patients with fever (<15days) with altered sensorium, with or without seizures and who stay in hospital long enough to complete essential diagnostic work up which includes (CBC with peripheral smear, RFT, LFT, MP, S. electrolytes, CSF, MRI brain).
Results: The final study group comprised of 60 patients with age group 1-14 yrs and male to female ratio was 1.07:1. Patients with diagnosis of cerebral malaria were 17. High grade fever, headache, altered sensorium, generalized seizures In general examination pallor was present in 52.9%, icterus in 35.29% cases of cerebral malaria. Splenomegaly (70.5%) was more common finding than hepatomegaly (58.8%) in cerebral malaria. GCS was>6 in most cases, fundus abnormality and meningeal irritation was absent in all cases of cerebral malaria. MRI of brain in cerebral malaria was mostly normal, in (47.05%), second most common we get hyperintensity in periventricular and corpus callosum areas (23.52%), hyperintensity in basal ganglia and thalamus was found in17.64% cases and white matter changes in 2 cases. The final outcome of all cerebral cases was good, all were discharged, and there was no mortality.
Conclusions: Our result demonstrate that cerebral malaria is a common cause of acute febrile encephalopathy in children. Presence of plasmodium falciparum is essential for diagnosis of cerebral malaria. No specific lesions have been identified in MRI brain.

Keywords: Acute febrile encephalopathy, Cerebral Malaria, Acute encephalitis syndrome

INTRODUCTION

Acute encephalitis syndrome (AES) is defined as a person of any age group, at any time of the year with the acute onset of fever and change in mental sensorium (including confusion, disorientation, coma or inability to talk) and/or new onset of convulsions (excluding febrile seizures). Encephalitis is an inflammation of brain tissue which presents as a diffuse and/or a focal neuropsychological dysfunction and inflammation of adjacent meningitis.[1-4] The world health organization defines cerebral malaria as a clinical syndrome characterized by coma for atleast 1/2 hour after

termination of a seizure or correction of hypoglycemia, asexual varieties of Plasmodium falciparum parasites on peripheral blood smears and no other cause to clarify the coma.[11]

In many children with AES, there is a prodromal period of infectious symptoms from the upper respiratory tract or gastrointestinal tract precede the onset of central nervous system (CNS) symptoms.[1-4] Most children with acute CNS infection will present with fever or a recent history of fever, but not all other symptoms may be headache, vomiting, seizures, altered sensorium, abdominal pain. There are various causative agents that may cause AES like viruses, bacteria, parasite, fungi, autoimmune.[1,3-5]

A detailed history of travel, vaccination, area of residence will be helpful in giving a clue to etiology. Various important investigation complete blood count (CBC) with peripheral smear for malarial parasite, cerebral spinal fluid (CSF) examination including microscopy, culture, acid fast bacilli (AFB) stain, polymerase chain reaction (PCR) for viruses like herpes, Japanese encephalitis (JE). MRI (magnetic resonance imaging) brain also contributes in making a diagnosis like inflammatory lesions or necrosis within the fronto temporal regions in Herpes simplex encephalitis (HSV).[6-8] In arboviruses like west nile virus (WNV) lesions are often visualized in deep grey matter in thalami, basal ganglia and in cerebellum, and enterovirus (EV) 71 virus shows lesions within the brainstem.[8-10] But there are no significant studies showing any specific lesions present in patients of cerebral malaria.

In this study, an attempt has been made to identify clinical symptoms and signs specific to etiological agents of AES with special attention to cerebral malaria and specific MRI findings of brain in patients with cerebral malaria.

METHODS

It was a hospital based prospective study of the patients with acute febrile encephalopathy syndrome admitted in the Department of Pediatrics in our institute from 1 March 2016 to 30 September 2017 in collaboration with pathology department and radiology. All the cases admitted pediatric intensive care unit (PICU) have been studied based on the following inclusion criteria:1) All those children who were previously neurologically normal, of age 1-14 years 2) Patients with fever (<20days) with altered sensorium, with or without seizures 3) Who stay in hospital long enough to complete essential diagnostic work up which incorporates (CBC with peripheral smear, Renal function, Liver function test, malaria parasite, Serum, electrolytes, CSF, MRI brain).

All the relevant clinical and demographic information were recorded in pre structured proforma together with positive findings of physical examination at the time of admission. A record patients' progress in hospital was maintained. With the results of all investigations: Complete hemogram, peripheral smear for plasmodium falciparum, renal function test, liver function test, serum electrolytes, random blood sugar, blood culture and sensitivity, CSF examination for gram stain, culture, AFB.

Patients were diagnosed to possess cerebral malaria supported on the detection of plasmodium falciparum parasite in peripheral smear of blood. Patients were suspected to possess viral etiology supported the subsequent criteria: absence of bacteria on direct microscopy or culture, with or without a CSF pleocyotsis with lymphocytic predominance. No viral isolation and serology were done because it was unavailable in our institute. MRI brain was done in all patients. All the patients were treated in step with standard treatment protocols. This included supportive care e.g. inotropic agents were used when patient was hemodynamically compromised, intravenous antibiotics, antimalarials, anticonvulsants, decongestive measure for raised intracranial pressure. During the recovery phase, patients underwent rehabilitation under physiotherapy department. The study was approved by institutional ethics committee.

RESULTS

A total of 60 patients with diagnosis of acute febrile encephalopathy were admitted. We had patients old starting from 1-14 years, maximum incidence being within 6-10 years in cerebral malaria. The male to female ratio was 1.07:1 among all 60 patients. The age-wise distribution in cerebral malaria and other AES is shown in (Table 1).

Table 1: Age group.

Age (years)	Cerebral malaria		Other	
	Count	%	Count	%
1-5	7	41.11	27	62.79
6-10	9	52.9	11	25.58
11-14	1	5.8	5	11.6

All the 60 cases were investigated thoroughly to identify the etiology. Among 60 cases 28.3% were cerebral malaria cases, 16.6% were herpes simplex encephalitis, 16.6% were pyogenic meningitis, 10% were tubercular meningitis and 8.33% were cases of acute disseminated encephalomyelitis (ADEM), 4 cases were of autoimmune encephalitis, 3 unknown encephalitis, 2 were of varicella and 2 cases were of Japanese encephalitis. Only 1 patient had dengue encephalitis. Table 2 shows etiology of AES case.

The most common symptom in cerebral malaria was fever 100%, followed by altered sensorium 76.47,

headache in 70.58% generalized seizures 70.58%, 6 patients had abdominal pain, 3 had vomiting, 2 were drowsy and a pair of had tonic posturing. In other encephalitis the foremost common symptom was fever 100%, followed by generalized seizures 65.11%, altered sensorium 55.8%, 37.2% were drowsy, 32.55% had vomiting and headache, 23.2% had tonic posturing, 2 patients had abdominal pain, 7 had cough, 4 had focal seizures, 3 had rashes. Pallor was present in 52.9% of cases and icterus was present in 35.5% of cases whereas in other encephalitis pallor was present in mere 6.9% and icterus in 4.6% cases hepatomegaly was present in 58.8% and splenomegaly in 70.5% cases. In other encephalitis hepatomegaly was present in 9.3% and splenomegaly in 4.6% cases. (Table 3) shows clinical profile of cerebral malaria cases.

Table 2: Etiology of AES case.

Diagnosis	No. of cases	Percentage
ADEM	5	8.33
Autoimmune Encephalitis	4	6.66
Unknown encephalitis	3	5
Cerebral Malaria	17	28.3
Dengue Encephalopathy	1	1.6
Herpes simplex	10	16.6
Pyogenic Meningitis	10	16.6
Japanese Enceph	2	3.3
Tubercular Meng	6	10
Varicella enceph	2	3.3
Total	60	100

Table 3: Clinical profile of cerebral malaria cases.

Signs and symptoms	Cerebral malaria cases (%)	Other encephalitis
Fever	17(100%)	43(100)
Headache	12(70.8)	14(32.55)
Vomiting	3(17.6)	14(32.55)
Alter Sensorium	13(76.47)	24(55.8)
Drowsy	2(11.76)	16(37.2)
Generalised Seizures	14(82.35)	38(88.3)
Focal Seizures	-	4
Abdo Pain	6	2
Pallor	52.9%	6.9%
Icterus	35.5%	4.6%
Hepatomegaly	58.8%	9.3%
Splenomegaly	70.5%	4.6%

In CSF analysis cerebral malaria cases had CSF cells <5, all were lymphocytes, glucose and protein were within the normal range. But in other encephalitis, 32.5% cases had cell between 10-100, followed by 0-5 cells in 30.2%, 23.2% had >500 cells, 6 cases had 100-500 cells. In 76.7% CSF lymphocytic pleocytosis was present, 23.2% neutrophilic pleocytosis was present. Glucose was<40 gm/dl in 65.1% CSF, protein<40 gm/dl was present in 86.0% CSF. Among 17 cases of cerebral malaria, 88.23% cases had peripheral smear +ve for plasmodium falciparum and RDT (rapid diagnostic test) was +ve in 70.58% cases. MRI brain was done in all 60 admitted patients and also the report showed that MRI brain of cerebral malaria cases was normal in (47.05%), hyperintensity in periventricular and corpus callosum areas was present in 23.52% cases, (Figure 1) hyperintensity in basal ganglia and thalamus was found in 17.64% cases (Figure 3) and white matter changes in 2 cases (Figure 2). In other AES cases, hyperintensity in basal ganglia and thalamus was present in 4.6% cases and in remainder of the cases various non-significant MRI findings were present.

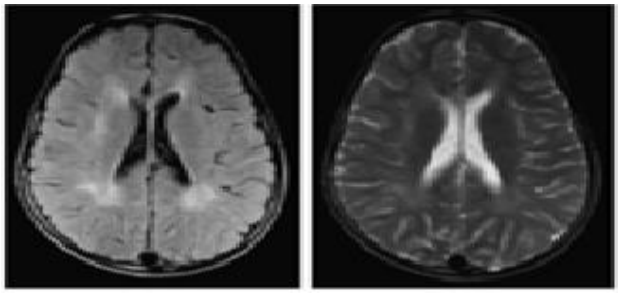

Figure 1: Periventricular white matter abnormalities in cerebral malaria case on T2 image.

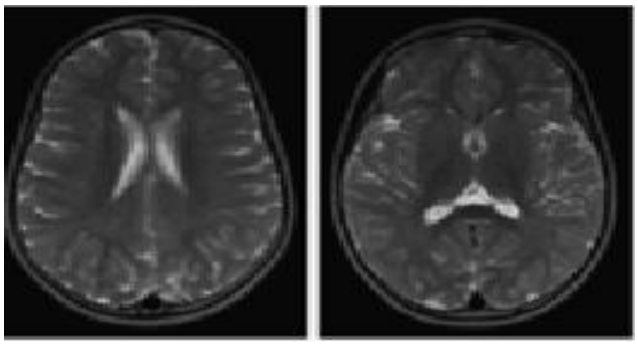

Figure 2: White matter changes in cerebral malaria on T2 image.

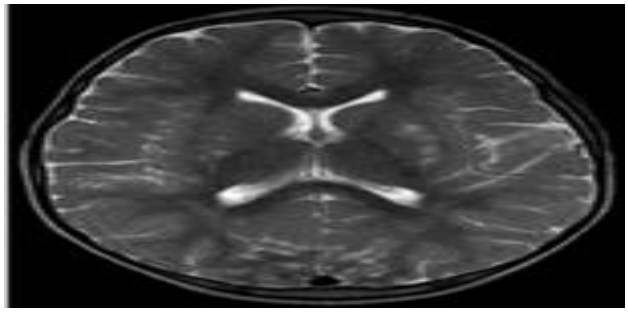

Figure 3: Hyperintensity in basal ganglia in cerebral malaria case on T2 image.

Out of 17 cases of cerebral malaria 15 patients were discharged and 2 went left against medical advice (LAMA) and among 43 cases of other encephalitis, 31 were discharged, 5 went LAMA and 7 patients died due to complications.

DISCUSSION

This study is a hospital based prospective study of the patients of acute febrile encephalopathy admitted in the PICU in our institute. Only patients with fever for lesser than 20 days with altered sensorium were included in the study to exclude other chronic causes of encephalopathy. We aimed to review clinical profile of acute febrile encephalopathy with special reference to cerebral malaria.

Cerebral malaria is fatal entity, if not treated properly because it can cause brain injury, metabolic derrangment. The clinical hallmark of cerebral malaria is impaired consciousness with coma the most severe manifestation. There is sequestration of parasitised RBCs within the cerebral capillaries and where they release local inflammatory factors which causes the cerebral edema. Systemic response includes hyperpyrexia, seizures, hypoglycemia.[12] Microhemorrhages are often seen in cerebral white matter. Plasmodium falciparum is epileptogenic and degree of parasitemia increases the chance of siezures. Prolonged siezure acitvity can cause irreversible neuron damage which will cause poor neurological outcome.[13] During this study, the most common finding in cerebral malaria was high grade fever (100%), headache (70.58%), altered sensorium (76.47%), generalized seizures in (70.58%), and tonic posturing in (11.76%) cases. The mean duration of fever was 6 days. In general examination pallor was present in 52.9%, icterus in 35.29% cases of cerebral malaria. Splenomegaly (70.5%) was more common finding than hepatomegaly (58.8%) in cerebral malaria. GCS was>6 in most cases, fundus abnormality and meningeal irritation was absent in all cases of cerebral malaria. The mean Hb level in our study was 9.56 gm/dl. Platelet count was less than 99000 in 64.7% cases of cerebral malaria. CSF examination was within normal limits in all 100% cases of cerebral malaria. Most patients had no secondary complications, only 3 had aspiration pneumonia. MRI brain in cerebral malaria was normal in (47.05%) cases hyperintensity in periventricular and corpus callosum areas (23.52%), hyperintensity in basal ganglia and thalamus was found in 17.64% cases and white matter changes in 2 cases. The final outcome of all cerebral cases was good, all were discharged, and there was no mortality.

In study among 60 cases 28.3% were cerebral malaria cases, 16.6% were herpes simplex encephalitis,16.6% were pyogenic meningitis, 10% were tubercular meningitis and 8.33% were cases of ADEM. 4 cases had autoimmune encephalitis, 3 unknown encephalitis, 2 were of varicella and a pair had Japanese encephalitis. Only 1 patient had dengue encephalitis.

Cerebral malaria needs special consideration especially within the post-monsoon period. There are not any distinguishing clinical or radiological features to differentiate the varied causes of viral encephalitis and therefore the clinical and radiological findings in encephalitis should be interpreted within the other epidemiological background.

CONCLUSION

To conclude that diagnosis of cerebral malaria can be made on the basis of clinical features and basic investigations. There is no requirement of brain imaging, CSF examination or serological testing. MRI, CSF examination is required to exclude other causes. Cluster of findings like fever, altered sensorium, pallor, hepatomegaly, thrombocytopenia is more common in cerebral malaria. Cerebral malaria is believed to be more common explanation of acute febrile encephalopathy during monsoon and post monsoon period.

Diagnosis of other encephalitis needs specific serological test. MRI findings are not helpful in distinguishing different viral encephalitis except Japanese and herpes simplex encephalitis where specific effected areas of brain are known. Mortalities in some viral encephalitis like herpes simplex encephalitis are often reduced by early diagnosis, proper referral and early treatment.

The incidence of pyogenic meningitis, Japanese encephalitis and, tuberculous meningitis can be reduced by vaccination in rural and endemic areas. Cerebral malaria and other vectors born encephalitis can be controlled by using insecticides.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

REFERENCES

1. Galanakis E, Tzoufi M, Katragkou A, Nakou I, Roilides E. A prospective multicenter study of childhood encephalitis in Greece. Pediat Infect Disea J. 2009;28(8):740-2.
2. Wang IJ, Lee PI, Huang LM, Chen CJ, Chen CL, Lee WT. The correlation between neurological evaluations and neurological outcome in acute encephalitis: a hospital-based study. Europe J Paediat Neurol. 2007;11(2):63-9.
3. Tobias IF, Donati F, Vassella F, Schaad UB, Bianchetti MG. Acute encephalitis in Swiss children: aetiology and outcome. Europe J Paediat Neurol. 1998;2(5):233-7.
4. Granerod J, Ambrose HE, Davies NW, Clewley JP, Walsh AL, Morgan D, et al. Causes of encephalitis

and differences in their clinical presentations in England: a multicentre, population-based prospective study. Lanc Infect Disea. 2010;10(12):835-44.
5. Le VT. Viral etiology of encephalitis in children in southern Vietnam: results of a one-year prospective descriptive study. PLoS Negl Trop Dis. 2010;4(10):e854.
6. Whitley RJ, Kimberlin DW. Herpes simplex: encephalitis children and adolescents. Semin Pediat Infect Diseas. 2005;16(1)17-23.
7. Kennedy PG. Viral encephalitis: causes, differential diagnosis, and management. J Neurol Neurosurg Psychiat. 2004;75(1):i10-5.
8. Maschke M, Kastrup O, Forsting M, Diener HC. Update on neuroimaging in infectious central nervous system disease. C Opini Neurol. 2004;17(4):475-80.
9. Horger M, Beck R, Fenchel M, Ernemann U, Nägele T, Brodoefel H, et al. Imaging findings in tick-borne encephalitis with differential diagnostic considerations. Americ J Roentgenol. 2012;199(2):420-7.
10. Huang MC, Wang SM, Hsu YW, Lin HC, Chi CY, Liu CC. Long-term cognitive and motor deficits after enterovirus 71 brainstem encephalitis in children. Pediat. 2006;118(6):e1785-8.
11. World Health Organization. Severe falciparum malaria. World Health Organization, communicablediseases cluster. Trans R Soc Trop Med Hyg. 2000;94:S1–90.
12. Clark IA, Alleva LM. Is human malarial coma caused, or merely deepened, by sequestration? Trends Parasitol. 2009;25:314-8.
13. Idro R, Ndiritu M, Ogutu B, Mithwani S, Maitland K, Berkley J, et al. Burden, features, and outcome of neurological involvement in acute falciparum malaria in Kenyan children. J Americ Medic Assoc. 2007;297:2232–40.

Cite this article as: Yadav V, Thora S, Choudhary P. MRI brain findings of cerebral malaria in children with acute encephalitis syndrome: a prospective study in 60 patients. Int J Res Med Sci 2020;8:4001-5.