

Haemorrhological Study in Cerebral Malaria: A Hospital Based Study

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ABSTRACT

Background: The World Health Organization defines cerebral malaria as a clinical syndrome characterized by coma at least 1 hour after termination of a seizure or correction of hypoglycaemia, asexual forms of plasmodium falciparum parasites on peripheral blood smears and no other cause to explain the coma.

Aim of the study: To evaluate the incidence of hemorrhagic manifestations in cerebral malaria patients.

Materials and Methods: The study was conducted in the department of general medicine of Haridev Joshi Hospital, Dungarpur, Rajasthan, India. 40 patients admitted to the surgical medical ward with symptoms of cerebral malaria were included in our study. The patients included in the study had symptoms like fever with chills and rigors for the more than 7 days. Their liver function and renal function tests were deranged and the peripheral smear was positive for malarial parasites. For the evaluation of cerebral hemorrhage patients were subjected to MRI. The findings of the MRI were recorded and subjected to statistical analysis.

Results: A total of 40 patients were included in the study. The number of male patients in the study was 22 and number of female patients was 18. The mean age of the patients was

43.23±2.9 years. The basal ganglia infarct was seen in 10% patients, thalamus infarct in 10% patients, cerebellum infarct, pontine infarct, parietal occipital lobe infarct and other findings were seen in 5% of patients each.

Conclusion: Within the limitations of the study we conclude that patients with cerebral malaria are at high risk for cerebral hemorrhage and MRI should be conducted for each patient for diagnosis at early stage.

Keywords: Malaria, Cerebral Hemorrhage, Plasmodium.

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INTRODUCTION

Malaria is still a global health problem. India accounts for 40% of all malaria cases with Plasmodium vivax infection, contributing to two-third of them. Plasmodium vivax is usually presumed to cause only uncomplicated malaria, but in the past few years, there have been several reports of complicated malaria, including cerebral malaria.¹⁻³ The World Health Organization defines cerebral malaria as a clinical syndrome characterized by coma at least 1 hour after termination of a seizure or correction of hypoglycemia, asexual forms of Plasmodium falciparum parasites on peripheral blood smears and no other cause to explain the coma.⁴ There is an estimated mortality rate of between 15% and 25% even with appropriate treatment and intensive care. However, patients who survive often recover fully with no long-term consequences.⁵ Early diagnosis and treatment is therefore crucial to obtain the best outcome. With the availability of MR scanners in developing countries, where malaria is still an endemic health issue, a few case reports and series have already been published on the role of MR imaging in cerebral malaria.⁶ Hence, we planned the present study to evaluate the incidence of hemorrhagic manifestations in cerebral malaria patients.

MATERIALS AND METHODS

The study was conducted in the department of general medicine of the Haridev Joshi Hospital, Dungarpur, Rajasthan, India. The ethical clearance for the study was obtained from the ethical board of the institute prior to commencement of the study. 40 patients admitted to the surgical medical ward with symptoms of cerebral malaria were included in our study. Patients below 12 years, pregnant women, patients unfit for MRI and those having other systemic conditions such as diabetes, leukemia were excluded from the study. After obtaining an informed consent, all patients were subjected to a preoperative work up. The patients included in the study had symptoms like fever with chills and rigors for the more than 7 days. Their liver function and renal function tests were deranged and the peripheral smear was positive for malarial parasites. Majority of patients had brief episodes of loss of consciousness and few episodes of focal seizures that responded to anticonvulsants. All the patients were subjected to anti-malarial treatment along with supportive treatment. The treatment provided included administration of intravenous quinine dihydrochloride, intravenous fluids, antipyretics, and anti-inflammatory drugs. For

the evaluation of cerebral hemorrhage patients were subjected to MRI. The findings of the MRI were recorded and subjected to statistical analysis.

The statistical analysis of the data was done using SPSS version 20.0 for windows. The Student's t-test and Chi-square test were used to check the significance of the data. The p-value less than 0.05 was predetermined as statistically significant.

Table 1: Demographic data of the patients

Variables	Frequency
Total no. of patients	40
No. of male patients	22
No. of female patients	18
Mean age of the patients (years)	43.23±2.9

Table 2: Pattern of hemorrhagic manifestations in cerebral malaria patients

Area of Hemorrhagic infarct	Prevalence (N = 20)	Percentage
Basal ganglia infarct	2	10
Thalamus infarct	2	10
Cerebellum infarct	1	5
Pontine infarct	1	5
Parietal occipital lobe infarct	1	5
Other	1	5
Total	8	40

RESULTS

Table 1 shows demographic data of the patients. A total of 40 patients were included in the study. The number of male patients in the study was 22 and number of female patients was 18. The mean age of the patients was 43.23±2.9 years. Table 2 shows the pattern of hemorrhagic manifestations in cerebral malaria patients. In total 40% patients were diagnosed from the MRI having cerebral hemorrhagic infarct. The basal ganglia infarct was seen in 10% patients, thalamus infarct in 10% patients, cerebellum infarct, pontine infarct, parietal occipital lobe infarct and other findings were seen in 5% of patients each. The results were compared and found to be statistically significant. ($p < 0.05$)

DISCUSSION

In the present study we observed that out of 40 patients who participated in the study, 40% patients were found to be having cerebral hemorrhage. The basal ganglia infarct was seen in 10% patients, thalamus infarct in 10% patients, cerebellum infarct, pontine infarct, parietal occipital lobe infarct and other findings were seen in 5% of patients each. The results were statistically significant. The results were compared with previous studies and results were found to be consistent. Olumese PE et al examined the fundi of 73 children aged between six months and six years with confirmed diagnosis of cerebral malaria at the Children's Emergency Ward of the University College Hospital, Ibadan. Normal fundi, papilloedema and retinal haemorrhages were present in 38(52.1%), 18(24.7%) and 17(23.3%), respectively on admission. There were no significant differences between the

three groups with respect to age, sex, admission coma score, posture, packed cell volume, parasite density, serum glucose, and serum electrolyte profile on admission. The mortality rates were 16%, 22% and 47% in the normal, papilledema and retinal hemorrhage groups, respectively. Retinal hemorrhage was significantly associated with death. The association was still present after adjusting for other known risk factors for mortality, including age, sex, acidosis, parasite density, anemia, deep coma, and hypoglycemia. Papilledema alone was not associated with mortality when compared with normal fundi. It is concluded that fundoscopic abnormalities are common in children with cerebral malaria, and that retinal hemorrhage is associated with a poor prognosis in such children with cerebral malaria. Greiner J et al compared clinical retinal findings and retinal and cerebral histopathological changes in a series of patients in Blantyre, Malawi, who died of CM. The features systematically compared in the same patient were: (1) clinical, gross and microscopic retinal hemorrhages with microscopic cerebral hemorrhages, (2) retinal and cerebral hemorrhage-associated and -unassociated axonal damage, and fibrinogen leakage, and (3) differences in the above features between the pathological categories of CM without microvascular pathology (CM1) and CM with microvascular pathology (CM2) in retina and brain. Forty-seven patients were included: seven CM1, 28 CM2, and 12 controls. In the 35 malaria cases retinal and cerebral pathology correlated in all features except for non-hemorrhage associated fibrinogen leakage. Regarding CM1 and CM2 cases, the only differences were in the proportion of patients with hemorrhage-associated cerebral pathology, and this was expected, based on the definitions of CM1 and CM2. The retina did not show this difference. Non-hemorrhage associated pathology was similar for the two groups. As postulated, histopathological features of hemorrhages, axonal damage and non-hemorrhage associated fibrinogen leakage correlated in the retina and brain of individual patients, although the difference in hemorrhages between the CM1 and CM2 groups was not consistently observed in the retina. These results help to underpin the utility of ophthalmoscopic examination and fundus findings to help in diagnosis and assessment of cerebral malaria patients, but may not help in distinguishing between CM1 and CM2 patients during life.^{7,8}

Idro R et al reported that cerebral malaria is a well-known complication of Plasmodium falciparum malaria. Over recent years, however, Plasmodium vivax also has been reported to cause cerebral malaria with or without co-infection with P. falciparum. They reported a boy aged 10 years presenting with acute febrile encephalopathy with raised intracranial pressure to the emergency, who was later diagnosed to have P. vivax malaria. His neurological status improved gradually during 6 weeks of pediatric intensive care unit stay. They reported this case to highlight the unusual radiologic findings in the patient, such as multifocal hemorrhagic infarcts in the brainstem, bilateral thalami, frontal cortex and basal ganglia, which have not been reported with P. vivax malaria. Rasalkar DD et al conducted a retrospective institutional review of clinical data and radiological findings of cerebral malaria patients presenting to a tertiary center in India, which is an known to be endemic for malarial disease. The present series describes MRI in four cases all of which revealed bithalamic infarctions with or without haemorrhages in patients with cerebral malaria, and this review examines a subset of

patients with this condition. In addition, acute haemorrhagic infarctions were also seen in the brain stem, cerebellum, cerebral white matter and insular cortex in two of the four patients. In this series, the patient with cerebellum and brain stem involvement died. The remaining three survived with antimalarial and supportive treatment. No neurological symptoms were noted on clinical follow-up. MRI follow-up was obtained in only one of the three patients (3 months post-treatment) and showed resolution of thalamic infarctions. These imaging features may help in the early diagnosis of cerebral malaria so that early treatment can begin and improve the clinical outcome.^{9,10}

CONCLUSION

Within the limitations of the study we conclude that patients with cerebral malaria are at high risk for cerebral hemorrhage and MRI should be conducted for each patient for diagnosis at early stage.

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