ELECTROENCEPHALOGRAPHY IN CEREBRAL MALARIA

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Abstract. Electroencephalography (EEG) was performed in 13 male patients with cerebral malaria during the first 24 hours of admission, using a 10-channel, 10-20 system EEG machine (6 montages, 20 minute duration). The EEG patterns were of theta and delta waves from both sides of cerebral hemisphere suggesting diffused cortical dysfunction. No epileptic pattern was found in patients who had seizures prior to, or after admission. The initial EEG performed on the day of admission did not show any specific pattern attributable to any pathological condition. It was also unable to predict the prognosis of the 2 dead patients. However, one cerebral malaria patient with left hemiplegia was subsequently found to have right basal ganglia hemorrhage in CAT scan, high amplitude delta waves and theta waves in the tracings of the right hemisphere. The study suggests that a single EEG data on admission can hardly give enough information for prediction of the clinical course and outcome of cerebral malaria. Serial EEGs probably provide more useful information regarding the prognostic signs in this group of patients. Nevertheless, EEG could be useful to rule out some cerebral pathology such as space occupying lesions, epilepsy or any other causes of unconsciousness that could produce similar cerebral symptoms in malaria patients.

INTRODUCTION

Cerebral malaria is one of the severe manifestations of falciparum malaria with high mortality (WHO, 1990). It often presents with fever, followed by persisting unconsciousness of varying levels. Apart from convulsions, it could also present with various combinations of other signs and symptoms of diffused cerebral dysfunction namely severe headache, delirium, neck stiffness and extensor posturing, but rarely with focal neurological signs (Bradley *et al,* 1987; WHO, 1990). The pathophysiology of cerebral malaria is not fully understood; obstruction of cerebral microvasculature with cerebral hypoxia is assumed to be the cause of cerebral dysfunction and coma (MacPherson *et al,* 1985; Bradley *et al,* 1987; Aikawa 1988; WHO, 1990). An electro-encephalo-(EEG) is visible amplified record of electrical activities generated by nerve cells of the brain and it can be used as a tool for investigation of changes of state in cerebral activity (Pedley and Emerson, 1991). There is only one previous report of EEG pattern in 2 cerebral malaria patients (Chen *et al,* 1991); however, the pattern in cerebral malaria patients is not clearly defined. This study was designed to elucidate the EEG patterns in cerebral malaria. The correlation between EEG patterns and the prognostic outcome of the treatment, as well as the predictive signs in EEG for convulsion, were also investigated.

MATERIALS AND METHODS

The study was carried out in Phra Pok Klao Hospital, Chanthaburi Province, eastern part of Thailand, the area where multidrug resistant falciparum malaria is endemic.

Subjects

Thirteen male patients with cerebral malaria were recruited into this study. Cerebral malaria was diagnosed when the patients came in with fever, asexual form of *Plasmodium falciparum* in peripheral blood smear, and alteration of consciousness, after excluding other possible causes from history. All of the patients were admitted to medical ward or intensive care unit according to the severity of illness. They were treated with standard treatment for severe or complicated malaria with either quinine or artemether.

Investigations

Complete physical examination, including a thorough neurological examination and laboratory

investigations (LFTs, BUN, creatinine, electrolytes, glucose, CBC) were done immediately on admission and then daily until 7 days (study period) or till the results returned to normal. Lumbar puncture was done and CSF was examined, to exclude other central nervous system (CNS) infections and hemorrhage. Serum and CSF samples were kept and transported to Bangkok for measurement of antibody titer of Japanese-B encephalitis, the most common viral encephalitis in Thailand which is sporadic in this area.

Electroencephalographic study

Electroencephalography (EEC) was performed within the first 24 hours of admission by using a 10-channel, 10-20 system EEG machine, with 6 montages for 20 minutes duration.

RESULTS

Thirteen cerebral malarial patients were recruited in this study. Median (range) of age and serum creatinine level were 27 (19-44) years and 2 (0.4 - 16.5) mg/dl respectively.

Six stuporous (Glasgow coma score > 8) and 7 comatose (Glasgow coma score < 8) cerebral malaria patients had nearly the same basic EEG patterns. The EEG showed generalized asynchronous slow waves; most were of theta waves which presented at 4-7 cycles per second (Fig 1). Some delta waves (1.5 - 3 cycles per second) occurred between the theta waves. The range of amplitude was between 20 and 200 microvolt. Two comatose patients had wave amplitude of less than 50 microvolt. One comatose and one stuporous patients had amplitude of more than 150 microvolt.

Beta activities (more than 13 cycles per second) occurred between the slow baseline waves in 3 comatose patients. No alpha wave (8-13 cycles per second) was found in any of the cerebral malarial patients except one with left hemiplegia grade 0 on admission. In this particular patient, alpha waves were found in some duration between theta waves from the left hemisphere with the amplitude of 50-100 microvolt (Fig 2). In this patient, high amplitude delta waves and theta waves were found in right hemisphere. Brain CAT scan was done and revealed the right basal ganglia hemorrhage.

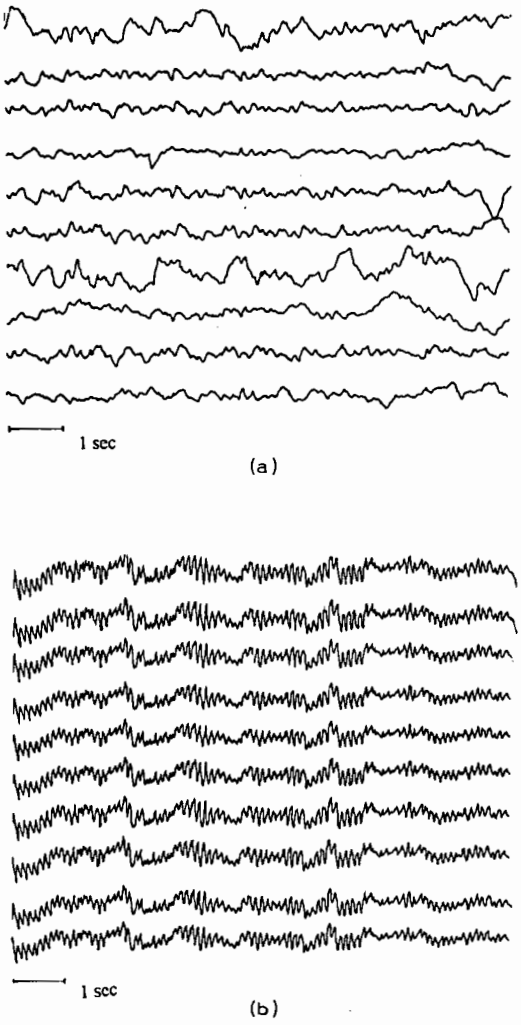

Fig 1–EEG pattern in cerebral malaria (a) and normal EEG (b).

Craniotomy and evacuation of blood clot were done. No evidence of arteriovenous malformation was seen. This patient survived with some neurological deficits.

One stuporose and 3 comatose patients had convulsion without any previous history of epilepsy. The EEGs of these patients showed the same pattern with other cerebral malaria patients. Focal spike, sharp wave, spike and wave complex, sharp and slow wave complex and polyphasic complexes were not found in any of these 4 patients.

Two comatose patients died from pulmonary complications on days 6 and 7 after the regaining

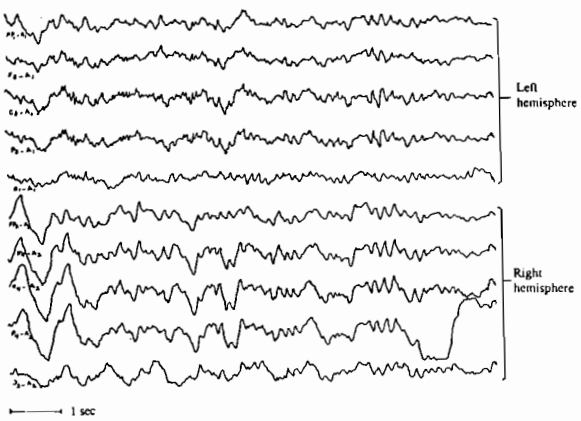

Fig 2–EEG pattern in cerebral malaria patient with left hemiplegia.

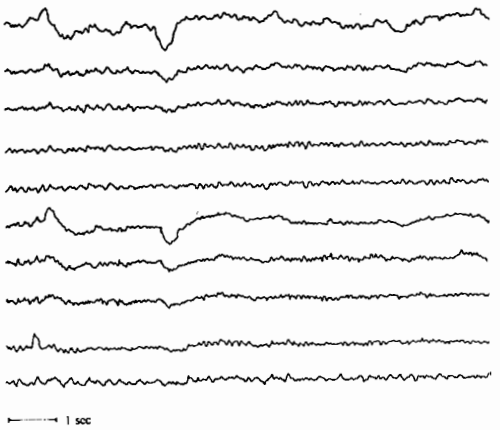

Fig 3–EEG pattern in recovery phase of cerebral malaria.

of consciousness and clearance of parasitemia. The basic patterns of EEG tracings done within 24 hours after admission were not significantly different from the ones who survived.

Four patients (2 stuporose and 2 comatose patients) had episodes of mild degree hypoglycemia (blood glucose levels of 41-58 mg/dl). The EEG patterns in these patients were not significantly different from the others.

Six patients (4 stuporose and 2 comatose) with direct bilirubin of greater than 3 mg/dl (3.07-15.2 mg/dl) had triphasic wave from bifrontal region. In one patient with serum direct bilirubin of 15.2 mg/dl, the occurrence of triphasic wave was markedly increased.

The follow-up EEG was done in 5 patients (4 stuporose and 1 comatose), after regaining full consciousness, between days 2 and 5. Alpha activity was found to be the basic background in 3 patients (1 on day 2 and 2 on day 5) with beta waves on top (Fig 3). The other 2 patients showed slow waves of theta and delta activities (1 on day 2 and 1 on day 5) even after they had regained full consciousness. In these 2 patients however, serum creatinine level was high (5.2 and 7.3 mg/dl) on the day the follow up EEG was done. Further follow-up EEG tracings were done when creatinine levels returned to normal, the reappearance of alpha activity with no theta nor delta waves was seen.

DISCUSSION

Cerebral malaria is one of the major causes of death in falciparum malaria. The mortality rate ranges from 20-50% in the treated patients (WHO, 1990). Most of the deaths occur within the first 24 hours of admission (White and Krishna, 1989). The pathophysiological processes causing death in cerebral malaria is still controversial (WHO, 1990). There is only one previous report of EEG pattern in 2 cerebral malaria patients by Chen *et al* (1991). The EEG patterns were shown as bursting polymorphous slow wave complexes lasting 1-2 seconds, followed by a period of quiescence lasting for 2-3 seconds in 1 patient with grand mal seizure. Another patient with flaccid paraplegia with hyporeflexic deep tendon reflexes of the lower limbs, showed generalized continuous theta activities on his EEG prior to antimalarial treatment.

In this study, the initial EEG performed on the day of admission did not show any specific EEG pattern attributable to any pathological condition. It was unable to predict the prognosis of the 2 patients who died. However, the causes of death in these two patients may not have been entirely attributed to cerebral pathology. They died of pulmonary complications on days 6 and 7 after regaining consciousness. More studies with serial EEGs should be carried out to define the patterns in the patients with different clinical outcomes.

The EEG patterns in cerebral malaria patients in the present study were of theta and delta waves. Widespread asynchronous slow waves were noticed in both sides of cerebral hemisphere suggesting diffused cortical dysfunction. This finding is in agreement with that reported by Chen *et al* (1991).

However, this pattern can also be found in anoxic encephalopathy and viral encephalitis (Brenner, 1985; Tyner *et al,* 1989). Non-specific characteristic of EEG patterns in cerebral malaria makes it difficult to rule out these two conditions in unconscious patients who present with asexual form of falciparum malaria in their peripheral blood. In viral encephalitis, the epileptic patterns were seen in patients with seizures (Tyner *et al,* 1989). In this study, however, we did not see the epileptic patterns in patients who had seizures prior to, or after admission. Seizures in cerebral malaria may be the result of transient functional abnormalities due to complex factors (Mac Pherson *et al,* 1985; White *et al,* 1988). It is unlikely that admission EEG can be used for prediction seizures in cerebral malaria.

One patient with left hemiplegia who was subsequently found to have right basal ganglia hemorrhage in CAT scan; alpha waves (unusual finding in acute phase of cerebral malaria) were found in some duration between theta waves from the left hemisphere with the amplitude of 50-100 microvolt. However, high amplitude delta waves and theta waves, were found in the tracings of the right hemisphere (Fig 2). The unusual finding of alpha waves during acute illness with cerebral malaria and asymmetrical wave patterns from the two hemispheres should alert the physician to perform further investigations.

In conclusion, a single EEG data on admission cannot give enough information for prediction of the clinical course and outcome of cerebral malaria. Serial EEG probably provide more useful information regarding the prognostic signs in this group of patients. More complicated neurological electrophysiological assessments such as nerve conduction velocity, brain stem auditory evoked potential and auditory evoked potential may reveal the cause of some rare manifestations in cerebral malaria (Chen *et al,* 1991). Nevertheless, EEG could be useful to rule out some cerebral pathology such as space occupying lesions, epilepsy or any other causes of unconsciousness that could produce similar cerebral symptoms in malaria patients. However, it needs special sophisticate equipment, experienced technologist and neurologist. It also requires cooperation from the patient during the recording time which is rather difficult in cerebral malarial patients, and as a consequence unlikely to be practical for routine investigation of all cerebral malaria patients in community hospitals.

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