Neurologia et Psychiatria

CEREBRAL MALARIA

A neurological report of 49 patients

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Abstract: A consecutive neurological study of 48 patients with the cerebral form of Plasmodium falciparum malaria is presented, having been under treatment at the hospital of Mnero, Tanzania. Diagnosis was based on neurological features and on demonstration of the parasites in peripheral blood. In 1 additional case with imported malaria the involvement of the central nervous system (CNS) was recorded by electroencephalogram (EEG) and cranial computed tomography (CT) follow-up examinations. EEG alterations in the acute phase are not helpful in diagnosis as well as CT studies are disappointing in the context of the severe brain disease. The low mortality rate of 18 per cent is due to early diagnosis and immediate begin of the treatment.

Introduction

Malaria is widely distributed in the tropics and subtropics, in European countries malaria is almost extinct, however, epidemic malaria is still present in Turkey. Foreign travellers import malaria very often, for example, as many as 539 malarial diseases were observed in West-Germany in 1978, about 150 malarial patients have been treated in Austria during the past 10 years (16, 26).

The cerebral form of malaria is a well-recognized complication of infection by the malarial parasite Plasmodium falciparum. It is a dramatic and potentially fatal condition, which was first discussed as "febris perniciosa comatosa" by KRAEPELIN (1881). Later on many authors reported on malaria complicated by various symptoms of the CNS (4,7,8,9). The clinical informations are usually derived from single cases. NEIGALIGH described neurological symptoms caused by Plasmodium falciparum in 203 patients (14), recently 39 cases of cerebral malaria in children were reported by BERNER (1). Some papers are available of EEG alterations in cerebral malaria (6). Few neuroradiological findings were described (25), however, no CT study has been previously reported.

This study is made to analyze neurological features of 48 children taken ill with cerebral malaria and in addition to evaluate EEG and CT follow-up findings in 1 adult with imported malaria.

Material and methods

This study covers a period of 2 years (1979 and 1980) and represents a consecutive one. In 5430 patients Plasmodium falciparum was proved, in 408 patients Plasmodium vivax and malaria were made visible by blood film. Of 49 patients with cerebral malaria 48 were Tanzanian children, treated at the hospital in Mnero, and 1 adult with imported malaria was studied at the Department of Neurology, University Hospital, Innsbruck. The diagnosis in reported patients based on clinical features (impairment of consciousness, acute convulsions and local signs) and on blood film or thick smears of the blood contained abundant numbers of Plasmodium falciparum. Cerebrospinal fluid examination was done in all patients to differentiate meningoencephalitis of other origin. EEG and CT follow-up studies were made in 1 patient. CT scans in the transverse axial plane were performed on a "Delta 25" Scanner using a 256 x 256 matrix.

Our patients with cerebral malaria were treated with Chloroquin 20 mg/3 kg/ KG im. initially, repeated after 12 hours and given three times on the second day, twice on the third day and once on the following days. Dexamethasone was used in management of cerebral edema.

Results

From 5430 patients infected by Plasmodium falciparum 48 patients developed cerebral malaria (0,88 per cent). The monthly distribution of 1979 and 1980 is shown in table Ia and Ib. The distribution of age shows that malaria in endemic regions is interpreted as a children's disease. Table 2 demonstrates the age peak between the first and third year of life.

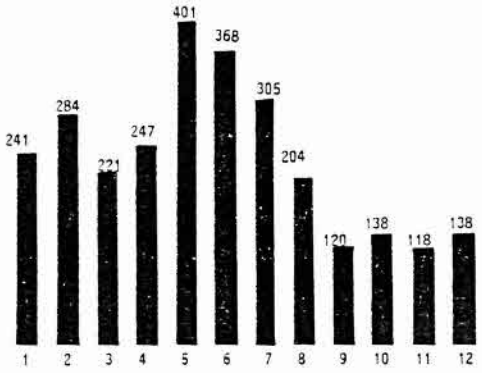

Table Ia

Monthly distribution of 2855 malarial diseases in 1979

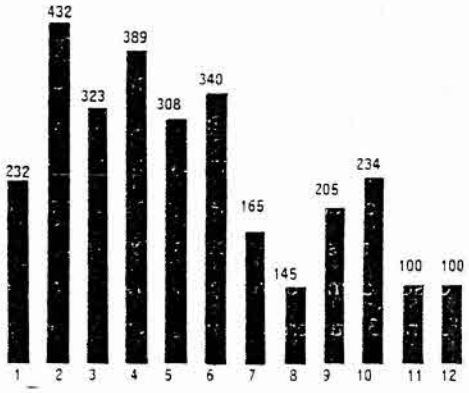

Table Ib

Monthly distribution of 2983 malarial diseases in 1980

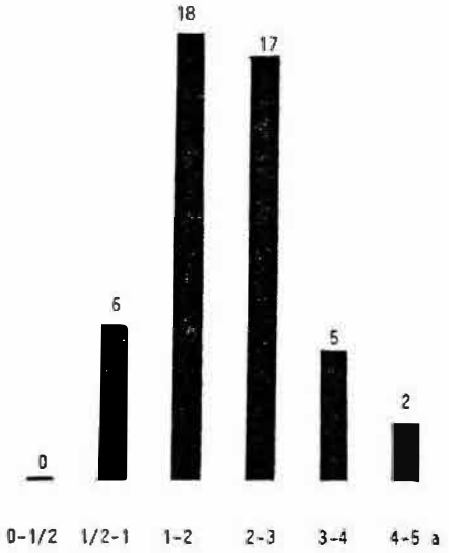

Table II

Age-distribution in 48 patients with cerebral malaria

The neurological features of the 48 children are subdivided in table 3. A sudden onset is described in 39 patients. Initially, acute generalized convulsions linked to hyperthermia are the most frequent symptoms. The impairment of consciousness ranged from acute confusion to somnolence, stupor and coma. In 32 cases coma developed, which was reversible in 23 patients. Local signs were seen in 25 per cent, but only in one case left hemiparesis remained. Organic brain symptoms were observed in 10 patients. Meningeal signs occured in 8 patients, 28 children complained of a headache.

Table III

Outcome of 48 patients with cerebral Malaria

Sequels	number
No residuals	32
Organic brain syndrome	5
Hemiparesis	1
Residual epilepsy	1
Deaths	9

Special interest on our part led to table 4, which contains the outcome of the 48 children infected by cerebral malaria. 9 patients died with the signs of a bulbar-brain-syndrome. A reexamination after six months of the acute illness revealed 32 patients without any defect, one child showed slight left hemiparesis and residual epilepsy was diagnosed in one patient too. In 5 children symptoms of an organic brain syndrome were found.

Table IV

Neurological findings in 48 patients with cerebral malaria

Acute convulsions	34	70,8 %
Coma	32	66,7 %
Hyperthermia	44	91,7 %
Headache	28	58,3 %
Meningeal signs	8	16,7 %
Local signs	12	25,0 %
Organic brain syndrome	10	20,8 %
Sudden onset	39	81,3 %

27 patients underwent lumbal puncture to exclude meningoencephalitis of any origin.

The case history of the adult with imported malaria is given in detail. The 29 year-old man was on holiday in Togo, West-Africa, from August 22nd until August 30th, 1980. Chemoprophylaxis (Fansidar^{R}) was taken on August 21st, on the 23rd, 29th and 31th, one tablet each time. On September 5th he was referred to a hospital because of fever. Hepatosplenomegaly of unknown origin was diagnosed and treated with steroids and a fixed dose combination of trimethoprim and sulfamethoxazole. After recovery the patient was discharged on October 3rd. Three weeks later, the patient was referred to our hospital because of increased impairment of consciousness. Confusion, stupor and later on coma developed. Slight left hemiparesis with hyperreflexia and bilateral pyramidal signs were found. After 4 hours myoclonic jerks of trunk and limb muscles were seen. In the face of the evidence of Plasmodium falciparum in the blood film Chloroquintherapy was started and the patient recovered promptly. At discharge cerebellar disorders and organic brain symptoms remained.

The illustration 1a shows the EEG at admission. A diffuse 2,5 - 7/sec. - slow activity was recorded. Seven days later, slow 8 - 8,5/sec. - activity but no definitive abnormalities were seen (Illustration 1b).

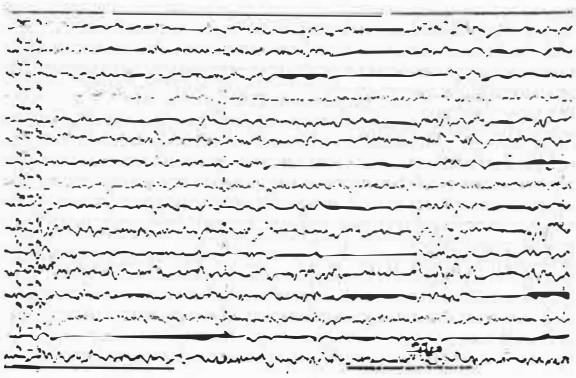

Fig. 1a 29 year-old man, EEG at admission: diffuse 2,5 - 7/sec slow activity.

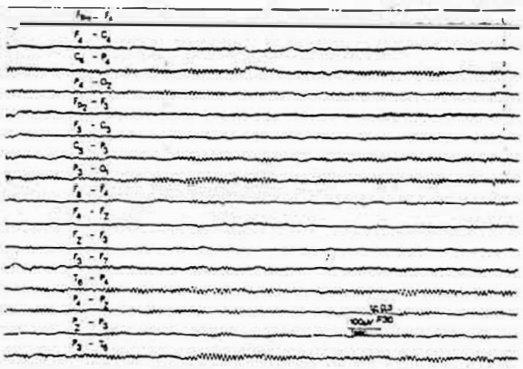

Fig. 1b EEG recording seven days after admission: Slow 8 - 8,5/sec activity, but no definitive abnormalities.

CT studies were normal except a slight frontal atrophy.

Discussion:

The frequency of cerebral malaria in relation to all reported Plasmodium falciparum infections is 0,88 per cent, in comparison with other papers this percentage is low (7, 11). The incidence and frequency of cerebral malaria between the first and third year of

life, as table II demonstrates, is substantiated by following facts. Newborns receive merozoites-blocking antibodies of the Ig G type via Placenta. This passive immunity decreases during the first months. Under further production of Ig M antibodies the infants are not able to synthesize Ig G (5, 28). However, recent studies suggest that Plasmodium faiciparum may preferentially invade young metabolically active erythrocytes (13, 15, 19). PASVOL (1976) found out that erythrocytes containing fetal Hb F are more resistant to infection by Plasmodium falciparum than those containing adult Hb A. After diminution of passive immunity and the shift from Hb F to Hb A the critical period for the child starts.

Cerebral malaria in reported children has an abrupt and dramatic onset. Headache, fever and tonic-clonic convulsions are the most frequent symptoms of the acute stage. Very often, acute convulsions introduce the comatose state. The invasion, alteration and destruction of red cells by malaria parasites, systemic and local circulatory changes and immune phenomena are probably all important in the pathophysiology of cerebral malaria. This species also induces physical changes in parasitized cells resulting in intravascular coagulation. Complement activation should be added to the pathogenetic mechanism too (3, 17, 19, 20, 24). The impairment of microcirculation of the CNS result in diffuse cerebral dysfunction and lead to brain edema and increased intracrnial pressure (2, 27).

It should b pointed out, that common concomitants of cerebral malaria, which are often seen in some other parts of the world (12), do not have a decisive significance for differential diagnosis in reported patients. However, postmortem findings showed in 2 of 9 cases pulmonary involvement which was not proved in clinical condition. Diarrhoea, vomiting and abdominal pain were seen in 14 patients as an evidence of obstructed splanchnic capillaries. In association with reported cases blackwater-fever was found in none of the patients.

Cerebral malaria occurs in higher frequency in persons not immune to this parasitic condition. Adults, usually foreigners to endemic areas, have their first exposure during temporary residence in a malarial zone. The cerebral malaria in adults develops when they have had symptoms of Plasmodium falciparum for more than a week. Fever, headache and influenza-like symptoms precede and then neurological symptoms appear as it is demonstrated. In our case the antimalarial chemoprophylaxis was insufficient, however, according to our experiencies the prescribed dosis might be inadequate.

EEG abnormalities in the acute phase of cerebral malaria are described by COLLOMB (6). It is discussed that the EEG alterations are caused by hypoxic, metabolic and toxic disturbances. The EEG features were highly correlated with the neurological findings and envolved quickly after oppurtune treatment.

No CT studies of cerebral malaria has been previously published. The CT scans of our case showed no abnormalities except a slight frontal atrophy, which might not correlate to the CT features of cerebral malaria. Cor-

responding to the neuropathological data no particular findings can be expected by CT.

One of the remarkable features of cerebral malaria is that survivors are free of residual disability although exceptions do occur (7, 21, 25), in this study only in 2 patients residual findings were observed.

In various reported series the mortality rate ranges between 48 and 29 per cent. Cerebral malaria is considered to be a medical emergency and includes supportive measures. Antimalarial therapy and Dexamethasone should be given as soon as possible (10, 18, 22, 23). The treatment by high dose of chloroquin - as mentioned above - showed no other than usual side-effects. Together with the early diagnosis and the immediate begin of therapy it may even have contributed to the remarkable low mortality rate of 18 per cent.

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