CEREBRAL MALARIA

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A consecutive neurological study of 66 patients with the cerebral form of plasmodium falciparum infection is presented having been diagnosed, under treatment and reexamined at the hospital Mnero, South-East Tanzania. Beside epidemiological aspects and the pathology of cerebral malaria, it's clinical-neurological-symptoms, it's therapy and the results of reexamination within half a year after discharge from the hospital are decribed in detail.

Introduction

Malaria is widely distributed in tropics and subtropics; in European countries malaria is almost extinct (5 , 38 . 39). However, foreign travellers import malaria very often (7,13,18,25,27,41,50,51,52). In West-Germany there is a steady rise of such imported cases from 30 per year in 1965 to 539 cases in 1978 as table 1 shows (51). 43,3 % of these cases were plasmodium falciparum infections. According to WEISE (51) almost 5 % of these imported plasmodium faciparum infections ended fatally.

The cerebral malaria represents one of the most threatening courses of a plasmodium falciparum infection. It has been described first as "febris perniciosa comatosa" by KRAEPELIN (1881). Later on many authors reported on malaria complicated by various symptoms of the central nervous system (6, 12,15,16,36). In 1975 39 cases of cerebral malaria in children were reported by BERNER (2). In 1981 52 cases of cerebral malaria were described by NAPARSTEK et al. and in 1982 a series of 100 patients with cerebral malaria was reported by WARRELL et al. from Thailand. Some papers are available of EEG alterations in cerebral malaria (1,11). Only few neuroradiological findings are described (1,47).

Epidemiology

Whereas in non-immune individuals cerebral malaria occurs at all ages, in holoendemic areas, i. e. areas in which more than 75 % of the children between 2 and 10 years of age show a splenomegaly and the adult have no more splenomegaly,

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cerebral malaria strikes preferentially in children under 5 years of age (2,32). This age distribution can also clearly be seen in the 66 patients treated at Mnero Hospital, as table 2 shows. The peak lies between the 2nd and 3rd year of age. No cases could be observed in newborn and infants aged less than half a year. This is substantiated by following facts: Fetuses receive merozoites-blocking antibodies of the IgG type via the Placenta. The passive immunity decreases during the first month of life. Under further production of IgM antibodies the Infants are not able to synthesize IgG (10,54). However, recent studies suggest that plasmodium faciparum may preferentially invade metabolically active erythrocytes (34, 37,42). PASVOL (1976) found out that erythrocytes containing fetal HbF are more resistant to infection by Plasmodium falciparum than those containing adult HbA. After diminution of passive immunity and the shift from HbF to HbA the critical period for the child starts (37)

At Mnero Hospital, Tanzania 8456 cases of malaria were parasitologically diagnosed during the 3 years period 1979–1981 by mostly thick film method by (the methods of thickfilm,) but in many cases thin film method was used for further parasitological differentiation. Out of these 8456 cases of malaria 541 (6,4 %) were Plasmodium vivax infections and 7915 (93,6 %) were Plasmodium falciparum infections. Out of these 7915 patients infected by Plasmodium falciparum 66 (0,83 %) developed cerebral malaria.

Table 3 shows the seasonal and monthly distribution of all malaria infections at Mnero Hospital from 1979–1981. It shows clearly a maximum of frequency in the months February to June, a fact which closely correlates to the climatic situation in South–East Tanzania. The rainy season starts early in December with a first precipitation maximal early in January and a second at the end of March/April. At the latest around mid-May rain stops completely. As table 4 shows the incidence of cerebral malaria is high during the months of the rainy season and continues to stay high for two more months. A very high mortality rate could be observed during the months May and June (36% and 40%). respectively. The average mortality rate of all cerebral malaria infections was 18,2%. An important cause for this phenomenom seems to be the fact that the people of Southern Tanzania cultivate their fields on a subsistence level. The stable food is maize and millet which are harvested in May and in June. That means that the months before the harvest is brought in, are in many cases characterized by lack of sufficient food. On top of that we found out that the morbidity rate of diarrheal diseases and decompensated anaemias in children has its peak during the rainy season months. Beside the intensity of Plasmodium falciparum infection these three conditions - malnutrition, diarrhea, anaemia - seem to play a decisive role in the outcome of cerebral malaria.

Pathology

The disintegration of parasitized erythrozytes plays the decisive role in pathogenesis of the damag of different organs (43). It leads to the literation of substances with toxinlike effects (24,31) This changes the rheological properties of the parasitized erythrozytes (33,34) and causes impairment of the microcirculation in various organs, e.g kidney, lung but especially the brain (3,4,24,26,29,31,43,45,46).

The brain of patients with cerebral malaria shows edema, a diffuse hyperemia, petechial hemorrhages into the white substance and densely packed erythrocytes within the lumen of capillaries and venules (42,46). This stasis is thought to be the main cause for the brain dema and hemorrhages into the brain (43).

Clinical Symptoms

The first symptoms of cerebral malaria in the patients treated at Mnero Hospital were hyperpyrexia; headache, vomiting and restlessness. Their onset usually was abrupt and dramatic. Soon many children developed convulsions, followed by a coma with all the signs of midbrain syndrome and some cases showed lateralization.

In all 66 patients blood slide was positive for Plasmodium falciparum. The lumbar

puncture revealed in a high percentage a raised CSF pressure a slightly to moderately positive pandy reaction and sporadically lymphocytes.

Table 5 shows the breakdown of symptoms of all the patients with cerebral malaria who were admitted at Mnero Hospital during the 3 years period 1979–81 : 16 had focal signs as hemiparesis, hemihypaestesis or focal epileptic fits. 42 showed generalized convulsions. 48 patients developed a coma.

COLLOMB (11) described diffuse EEG abnormalities in the acute phase of cerebral malaria. Hypoxic disturbance are discussed as possible cause. The computed tomography performed in one patient suffering from imported cerebral malaria did not show any relevant pathological findings. Despite midbrain syndrome phase 2-3 (1), This shows that additional electroneurological and neuroradiological examinations are of the only limited diagnostic value.

Table 6 contains the result of the reexamination of the 66 children who had suffered from cerebral malaria. 12 children died with the signs of bulbar brain syndrome. The reexamination within half a year after discharge from the hospital showed 39 children completely free of any symptoms, 5 had signs of a slight to moderate organic psychosyndrome, 3 had a spastic hemiparesis, 2 children suffered from a residual epilepsy and one child with a residual epilepsy showed also a slight paresis of the left upper limb. 5 children could not be included into the follow up examination.

Decisive for the course of cerebral malaria is the application of schizontozides early as possible (8,17,19,21,29,32). GENTILINI (1979) recommends the sole use of Quinin, 25mg/kg bodyweight per 24 hours in an i.v. drip of Glucose 5%. Similarly important are supportive measurements (17,44,53) like treating a concomitant anaemia, application of Diazepam or Phenobarbital in the case of convulsions, correction of renal insufficiency and keeping an acidosis under control or, if necessary, to start positive pressure breathing (17,32)

At Mnero Hospital a simple scheme was worked out in order to ensure an efficient therapy of cerebral malaria which could be carried out properly by paramedical staff of the hospital. Table 7 shows this scheme: Chloroquin base is given in a dosage of 5–7,5 mg/kg bodyweight i.m. (23), i.e. 0,5 ml per 3 kg bodyweight i.m. This dose is to be given immediately after establishing the diagnosis and has to be repeated 1 hour and 12 hours after the first injection. On the 2nd and 3rd day this intramuscular dose has to be continued twice daily. At the same time 3 mg Dexamethasone/kg bodyweight are administered i. m. In the case of epileptic convulsions the patient gets Diazepam 10 mg i. m. If necessary an i. v. drip has to be established for rehydration, blood transfusion, i. v. application of Digitalis and repeated i. v. administration of Diazepam and Dexamethasone. Patients in comatose state have to get NG-tubes for feeding purposes and urinary catheter for checking output.

Summary

Cerebral malaria is a lifethreatening course of a Plasmodium falciparum infection. In holoendemic areas the age distribution shows its peak between the 2nd and 3rd year of age. As we could see there is a direct correlation between morbidity/mortality of cerebral malaria and climatic conditions, supply of staple food in rural areas where agriculture is run on a subsistence level, furthermore diarrheal diseases, decompensated anaemia and malnutrition.

The onset of cerebral malaria in children is usually very abrupt and dramatic.

In various reported series mortality ranges from 4-48% (1,2,35,48) In our series of 66 children it was 18%. The percentage of cerebral malaria of all parasitologically proved Plasmodium falciparum infections was 0,83% which, compared with 1,5% in similar reports (12,28), appears to be low. The main reason seems to be the very simple but dense medical infrastructure of Tanzania with first Aid Posts and Dispensaries.

In areas, in which resistance to 4 aminoquinoline (8,9,40) does not yet exist, Chloroquine is still the first drug of choice-as schizontozide-in therapy of cerebral malaria. The importance of Dexamethasone in the treatment of raised intracranial pressure in cerebral malaria seems to be questionable (20,22,48,53).

Although in this series of children suffering from cerebral malaria, treated in a rural East-African hospital, the mortality rate is rather low (18%) the percentage of children in whom within half a year after discharge from hospital, in a neurological control examination, some degree of disability could be detected, is rather high. This is in contrary to the very few series which looked distinctly for this fact (49) but it might mean that the true rate of disability as a consequence after cerebral malaria is higher than usually assumed.

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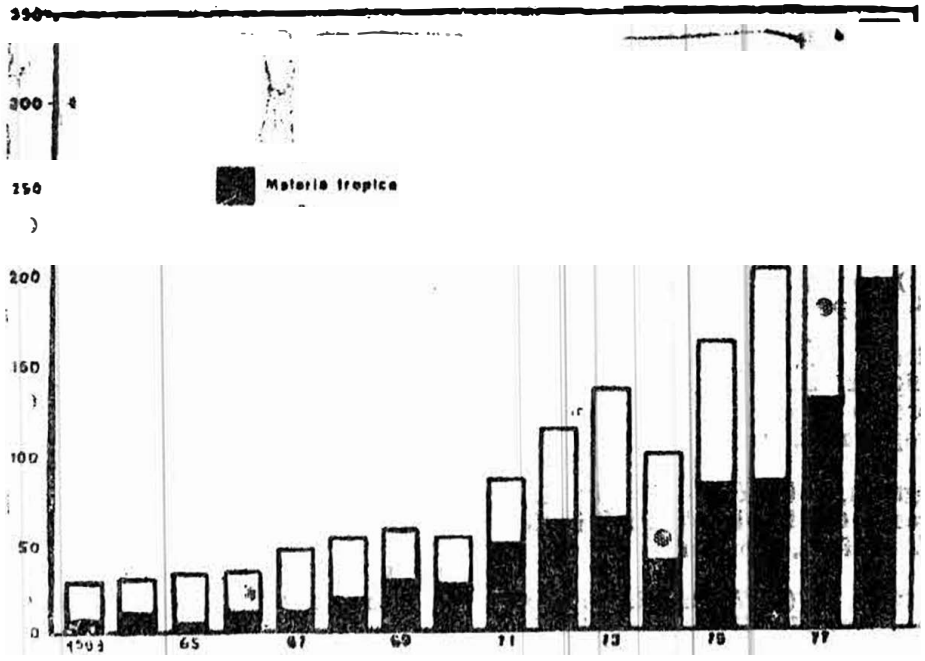

Table 1 : Imported malarial diseases in Federal Republic of Germany (inclusive & West-Berlin) - acc. to WEISE, H J. (51)

Table 2

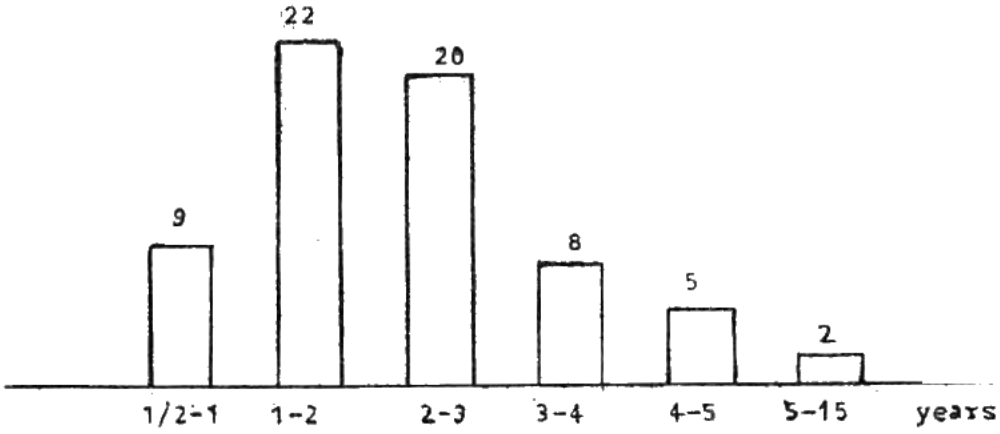

Table 2: Age distribution in 66 patients with cerebral Malaria

Table 3

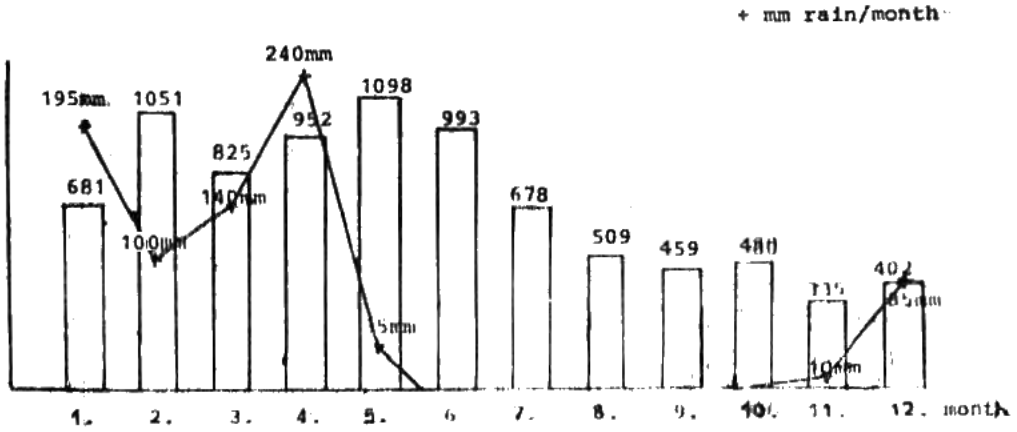

Table 3: Monthly distribution of 8456 malarial diseases 1979-981. In comparison to it the monthly average of rain 1979-1981.

Table 4

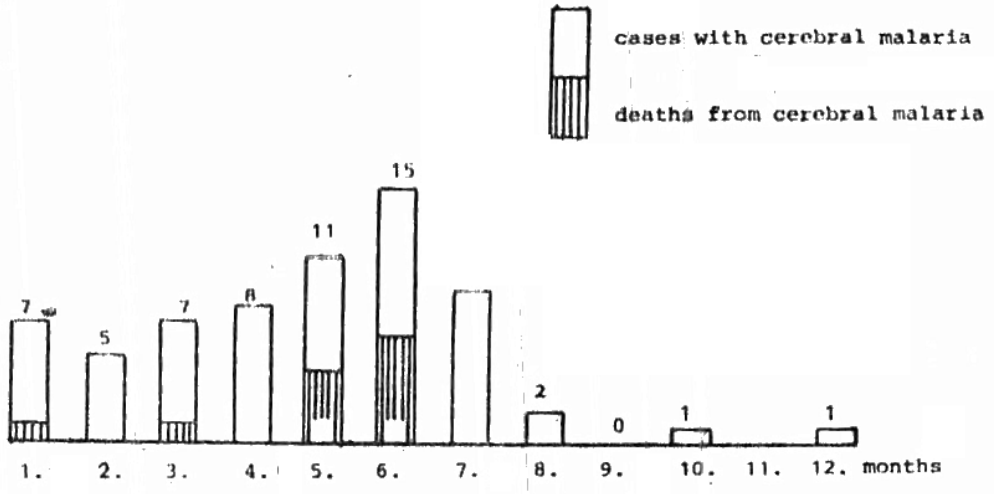

Table 4: Monthly distribution of 66 patients with cerebral malaria and deaths per month.

Table 5

1.	Hyperthermia	62	94%
2.	headache	31	47%
3.	vomiting	40	60,6%
4.	neckstiffness	10	15,2%
5.	organic psychosyndrome	10	15,2%
6.	epileptic fits – focal or generalized	42	63,3%
7.	Comatous state with signs of midbrain syndrome	48	72,7%
8.	focal signs	16	24,2%
9.	abrupt onset of symptoms	53	80,3%

Symptoms of cerebral malaria of patients who were admitted to Mnero-Hospital during th e3 years period 1979–1981

Table 6

no residual symptoms	39	59%
organic psychosyndrome	5	7,5%
hemiparesis/hemihypaesthesia	3	4,5%
residual epileptic fits with residual hemiparesis	1	1,5%
residual epileptic fits	2	3%
death in bulbar brain syndrome	2	3%
patient who did not undergo control examination	5	7,5%

results of the reexamination of 66 patients with cerebral malaria within half a year after discharge from hospital 1979-1981

Table 7

Therapy Scheme for cerebral malaria worked out at Mnero Hospital:

1) Chloroquine-base: 5-7,5 mg/kg bodyweight i.m.; initial dosage immediately after admission, repetition after 1 and 12 hours time, and twice daily on the 2nd and 3rd day.
2) Dexamethasone: 1-3 mg/kg bodyweight i.m.
3) Diazepam: 0 mg i.m., in case of epileptic convulsions
4) establishing an i.v. drip for rehydration, blood transfusion and application of Digitalis, if necessary
5) in comatous patients: NG-tube, urinary catheter