EARLY MENTAL AND NEUROLOGICAL SEQUELAE AFTER JAPANESE B ENCEPHALITIS

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Abstract. Japanese B encephalitis is a disease with high mortality and many of those surviving suffer from serious sequelae. During the 1992 epidemic in northern Vietnam 50 patients treated at the Institute for Protection of Children's Health in Hanoi were studied concerning the type of sequelae and the development of the symptoms during the first two months of the disease. The age span was 1 to 15 years. 29 of the patients (58%) did not recover fully during the observation period. Fifteen (30%) showed signs of both neurological and mental disturbances. Nine (18%) only had mental symptoms while 5 (20%) suffered from isolated nerological sequelae. EEG was pathological in 9 out of 30 tested cases (30%); 9 of 23 patients (39%) performed subnormal IQ tests. Deep coma, bronchopneumonia with cyanosis, apnea attacks, prolonged fever and coma were all correlated (without statistical significance) to a higher risk for subsequent sequelae.

INTRODUCTION

Outbreaks of Japanese B encephalitis have occurred in Vietnam since 1960 (Le Duc, 1988). The disease is linked with a substantial mortality and often results in mental and/or neurological sequelae (Tran, 1991). According to WHO, mental retardation is a major health problem in many countries. In recent years this condition has been reported in people having suffered from Japanese B encephalitis (Le Duc, 1988).

According to a Vietnamese study (Le Duc, 1988) Japanese B encephalitis is the most common cause of mental retardation in Vietnam. Another study showed that the leading cause of mental retardation in children in Vietnam is infections (Hoang, 1991).

The patients treated for sequelae after Japanese B encephalitis today constitute the largest group at the Department for Traditional Medicine at the Institute for Protection of Children's Health (IPCH) in Hanoi. However, we still lack reliable assessments concerning the risk for mental and neurological sequelae after Japanese B encephalitis. This report monitors these sequelae during the two first months after the disease and considers symptoms and signs predicting the sequelae.

MATERIALS AND METHODS

Fifty patients treated for Japanese B encephalitis at the IPCH in Hanoi, between June 6 and September 30, 1992, were included in the study. These patients constituted only a part of those admitted for the disease during the study period. They were included after having been placed randomly in the rooms supervised by the first author.

The diagnosis was made by clinical methods and confirmed by ELISA technique. Only those with significant titers (Hoang, 1991) were included. Those who died during the comatous phase were not included in the study.

The age span was 1-15 years and the mean age was 6.8 years; 19 (38%) were girls and 31 (62%) were boys (Table 5).

During the comatous phase mannitol 2g/kg/24 hours was given to all patients to minimize the cerebral edema and intravenous saline transfusion was administered according to the electrolyte status. When the patient had regained consciousness different drugs were added. Norakin (Trihexphenidyl clohydrate) was given to treat extra-pyramidal symptoms. Majeptil (Thioproparzin), Neuleptil (periziazine) and Aminazin (chlorpromazine) were used together with Garde nal (phenobarbital) Tegritol (carbamazepin) and Seduxen (diazepam) in different forms of mental disturbances. Treatment was administered individually according to the needs.

All patients received physical exercise and the parents were encouraged to follow the advice given concerning training of impaired mental and physical

functions.

The patients were examined and symptoms were assessed during the hospital stay and at planned visits to the outpatient department after discharge.

During the comatous phase the following symptoms were registered: Number of days in coma, maximum degree of coma (I-III), number of days with fever, the occurrence of convulsions and breathing difficulties which was defined as the presence of cyanoses. Lumbar puncture was made on the day of admission to examine the number of leukocytes and the protein content of the cerebrospinal fluid (CSF).

Fundoscopy was performed in 20 patients, randomly selected, during the comatose phase and an electrocephalogram was recorded in 30 participants during the second week of hospitalization.

Assessment of the sequelae were made on three occasions by the same individuals. The examining team consisted of a pediatrician, a pediatric psychiatrist and an educational psychologist. The first examination for the detection of early sequelae was made on the day when the patient regained consciousness. The second was performed 15 days later and the third 45 days later. The following points were specially observed:

1. Neurological symptoms and signs:
Muscular paralysis, increased tonus, clonus, chorea and appearance of a positive Babinski's reflex.
2. Mental symptoms:
Disturbance in contact, speaking, understanding, mood and general behavior. The intelligence was tested by the Denver test in children under the age of seven and by the Raven and the Gill tests in those of seven or older at the third assessment of the patient's sequelae. Statistical significance was tested by the chi square method, the student's *t*-test and Fischer's exact test.

RESULTS

The first evaluation of sequelae was performed when the patient regained consciousness which occurred on average 8 (± 3) days after the admission. At that examination only 4% of the patients were without mental or neurological symptoms while the vast majority (82%) showed disturbances in both these fields.

Table 1
Occurrence of sequelae in patients recovering from Japanese B encephalitis (n = 50).

Examination	Patients without sequelae (%)	Patients with remaining sequelae		
		Mental and neurological symptoms (%)	Mental symptoms (%)	Neurological symptoms (%)
1	2 (4)	41 (82)	4 (8)	3 (6)
2	16 (32)	21 (42)	6 (12)	7 (14)
3	21 (42)	15 (30)	9 (18)	5 (10)

Table 2
Disturbances in psychic functions in patients recovering from Japanese B encephalitis (n = 50).

Examination	Impaired responsiveness (%)	Impaired language functions			Mood disturbances		Behavioral disturbances	
		Difficulties to speak and understand (%)	Difficulties to speak (%)	Difficulties to understand (%)	Absence of emotional reactions (%)	Inappropriate cry or laughter (%)	Inappropriate sudden actions (%)	Hyperactivity (%)
1	39 (78)	32 (64)	4 (8)	2 (4)	42 (42)	3 (6)	6 (12)	4 (8)
2	16 (32)	6 (12)	8 (16)	1 (2)	16 (32)	6 (12)	4 (8)	7 (14)
3	14 (28)	5 (10)	6 (12)	2 (4)	18 (36)	11 (22)	5 (10)	11 (22)

Symptoms decreased with time and at the third examination 42% were free from symptoms leaving 58% with mental or neurological sequelae (Table 1). Disturbance in responsiveness was present in 78% of the patients while 76% had difficulties to speak or understand spoken language at the first evaluation (Table 2). The majority of those (64%) had both speaking and understanding impairment. Inappropriate crying or laughing was present in 6% and impulsive hyperactivity in 8%.

At the third examination 28% still had disturbance in responsiveness while 26% showed difficulties in speaking or understanding. The percentage of patients showing inappropriate crying or laughing had increased to 22%. This increase also occurred in the group showing cry or laughter without reason (22%) and hyperactivity (22%). Fifteen out of 22 patients tested (68%) had a normal result or better when examined with Denver's, Raven's or Gill's intelligence tests (Table 3).

Forty-four percent of the patients had signs of flaccid paralysis at the first examination and as many suffered from spastic paralysis. Some in both groups recovered and some with flaccid paralysis developed spastic symptoms during the observation period. At the third examination none remained with flaccid paralysis while 32% still showed signs of spastic paralysis (Table 4). The presence of Babinski's sign, decreased from 36% to 26% of the patients from the first to the third assessment.

Some neurological symptoms were more common at the end of the observation period. Thus the presence of clonus increased from 18% to 22%. Ataxia was seen in 16% initially and increased to 24% to the last examination (Table 4). There were some differences between those who recovered completely and those who did not (Table 5). Attacks of apnea occurred only in the group with sequelae (17%). 34% of those not recovering completely had suffered from bronchopneumonia during the acute phase compared to 14% of those without. Cyanosis was present in 50% of the patients developing sequelae during some part of the disease compared to 25% in those who did not. Corresponding figures for deep coma (grade III) were 28% and 10%.

Fever lasted on average one day longer in those developing sequelae as did the duration of coma. Patients with two periods of fever often had minor symptoms after the first phase and grow worse after the second.

Little difference were seen between the two groups concerning days of disease before admission (span 2-8 days), number of cells and albumin content of the CSF. A non-specific, pathological EEG pattern was found in 21 out of 30 tested cases. Nine patients had epileptiform activity. None of these showed clinical signs of epilepsy, however. All those examined by fundoscopy showed normal findings.

Table 3

Results of intelligence tests in patients recovering from Japanese B encephalitis (n = 23).

	Patients < 7 years old	Patients > 7 years old	
	Denver's test n = 5	Raven's test n = 8	Gill's test n = 10
Number of patients with normal result or better	3 (60.0%)	5 (62.5%)	7 (70%)

Table 4

Remaining neurological signs at different examinations in patients recovering from Japanese B encephalitis.

Symptom/sign		Examination		
		1 (%)	2 (%)	3 (%)
Flaccid	Hemiplegia	8 (16)	1 (2)	0 (0)
	Tetraplegia	14 (28)	4 (8)	0 (0)
Spastic	Hemiplegia	15 (30)	12 (24)	8 (16)
	Tetraplegia	7 (14)	8 (16)	8 (16)
Babinski's test positive		18 (36)	16 (32)	13 (26)
Increased muscular tonus		14 (28)	7 (14)	15 (30)
Clonus		9 (18)	6 (12)	11 (22)
Chorea		8 (16)	9 (18)	12 (22)
Impaired cranial nerve function		8 (16)	3 (6)	4 (8)

Table 5

Sex, age and symptoms from Japanese B encephalitis in relation to subsequent sequelae.

Recorded factor	Patients without sequelae (n = 21)	Patients with sequelae (n = 29)	Statistical significance (p-value)
Sex : M/F	1.6	1.6	> 0.8
Mean age	6.5	6.9	0.69
Duration of coma (days)	4.2	4.6	0.35
Mean depth of coma	1.5	1.7	0.37
Duration of fever (days)	5.8	6.8	0.09
Number with convulsions	14 (67%)	17 (59%)	0.57
Number with bronchopneumonia	3 (14%)	10 (34%)	0.10
Number with apnoea attacks	0 (0%)	5 (17%)	0.05
Mean number of leukocytes in CSF	147	177	0.53
Mean level of protein in CSF	59mg/100ml	63mg/100ml	0.72
Number of days of disease before admission	4.2	4.6	0.75

DISCUSSION

This study comprises 50 patients studied during two months. It is possible that a longer follow-up period would have somewhat changed the results due to late healing of the symptoms. A future follow up of the studied patients would thus be of interest.

However the present study indicates that both mental and neurological sequelae are common after Japanese B encephalitis. 38% of the patients showed improvement from the first to the third examination while as many as 58% were left with sequelae. The mental symptoms seemed to decrease more quickly than the neurological ones.

In fact in our study most mental disorders diminished during the observation period. In contrast, however, the occurrence of inappropriate laughter or crying rather tended to increase with time. We observed these phenomena specially in children older than 10 years.

Hoang (1991) found at a primary school that older healthy children had a higher incidence of behavioral disorders. Her conclusion was that this fact was due to the influence of puberty. Could prepubertal children be more vulnerable to these types of sequelae after encephalitis?

Nguyen (1988), in a group of 46 patients with mental retardation due to infectious disease affecting the nervous system, found impairment of language in 60% and sensibility in 89%. Cao (1988) and Ngo (1988) assessed the result of treatment of children at two schools for the mentally retarded. They found that symptoms could be diminished but the progress was slow. There were differences between that study and ours however. Their patients were treated late and activities concentrated on training and the management of existing handicaps. Most neurological symptoms also decreased during the treatment period. Thus 89% of the patients had some degree of paralysis at the first assessment compared to 30% at the third examination. We noticed that flaccid paralysis often changed into spastic paralysis before disappearing and that the appearance of clonus slightly increased which is in line with classical theories on the development of acute damage to the pyramidal tract. When the symptoms of paralysis had improved the patients could handle a toy, use chopsticks and spoon or walk down a stair-case, for example. However many still suffered from symptoms such as increased tonus, ataxia or muscular weakness.

Striking in this study was the different development regarding different symptoms. On the one hand, paralysis, specially the flaccid type, showed a good prognosis like the ability to contact others, while some symptoms like increased tonus, clonus or ataxia

remained fairly stable. On the other hand some mental symptoms like inappropriate crying or laughing and hyperactivity increased during the study period.

Several symptoms during the acute phase were more common in those later developing sequelae than in those who did not, without significant differences between the two groups however. This lack of significance might be due to the limited number of patients in the study. Since several symptoms were more common in the group with a worse outcome it is likely that patients having more of those symptoms stand an increased risk to develop sequelae.

Dao (1991) stated that late treatment will lead to more sequelae. In his study the recovery rate in patients hospitalized late and treated with acupuncture was 7.5%. In our study patients being admitted later than the average did not show more sequelae than the rest. In our opinion this finding is due to the fact that all patients came comparatively early for treatment. The diagnosis was early suspected at the district level since all cases occurred during an epidemic. One support of Doa's conclusion is our observation that several treatable symptoms during the acute phase of the disease were more common in those who later developed sequelae. This suggests that intensive care and careful monitoring for, *eg* breathing difficulties, pneumonia and fits is essential since vigorous treatment of these problems might prevent hypoxia which could be one of the etiological reasons for the sequelae. This circumstance was discussed in several studies in Vietnam and abroad (Tran, 1989; Nguyen 1991; Dau, 1989). Since the symptoms correlated to later sequelae occur early during the disease, observation and treatment should be started as soon as possible after the diagnosis is suspected.

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