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Epidemiological and Clinical Observations on Eosinophilic Meningitis and Meningoencephalitis of Children Caused by Infection with *Angiostrongylus Cantonensis* in Southern Taiwan

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Key words : parasite, *Angiostrongylus cantonensis*, eosinophilic meningitis, eosinophilic meningoencephalitis

Abstract

The epidemiological and clinical characteristics of 47-child cases of eosinophilic meningitis or meningoencephalitis were studied in the southern Taiwan from 1973 to 1981.

Although the worms of *A. cantonensis* were detected only in the spinal fluids of 4 cases, the clinical manifestations such as eosinophilic pleocytosis and some meningeal symptoms and signs of the other cases were almost the same as those of the proven 4 cases and those in the previous literatures. Therefore, most cases in the present study were considered as potentially infected with *A. cantonensis*. The majority of cases developed the first symptoms in the rainy summer season among the aborigines who lived in the eastern mountainous area, but no sex difference was noted.

Human angiostrongyliasis is still prevalent in the southern Taiwan and so continuing observations are necessary for better diagnosis, therapeutic control and prevention of the disease.

Introduction

Angiostrongylus cantonensis, a causative agent of human eosinophilic meningitis and meningoencephalitis, is widely distributed in the regions of the South Pacific Islands and Southeast Asia. In Taiwan, the parasite considered to be *A. cantonensis* in the lungs of wild rats was first reported in 1937.¹⁾ The parasite is now well established all over the island and more than 250 cases of the disease have been found in Taiwan.²⁾

Parasites have been rarely recovered in the cerebrospinal fluid by spinal tap. Therefore, the infection with *A. cantonensis* is indirectly diagnosed on the basis of the characteristic clinical symptoms, demonstration of eosinophilic pleocytosis in the

cerebrospinal fluid and history of eating the food known to be contaminated with infective larvae of *A. cantonensis* in the enzootic areas. The epidemiological and clinical features of the disease, however, are considered to be somewhat different among inhabitants in various localities. Their different ways of life and eating habits of food might play an important role of the infection.

The present report describes and discusses the recent epidemiological and clinical characteristics of the disease among children in southern Taiwan.

Patients

Cases studied were 47-child patients who were admitted in Cheng's Children's Clinic in Pingtung City, southern Taiwan from 1973 to 1981.

These patients showed an eosinophilic pleocytosis over 40 leucocytes per cu mm of cerebrospinal fluid with the characteristic signs and symptoms of meningitis or meningoencephalitis. Worms of *A. cantonensis* had been found in cerebrospinal fluid of 4 out of 47 patients. In addition to routine examinations, the date of onset of initial symptoms, past history with or without similar illness and food habits including the date of consumption of raw or rare animal food were recorded as much as possible.

Findings

1) Distribution of cases

The distribution of 47 cases studied was shown in Fig. 1. Most of patients (91.5 %) were from Pingtung Hsien (County) and remainings (8.5%) resided in the neighboring County, Kaohsiung Hsien. Nearly two-thirds of patients (63.8%) lived in the eastern mountainous areas and most of them were inhabitants in aboriginal villages such as Kaoshu, Santi and Maolin.

As shown in Fig. 2, most cases (70.2%) developed their first symptoms in the summer season from June to September.

The distribution of cases by age group and sex was shown in Fig. 3. Cases in the age group under 10 year-old amounted to 87.2 % of total cases, but there was little difference between both sexes (27 males and 20 females).

2) Incidence of clinical symptoms.

Incidence of clinical symptoms was summarized in Table 1. The intermittent or remittent fever was observed in all patients from the beginning of illness. Headache was a common symptom in the early stage of the disease. In many cases, the severity of headache decreased in intensity after a spinal tap and eventually disappeared after several spinal taps. Vomiting and nausea were also common and distressing symptoms. Intermittent somnolence was an early feature of the disease, and 40 % of patients had this symptom either from the onset of the disease or a few days thereafter. Patients were generally somnolent in the interval between their attacks of headache. Coma occurred in 4 patients and was associated with other manifestations of encephalitis in

a relatively later stage of the disease. All patients had some degree of malaise in the early stage of their illness and especially in 16 cases it was severe. Eleven patients complained of tremor and nine had occasional convulsion of short duration. Intermittent fine muscle twitching of short duration was also observed in 8 patients in the course of their illness. A dry cough occurred in 9 patients with symptoms resembling those of a common cold and a few of them had sneezing and /or rhinorrhea. Delirium, spasticity, disturbances of walking and swallowing, and chorea were also found in a few severe cases.

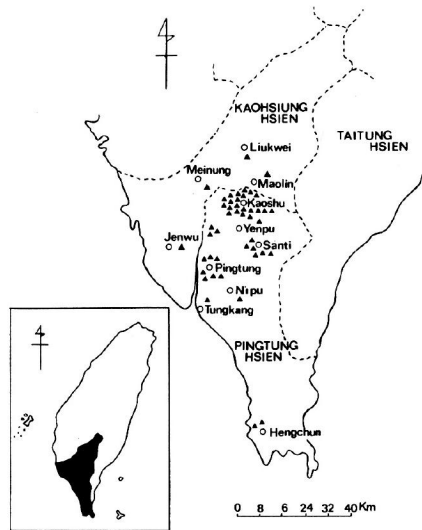


Fig. 1 Distribution of 47 cases of eosinophilic meningitis or meningoencephalitis in southern Taiwan by locality of residence.

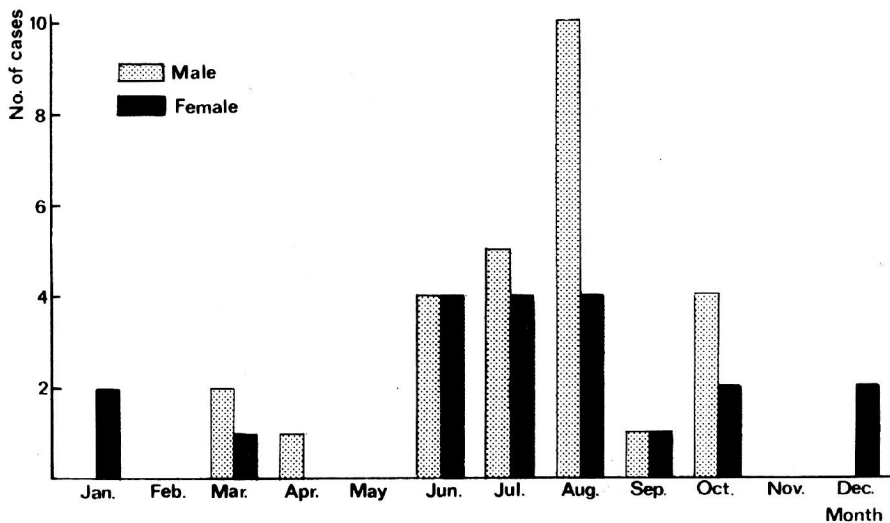


Fig. 2 Distribution of 47 cases by month of onset.

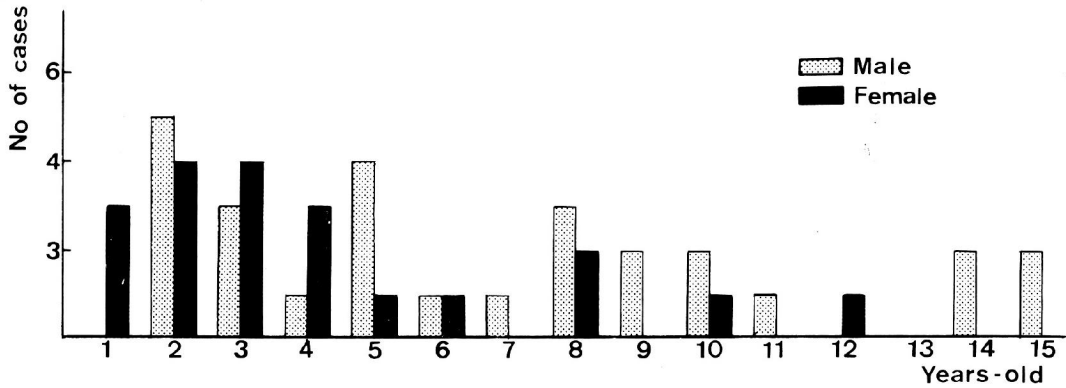


Fig. 3 Distribution of 47 cases by age group.

Table 1 Incidence of initial symptoms in 47 cases of eosinophilic meningitis or meningoencephalitis.

Symptom	No. of cases	Incidence(%)
Fever	47	100
Headache / vertigo	37	78.7
Vomiting / nausea	34	72.3
Somnolence	19	40.0
Malaise	16	34.0
Tremor	11	23.4
Convulsion	9	19.1
Cough	9	19.1
Twitching	8	17.0
Abdominal pain	6	12.8
Coma	5	10.6
Strabismus	4	8.5
Delirium	3	6.4
Spasticity	3	6.4
Walking disturbance	3	6.4
Swallowing disturbance	2	4.3
Chorea	2	4.3
Sneezing / rhinorrhea	2	4.3
Ptosis	1	2.1

3) Incidence of signs

Kernig's sign, neck stiffness and Brudzinski's sign, as shown in Table 2, were

commonly found in 70 % of patients or more. Kernig's sign was usually found at the first physical examination and disappeared within 2 weeks in most cases. There seemed to be little correlation between the intensity of the sign and the severity of the patient's illness. Neck stiffness was not pronounced at the first examination. It was persisted for several weeks and was temporarily improved after a spinal tap. Brudzinski's sign was also found in many patients but persisted for a shorter period than other meningeal signs such as Kernig's and neck stiffness. Most patients with positive Brudzinski's sign had positive Kernig's sign and neck stiffness concurrently. Babinski's sign was less frequent than the others. Pathological deep tendon reflex was demonstrated in one patient who showed negative knee jerk.

Table 2 Incidence of signs in 47 cases of eosinophilic meningitis or meningoencephalitis.

Sign	No. of cases	Incidence(%)
Kernig's	40	85.1
Neck stiffness	38	80.9
Brudzinski's	33	70.2
Babinski's	11	23.4
Negative knee jerk	1	2.1

4) Laboratory findings

Blood leucocyte count as well as gross appearance and protein measurement of cerebrospinal fluid of patients was summarized in Table 3. Leucocytosis ranging from 10,000 to 16,000 cells per cu mm were shown in 74.5 % of all cases. Peripheral eosinophilia was also common and marked. The peripheral eosinophils over 15 % were demonstrated in 61.7 % of patients. There were no remarkable changes in other blood leucocytes. Erythrocyte counts and hemoglobin values were generally within normal ranges. The gross appearance of cerebrospinal fluid was cloudy in most cases. Ground glass turbidity was observed in specimens with pleocytosis. Most patients were found to have a moderate elevation of protein in cerebrospinal fluid.

The distribution of the highest leucocyte counts and percentages of eosinophils in the cerebrospinal fluid of 47 cases were shown in Table 4. High leucocyte counts were found in all patients and more than 90 % of patients had pleocytosis over 100 leucocytes per cu mm. The eosinophils amounted to 30 % or more of cerebrospinal leucocytes in 85 % of cases. There was a positive correlation between the percentage of eosinophils and the total number of leucocytes in the cerebrospinal fluid, which reflects the eosinophilic pleocytosis of the cerebrospinal fluid of the disease.

In total, 125 worms of *A. cantonensis* were recovered from the cerebrospinal fluid

of 4 patients; 1 worm from each of 2 cases, 81 and 42 worms from another 2 cases, respectively.

Table 3 Laboratory findings in 47 cases of eosinophilic meningitis or meningoencephalitis.

A) Peripheral blood		No. of cases	Incidence (%)
1) W. B. C. /cu mm:	9,000-10,000	4	8.5
	10,000-16,000	35	74.5
	16,000-20,000	8	17.0
2) Eosinophils:	above 15%	29	61.7
B) C. S. F.			
1) Appearance:	Turbid	25	53.2
	Hazy	21	44.7
	Faintly	1	2.1
2) Protein:	Pandy's (+)	16	34.0
	(++)	20	42.6
	(+++)	11	23.4
3) Worm recovered		4	8.5

Table 4 Distribution of 47 cases of eosinophilic meningitis or meningoencephalitis by the cerebrospinal fluid leucocytes and percentage of eosinophils.

No. of leucocytes /cu mm in C. S. F.	Eosinophils as percentage in C. S. F.						Total (%)
	-10	11-30	31-50	51-70	71-90	-100	
-50	1						1 (2.1)
50-100		2	1				3 (6.4)
100-200		4	4	3			11 (23.4)
200-500			2	6	1		9 (19.1)
500-1,000			3	4	1		8 (17.0)
1,000-2,000			2	11	1	1	14 (29.8)
2,000-							1 (2.1)
Total (%)	1(2.1)	6(12.8)	12(25.5)	24(51.1)	3(6.4)	1(2.1)	

5) Treatment

The specific therapy for the disease is not well established yet. However, supportive and symptomatic therapy is primarily important. According to above principles, management of 47 cases was summarized as follows.

For releasing headache, the use of analgesics and an effort to reduce elevated intracranial pressure by repeated lumbar puncture, administration of hypertonic solution and manitol had been employed. Antipyretics was given when fever occurred. Appropriate fluid and nutritional elements were also given. Systemic use of antibiotics was provided for the prevention and treatment of bacterial complication. None was administered any anthelmintics in the course of treatment, though thiabendazole had been reported effective in the treatment of experimentally infected mice.

In the majority of patients most symptoms disappeared within one month of onset. One case died of purulent meningitis one year later.

Discussion

Forty-seven child-patients with eosinophilic meningitis or meningoencephalitis probably caused by infection with *A. cantonensis* in southern Taiwan were studied on its epidemiological and clinical characteristics. Among these cases, the worms of *A. cantonensis* were found from cerebrospinal fluid of only 4 patients. Therefore, the diagnosis of this disease is usually made on the basis of clinical symptoms, eosinophilic pleocytosis and history of eating food contaminated with infective larvae such as raw fresh water prawns, slugs and snails in the enzootic areas. It seems that the immunological examination may be useful in obtaining the correct diagnosis. The immunological diagnosis by immunodiffusion test, hemagglutination test and intradermal skin test has been successfully carried out on 9 cases in Japan.^{3,4)} Although immunodiagnosis was not performed to these cases in the present study, their clinical manifestations such as eosinophilic pleocytosis of cerebrospinal fluid and considerable meningeal symptoms and signs were indistinguishable from those of the proven 4 cases. In Taiwan, a similar clinical study on 125 cases has been carried out by Yii (1976).⁵⁾ The clinical findings of cases in the present study were almost the same as those in the previous study. From the results, it is certainly suspected that most cases in this study were indeed caused by potential infection with *A. cantonensis*. The mechanisms involved in the production of cerebrospinal angiostrongyliasis are not yet completely understood. In experimental animals, many larvae invaded become trapped and destroyed in the pulmonary lymphatic vessels and mediastinal lymph nodes.⁶⁾ It is not known, however, whether any larvae become trapped and destroyed in the lymphatic system in man before they migrate into central nervous system and produce meningeal symptoms of the disease.

Most cases developed the first symptoms in summer from June to September in Taiwan, while in the neighboring Okinawa in Japan, few cases were evenly seen throughout all seasons.⁴⁾ In Taiwan, summer months are known to be the rainy season

when *Achatina fulica*, a giant African terrestrial snail, is moving more actively. This is most likely source of human infection.²⁾

There was a clear excess of male patients on Pacific islands⁷⁾ and in Thailand.⁸⁾ In this study, however, the distribution of cases between two sexes was approximately equal, as it is in Okinawa, Japan.⁴⁾ The presence of a differential sex susceptibility to *A. cantonensis* infection has been shown in experimental animals.⁹⁾ This was considered to be one of the possible explanations for the higher number of cases among males than among females in Thailand.⁸⁾ However, the result in the present study did not support that males were more susceptible than females to the infection of *A. cantonensis*.

The patients examined were children who visited a children's hospital and the majority of the patients was infants under 5 years of age. Recently, angiostrongyliasis in Taiwan was reviewed by Chen (1979),²⁾ in which it was also indicated that most of Taiwanese patients (80%) were children below 14 years of age and that this was the most striking epidemiological feature of the disease in Taiwan as compared to the other areas. It has been logically suspected that the high proportion of cases among children is related to their propensity to play near the kitchen and yards of homes, where they exposed themselves to the debris associated with the preparation of *A. fulica* for eating. In a screening survey with the intradermal skin test for angiostrongyliasis, however, high positive rates were also obtained among the adult groups, suggesting that the latent infection might often occur among adults in this areas.¹⁰⁾ While, the positive rates in the same skin test among residents of the southern and eastern Taiwan were significantly higher than those of the northern and central areas. In Taiwan, it has been known that most of the patients were from the southern and eastern Taiwan, corresponding to the high incidence of the parasite in the intermediate and definitive hosts in the same areas.²⁾ The fact provided a reasonable evidence of the high positive rates in the skin test among residents in the southern and eastern Taiwan.

As mentioned above, the presence of different case distribution by area, age and sex probably suggests that the differences in the ways of life and in eating habits of inhabitants in various areas, as well as incidences of the parasite, are important factors for the prevalence of human angiostrongyliasis. Since the majority of cases in the present study were children below 10 year-old, their modes of infection could not be clarified in most cases. However, *A. fulica* has been considered to be important in conveying *A. cantonensis* to man of which the infection rate was 53.2% in the southern Taiwan in the previous survey.^{10,11)} There may be the greater number of cases among aborigines as compared with pure Chinese since the formers eat *A. fulica* more frequently than the latter do. The snails are rarely eaten by raw in Taiwan. Most patients may acquire infections during the process of preparing food. This may also be related to the more cases of female in Taiwan compared with those in the other areas.

From the results, angiostrongyliasis is still prevalent in southern Taiwan and it is necessary to continue various observations which are effective for better diagnosis, therapeutic control and prevention of the disease.

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