

# CLINICAL STUDIES ON ANGIOSTRONGYLIASIS CANTONENSIS AMONG CHILDREN IN TAIWAN

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**Abstract.** *Angiostrongylus cantonensis* is a disease commonly seen in Taiwan, especially in children during the summer rainy season. Most of the cases reported in other countries were adults and their clinical manifestations were different from children. Studies on special clinical characteristics of *angiostrongylus cantonensis* among 82 children in Taiwan were performed. Thirty-eight (46.3%) were male and 44 (53.7%) females, and 87% could be traced to a history of contact with the intermediate host, the giant African snail, *Achatina fulica*, which plays a major role in transmission. The incubation period (average: 13.2 days) was shorter in children than in adults (average: 16.5 days). In about one-third (30.5%) of the total cases, the clinical form was meningoencephalitis, which was higher than in adult cases seen in Thailand (5%). The most common clinical symptom was fever (91.5%), followed by vomiting and headache. The percentages of sixth and seventh cranial neuropathy associated with the disease were 19.5% and 11.0% respectively. Ophthalmologic funduscopy showed that 25.0% with papilledema which was significantly higher than seen in adults (12%) in Thailand. Most of the cases in this study had peripheral leukocytosis (above 10,000/mm<sup>3</sup>) and eosinophilia (above 10%); the percentages were 82.9% and 84.1%, respectively. The worm recovery rate from cerebrospinal fluid by lumbar puncture of 82 cases was 41.5%; 141 worms were collected from one female patient using a pumping method. In the recent 2 years, albendazole and levamisole were used clinically with good result.

## INTRODUCTION

Eosinophilic meningitis or meningoencephalitis caused by infection with *Angiostrongylus cantonensis* is an endemic disease of Taiwan. In the summer rainy season when snails are active in the field, children in rural or mountainous areas are infected by playing with the snails or eating them raw. Some are infected by innocent contamination with the mucus or viscera of snails which contain *A. cantonensis* third-stage larvae (Hwang and Chen, 1986). Over 80% of the cases in Taiwan occur among children under the age of 15 (Chen, 1979). Conversely, adults are more frequently infected than children in Thailand (Punyagupa *et al.*, 1970) and Tahiti (Rosen *et al.*, 1967) where people consume the intermediate or paratenic host. The clinical manifestations of eosinophilic meningitis or meningoencephalitis in children are different from those in adults and this study was done to determine the characteristic features of the disease in pediatric patients compared with those in adult patients.

## MATERIALS AND METHODS

### Subjects

Patients admitted to the study were diagnosed clinically and by laboratory examinations at the Pediatric Department of the Kaohsiung Medical College. A total of 82 patients were seen, 38 males and 44 females. The criteria of diagnosis included clinical manifestations of meningitis or meningoencephalitis, over 10% eosinophilic pleocytosis, history of contact with an intermediate host, and worm recovery from cerebrospinal fluid (CSF), eyes or other organs after autopsy (Cross, 1978).

### Methods

Special data forms were developed to record the history, chief complaints, symptoms and signs, physical and laboratory findings. Routine examinations: blood, urine, stool and CSF, liver function test, erythrocyte sedimentation rate, creatinine phosphokinase, EEG, CT and MRI were included in the laboratory findings.

Laboratory and neurological examinations were included. Patients were followed for at least 6 months after discharge to observe complications and sequelae.

Chi square and student *t*-test were used to compare the frequency of variables among patients from our series and to that from other published reports.

## RESULTS

### Age and sex

Among 82 cases, 34 were parasitologically proven. Their ages ranged from 10 months to 14 years, 58.5% were under 6 years of age and 80% (79.2%) were below 9 years of age. There were 38 (46.3%) males and 44 (53.7%) females. Females were 1.2 times more commonly infected than males.

### Monthly distribution

The distribution of cases showed an increase in numbers in the rainy season which is also the active season for *Achatina fulica*. Most (82%) of cases were seen during the Taiwan summer months of May, June, July, August, September and October.

### History of contact intermediate host

Of the total of 82 cases, 72 (87.8%) had a definite history of contact with intermediate hosts (Table 1). The most common intermediate host was *A. fulica* (69 cases). Slugs and the snail *Ampullarium* were also important intermediate hosts. Third-stage larvae were recovered from these molluscs after digestion and the larvae infected mice experimentally.

### Incubation period

The time of contact with an intermediate host and onset of the initial symptoms were determined for 72 cases. The average incubation period was 13.1 days and ranged from 2 days to 45 days. In the 28 worm-positive cases, the average incubation period was also 13.1 days. It was similar for that 44 worm-negative cases. There were no significant differences between these two groups ( $p > 0.05$ ).

Table 1

History of contact intermediate host among 82 patients with eosinophilic meningitis or meningoencephalitis.

History of contact intermediate host	No. of cases	%
<i>Achatina fulica</i>	68	82.9
Eaten	42	51.2
Played	11	13.4
Eaten + played	8	9.8
Contacted	7	8.5
<i>Achatina fulica</i> + slug	1	1.2
Eaten	1	1.2
<i>Ampullarium</i>	2	2.4
Played	1	1.2
Contacted	1	1.2
<i>Ampullarium</i> + slug	1	1.2
Played	1	1.2
Subtotal	72	87.8
Unknown	10	12.2
Total	82	100.0

### Clinical manifestations

The clinical manifestations of angiostrongylasis cantonensis may be meningitis, meningoencephalitis, radiculomyelitis, ocular or cranial nerve lesions (Hung and Chen, 1988). The manifestation maybe one or a combination of more than one of the above clinical forms. Of 82 cases, 57 or 69.5% had meningitis, and 25 or 30.5% meningoencephalitis. Twenty-four cases were complicated with cranial nerve lesions, 19.5% involved the abducent nerve and 11.0% involved facial nerve. Radiculomyelitis and ocular lesions were also found in 3 and 1 case respectively (Table 4).

### Initial symptoms and signs

The most common initial symptoms and signs in pediatric patients were fever (73.2%), followed by headache and vomiting. Of the total cases

14.6% and 12.2% had initial symptoms of cough and rhinorrhea, and were diagnosed initially as respiratory tract infections.

**Chief complaints**

Fever was the most common complaint in 53.7% (44) of total cases. The second most common complaint was headache (50.0%), followed by vomiting (25.6%) and neurological disorders including convulsion, lethargy and drowsiness. An ocular case, in which a worm was found in the anterior chamber, had red eyes. Strabismus as the chief complaint was also observed in one case.

**Clinical symptoms and signs during admission**

Over 90% of total cases had fever at admission. The other common symptoms were vomiting (72.0%) and headache (62.2%). Nearly one fourth (23.2%) of total cases had weakness of extremities. Strabismus and facial palsy occurred in 19.5% and 11.0% of total cases respectively. Four cases (4.9%) had hyperesthesia. The other 4 cases became comatose, 3 of them died (Table 2). Neck stiffness was seen in 79.3% at admission and positive Kernig's sign and Brudzinski sign were observed in 41 (50%) and 26 (31.6%) cases respectively. Forty-one cases (50%) had marked abdominal distension during the course of disease and 29.3% had hepatomegaly (> 4 cm below right costal margin) (Table 3).

**Fundoscopy findings**

Fourteen (25.0%) of 56 patients received fundoscopic examinations and revealed papilledema; 6 (10.7%) had a blurred optic disc and 36 (64.3%) a normal disc. A worm was recovered from the anterior chamber of the eye of one female patient.

**Laboratory findings**

The laboratory data included blood and cerebrospinal fluid (CSF) examinations at the time of admission to the hospital. The peripheral white blood cell count was > 10,000/mm<sup>3</sup> in 68 (82.9%) of 82 the patients and 69 (84.1%) patients had eosinophil counts of 10%.

The white blood cell count in CSF was less than 100/mm<sup>3</sup> in only 6 (7.4%) of the cases.

Table 2

Frequency of clinical symptoms in 82 cases of eosinophilic meningitis or meningoencephalitis.

Symptoms	No. of cases		Total	%
	(+)worm	(-)worm		
Fever	33	42	75	91.5
Vomiting	22	37	59	72.0
Headache	12	39	51	62.2
Anorexia	12	16	28	34.1
Irritability	13	12	25	30.5
Cough	11	11	22	26.8
Constipation	7	12	19	23.2
Weakness of extremities	11	8	19	23.2
Nausea	7	11	18	22.0
Abdominal pain	4	13	17	20.7
Somnolence	9	8	17	20.7
Convulsion	7	9	16	19.5
Strabismus	7	9	16	19.5
Drowsy	10	4	14	17.1
Malaise	6	7	13	15.9
Rhinorrhea	7	4	11	13.4
Myalgia	3	8	11	13.4
Facial palsy	6	3	9	11.0
Diarrhea	7	2	9	11.0
Semicoma	3	5	8	9.8
Spastic extremities	1	5	6	7.3
Dizziness	1	5	6	7.3
Urinary incontinence	3	2	5	6.1
Diplopia	0	5	5	6.1
Diplopia, blurred vision	0	5	5	6.1
Twitching	4	0	4	4.9
Coma	1	3	4	4.9
Hyperesthesia	1	3	4	4.9
Lethargy	1	2	3	3.7
Eyelids edema	1	2	3	3.7
Photophobia	1	1	2	2.4
Retroorbital pain	0	2	2	2.4
Nystagmus	1	1	2	2.4
Confusion	0	2	2	2.4
Insomnia	2	0	2	2.4
Paresthesia	1	1	2	2.4
Skin rash	1	1	2	2.4
Stupor	1	0	1	1.2
Eyeball protrusion	0	1	1	1.2
Arthralgia	0	1	1	1.2

Table 3

Frequency of signs in 82 cases of eosinophilic meningitis or meningoencephalitis.

Signs	No. of cases		Total	%
	(+)worm	(-)worm		
Neck stiffness	33	32	65	79.3
Kernig's sign (+)	21	20	41	50.0
Abd. distension	21	20	41	50.0
Brudzinski sign (+)	13	13	26	31.7
Hepatomegaly	11	13	24	29.3
Deep tendon reflex	3	4	7	8.5
Decreased	3	2	5	
Increased	0	2	2	
Paralysis of extremities	2	3	5	6.1
Anemia	0	4	4	4.9
Splenomegaly	1	0	1	1.2

Eosinophilic pleocytosis was found in 62.2% with eosinophil counts ranging between 51% and 90%. Protein in CSF was over 45 mg/dl in 41 (61.2%) of 67 patients. The levels of sugar of 40 (58.8%) cases were between 40 mg/dl and 7 mg/dl with 23 (33.8%) below 40 mg/dl. Worms were recovered from the CSF in 34 patients; 16 males and 18 females. The worm recovery rate in this study was 41.5% (Table 4).

Non-specific change of electroencephalogram (EEG) occurred in 13 of 28 cases subjected to EEG examination. Eight had diffused or focal cortical dysfunction, 3 borderline change, 1 flattening wave, and 1 paroxysmal spike and sharp waves.

Computerized tomography (CT) scan was performed on 16 patients, 9 were normal, 2 showed brain edema, 2 communication hydrocephalus, 2 meningitis, 1 prominent sylvian fissure and dilatation of the lateral ventricle. Magnetic resonance imaging (MRI) had been studied in one patient with non-specific finding.

The enzyme-linked immunosorbent assay (ELISA) was used to detect the specific antibodies in serum and CSF. High titers of specific antibodies were noted in the infective group including worm positive and worm negative cases. The titers were significantly higher than control groups.

### Treatments, complications and sequelae

Initially, patients were treated with glycerol, mannitol or steroids to reduce the intracranial pressure. Repeated lumbar puncture was also performed. In addition antibiotics and other supportive treatment were given to prevent secondary bacterial infections and relieve the clinical symptoms. Complications observed in 8 patients: 4 had pneumonia, 2 purulent meningitis, 1 pressure sore, 1 urinary tract infection. Sequelae, recorded after following up for 6 months, were slurred speech, poor perception, eyelid ptosis, weakness of extremities, blurred vision and poor school grades in 6.

Anthelmintics (levamisole 2.5 mg/kg/day, albendazole 10 mg/kg/day, for 3 weeks) had been given to replace the steroids recently. We experienced 22 cases without complications and sequelae.

### Course and prognosis

Seventy-two (87.8%) of 82 patients were considered completely recovered from their disease without definite sequelae. Seventy cases (85.4%) were released from hospital within 30 days after admission. No recurrent illness could be found. Four patients died with meningoencephalitis, 3 males and 1 female. All 4 were in coma at the time of admission. The mortality rate was 4.9%.

Table 4

Age and sex distribution of cases with eosinophilic meningitis or meningoencephalitis in Kaohsiung Medical College.

Age (year)	Male*( )	Female*( )	Total ( )	Worm recovery rate (%)
0 - 2	10 (9)	16 (10)	26 (19)	73.1
3 - 5	12 (4)	10 (5)	22 (9)	40.9
6 - 8	6 (2)	11 (1)	17 (3)	17.6
9 - 11	5 (1)	4 (1)	9 (2)	22.2
12 - 14	5 (0)	3 (1)	8 (1)	12.5
<b>Total</b>	<b>38 (16)</b>	<b>44 (18)</b>	<b>82 (34)</b>	<b>41.5</b>

( ) : No. of cases proved by parasite recovered from cerebrospinal fluid.

\* :  $\chi^2$  - test,  $p > 0.05$ , by Yate's correction.

## DISCUSSION

In Taiwan about 80% of patients with eosinophilic meningitis or meningoencephalitis are children under 15 years of age living in rural or mountainous areas. They innocently play with or eat snails, or ingest the mucus or viscera from the snails (Chen, 1979). Females are 1.2 times more frequently infected than males. Cases appeared yearly and over 75% were below 9 years of age. The reason is the poor personal hygiene of children in endemic areas where *A. fulica* is abundant and actively moving in the field in summer rainy season. In Thailand, Punyagupta *et al* (1970) reported cases throughout the year and about 70% were in the age group of 20-39. Males outnumbered females by more than two to one. In Tahiti, the highest prevalences were in the months of March through June (Rosen *et al*, 1967). Adults were more frequently infected than children. There was little difference in the distribution of cases by sex. The main source of infection in Tahiti is attributed to ingestion of raw freshwater prawns (*Macrobrachium*) or prawn sauce containing *A. cantonensis* larvae. In Thailand, an aquatic snail (*Pila* sp.) is the main source of infection.

The average incubation period in pediatric cases in Taiwan was 13.1 days; ranged from 2 days to 45 days, which is shorter than for adult cases reported in Thailand (16 days) (Punyagupta *et al*, 1970) and Tahiti (16.5 days) (Alicata and Brown, 1962). This indicates that clinical symptoms appear earlier in children.

Meningoencephalitis occurs more frequently in children than in adults (Yii *et al*, 1975; Cheng *et al*, 1984), but optic nerve involvement and radiculomyelitis is rarely found in children. However, the involvement of the sixth and seventh cranial nerve appeared in pediatric cases in Taiwan and presented as strabismus and facial palsy (Yii, 1976).

In the majority of our cases, the disease manifested with an abrupt development of fever, headache, vomiting and stiffness of the neck. However, headache was the most prominent symptom in Ponape, Tahiti and Thailand (Punyagupta, 1979). Fever was the most common symptom in pediatric cases and headache occurred in only 62.2% of total cases in this study. The frequency of abdominal symptoms including abdominal pain and diar-

rhea are similar to the report in Thailand (Punyagupta, 1979). These appeared in the early stage of the disease. The percentage of neck stiffness and positive Kernig's sign in this study was 79.3% and 50.5% respectively, which is significantly higher than adult cases in Thailand (Punyagupta, 1979). The most specific sign during the course of disease was abdominal distension involving half of the total cases and persisted for at least one month. Papilledema of the optic disc had been found in 25.0% of total cases, which is also higher than adult patients in Thailand (12%) (Kanchanaranya and Punyagupta, 1971).

Peripheral leukocytosis and eosinophilia were commonly seen in children compared to the adult cases in Thailand (Punyagupta *et al*, 1975). CSF findings, between adults and children, were similar except the worm recovery rate. The parasite apparently is more readily detectable in CSF on Taiwan than elsewhere (Yii, 1976). The worm recovery rate was 41.5% in this study. Moreover, the rate was improved by a pumping method created by us which has been proved in a case control study.

Recently, 22 cases treated with anthelmintics (levamisole 2.5 g/kg/day, albendazole 10 mg/kg/day) for 3 weeks gave good results. No complications, sequelae and mortality occurred in this group. We also experienced a case, from whom 141 worms were aspirated with CSF. This patient was cured by albendazole without the use of steroids.

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