

# Clinical Manifestations of Eosinophilic Meningitis Due to Infection with *Angiostrongylus cantonensis* in Children

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**Abstract:** Eosinophilic meningitis, caused by the nematode *Angiostrongylus cantonensis*, is prevalent in northeastern Thailand, most commonly in adults. Data regarding clinical manifestations of this condition in children is limited and may be different those in adults. A chart review was done on 19 eosinophilic meningitis patients aged less than 15 years in Srinagarind Hospital, Faculty of Medicine, Khon Kaen University, Thailand. Clinical manifestations and outcomes were reported using descriptive statistics. All patients had presented with severe headache. Most patients were males, had fever, nausea or vomiting, stiffness of the neck, and a history of snail ingestion. Six patients had papilledema or cranial nerve palsies. It was shown that the clinical manifestations of eosinophilic meningitis due to *A. cantonensis* in children are different from those in adult patients. Fever, nausea, vomiting, hepatomegaly, neck stiffness, and cranial nerve palsies were all more common in children than in adults.

**Key words:** *Angiostrongylus cantonensis*, eosinophilic meningitis, children, clinical manifestation

## INTRODUCTION

Eosinophilic meningitis (EOM) caused by *Angiostrongylus cantonensis* is prevalent in northeastern Thailand [1]. Most patients are adults and are infected by eating raw or undercooked freshwater snails or other paratenic hosts such as freshwater shrimps, frogs, or monitor lizards [2]. The diagnosis is mostly made clinically by the evidence of eosinophils in cerebrospinal fluid (CSF) constituting more than 10% of total CSF white blood cells [2,3]. A typical presenting symptom of EOM is acute severe headache without neurological deficits [4]. The diagnosis may be missed because meningism signs including fever and neck stiffness are found infrequently [5]. EOM in children is rarely reported in the literature. However, clinical manifestations in children may be different from those of adult patients. Here, we report a series of EOM cases in children in terms of clinical manifestations and outcomes in the endemic area of EOM associated with *A. cantonensis*.

## CASE DESCRIPTION

Twenty patients below the age of 15 were diagnosed as EOM associated with *A. cantonensis* at Srinagarind Hospital, Khon Kaen University, Thailand. One was excluded due to having spinal cord involvement. Medical records of the remaining 19 were reviewed. The diagnosis of EOM was made if CSF WBC count was  $> 10$  cells/mm<sup>3</sup> and more than 10% of these were eosinophils. Additionally, negative results should be yielded from the CSF by Gram, acid-fast and India ink staining, and cultures. We excluded patients with other possible causes of eosinophilic pleocytosis in CSF such as neurognathostomiasis, tuberculosis, or malignancy [6]. Clinical manifestations and outcomes were recorded including baseline characteristics, symptoms, physical signs, laboratory results, treatment, and outcomes. Data included age, gender, season of presenting symptoms defined by Thailand meteorology classification (winter, summer, or rainy), incubation period (number of days after the last exposure to snails or paratenic hosts to the first day of developing symptoms), duration of headache, history of paresthesia, history of nausea or vomiting, fever (oral temperature more than 37.8°C), general physical signs, cranial nerve abnormalities, cerebellar signs, papilledema, and neck stiffness. Laboratory results were complete blood count and

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CSF analyses. Treatment and clinical outcomes such as duration of headache, number of lumbar punctures were also reviewed. All data were presented using descriptive statistics and compared with the data of adult EOM patients.

All 19 patients presented with severe headache (100%). Most patients were males (78.9%), had fever (78.9%), nausea or vomiting (63.2%), a history of ingestion of raw freshwater snails (68.4%), neck stiffness (68.4%), and about half of them were infected during winter season (52.6%). The median incubation period was 22 (1-30) days. Six patients (31.6%) had papilledema or cranial nerve palsies. Abnormal cerebellar signs were found in 2 patients (10.5%). Hepatomegaly was found in another other 2 patients (10.5%). Median peripheral eosinophilia and CSF eosinophils were 20% and 58%, respectively. Three patients had thrombocytosis (more than 400,000 cells/ $\mu$ l). Data were summarized and compared with those from

adult patients as shown in Tables 1 and 2.

Corticosteroid was given to 5 patients (26.3%). Albendazole or mebendazole combined with corticosteroid was given to 1 patient (5.3%). The median duration of headache after treatment was 4 days (range 1-21 days) as shown in Table 3. Ten patients (52.6%) required repeated lumbar puncture to relieve headache. The median numbers of repeated lumbar puncture was 2.5 times (range 1-6 times).

## DISCUSSION

Clinical manifestations and outcomes of EOM in children were different from those in adults. Although our sample number is small, children with EOM revealed more systemic responses, as were apparent from the high proportion of patients with fever (78.9% vs 10%) and nausea/vomiting (63.2% vs 38.8%). Two children exhibited hepatomegaly, which was never seen in adult patients (10.5% vs 0%: Tables 1 and 2) [6]. In addition, cerebellar abnormality and thrombocytosis have never been reported in adult patients according to the literature [4,6-9].

Compared to adult patients [5], a higher proportion of children showed cranial nerve abnormalities (both cranial nerve VI and VII), neck stiffness (68.4% vs 47.5%), and papilledema (31.6% vs 2.5%). Clinical signs of meningism (fever, headache, and neck stiffness) were much more frequent in child patients compared with adults (68.4% vs 9.0%). In contrast, hyperesthesia, the specific sign for angiostrongyliasis in adults, was not found in children.

Regarding laboratory results (Table 2), all variables were quite comparable between children and adults except for thrombocytosis and high CSF opening pressure. These clinical features

**Table 1.** Clinical manifestations of eosinophilic meningitis in children and adults

Variables	Children (N=19)	Adults (N=80)
Age, years (range)	12 (4-14)	33.5 (15-70)
Male gender, N (%)	15 (78.9)	60 (75.0)
Summer season (%)	4 (21.1)	12 (15.0)
Snail ingestion, N (%)	13 (68.4)	80 (100)
Incubation period, days (range)	22 (1-30)	20 (1-90)
Headache, N (%)	19 (100)	80 (100)
Nausea or vomiting, N (%)	12 (63.2)	31 (38.8)
Fever, N (%)	15 (78.9)	8 (10)
Hepatomegaly, N (%)	2 (10.5)	0 (0)
6th cranial nerve palsy, N (%)	5 (26.3)	3 (3.8)
7th cranial nerve palsy, N (%)	1 (5.3)	2 (2.5)
Abnormal cerebellar signs, N (%)	2 (10.5)	0 (0)
Hyperesthesia, N (%)	0	9 (11.3)
Neck stiffness, N (%)	13 (68.4)	38 (47.5)
Papilledema, N (%)	6 (31.6)	2 (2.5)

**Table 2.** Laboratory results of eosinophilic meningitis in children and adults

Variables	Children (N=19)	Adults (N=80)
Blood test		
Total WBC, cell/mm <sup>3</sup> (range)	13,200 (6,400-22,500)	10,250 (4,700-23,500)
% eosinophils (range)	20 (5-48)	15 (1-45)
Thrombocytosis, N (%)	3 (15.8)	0 (0)
Cerebrospinal fluid examination		
Opening pressure, mmH <sub>2</sub> O (range)	400 (300-600)	280 (50-600)
Total WBC, cell/mm <sup>3</sup> (range)	637 (87-2,610)	765 (12-5,100)
% eosinophils (range)	58 (31-95)	49 (10-84)
Protein, mg/dl (range)	68 (34-240)	94 (17-470)
Glucose, mg/dl (range)	45 (26-114)	47 (20-134)
CSF/plasma glucose ratio (range)	45.2 (22.8-112.9)	45 (15-113)

**Table 3.** Treatment outcomes in children and adult patients with eosinophilic meningitis

Variables	Children (N=19)	Adults (N=55)
Median duration of headache, days (range)	4 (1-21)	13 (1-56)
No. of patients with repeated lumbar puncture, N (%)	10 (52.6)	22 (40)
Median numbers of repeated lumbar puncture, times (range)	2.5 (1-6)	NA

Adult patients received supportive treatment, while treatments for children were mentioned in the text. NA, not available.

recall a report from Taiwan that showed high proportion of fever (91.5%) in children with EOM [10]. The explanation may be due to systemic responses and high intracranial pressure, evidenced by higher CSF opening pressures in children than in adults (400 vs 280 mmH<sub>2</sub>O) as shown in Table 2.

Most clinical variables in this study and the study from Taiwan were quite comparable except numbers of patients with meningoencephalitis and worm recovery in the CSF (Table 4). In Thailand, the rate of meningoencephalitis was low particularly in adults (<5%). In this study, we did not find any children with EOM developed alteration of consciousness. The definition of meningoencephalitis may be different between Taiwan and Thailand studies. In Thailand, physicians defined meningoencephalitis only if the patients turned to permanent unresponsive or comatose condition. However, in Taiwan studies, patients were defined as meningoencephalitis if the patients had alteration in mental or consciousness level at presentation [10]. The worm recovery in the CSF was generally low [2,11], although it was reported to be 41.5% in a Taiwan study [10].

The treatment outcomes shown in Table 3 may not be realistic because data shown for adult patients included those who were treated with placebo [4], whereas children in the present study were treated with analgesics, corticosteroids, and anthelmintics. The duration of headache in children seemed to be shorter but a higher proportion required repeated lumbar puncture. This may imply that children with EOM may resolve more quickly than adults despite having more severe systemic responses as discussed earlier. Children with EOM, however, needed more frequent reduction of intracranial pressure by repeated lumbar puncture compared with adult patients (52.6% vs 40%, Table 3).

The limitations of this study were the small number of patients and incomplete data as a consequence of the retrospective nature of the study. Having a history of eating raw fresh-

**Table 4.** Clinical comparison between children with eosinophilic meningitis in Thailand and Taiwan

Variables	Thailand (N=19)	Taiwan [10] (N=82)
Male, N (%)	15 (78.9)	38 (46.3)
Season	Summer (21.1)	Mostly summer, rainy
Exposure to intermediate host, N (%)	13 (68.4)	71 (87)
Incubation period, days	22 (median)	13.2 (mean)
Fever, N (%)	15 (78.9)	75 (91.5)
6th cranial nerve palsy, N (%)	5 (26.3)	16 (19.5)
7th cranial nerve palsy, N (%)	1 (5.3)	9 (11)
Papilledema, N (%)	6 (31.6)	21 (25.6)
Worm recovery in CSF (%)	0	34 (41.5)
Meningoencephalitis (%)	0	25 (30.5)

Note. CSF, cerebrospinal fluid.

water snails is an important risk factor for angiostrongyliasis, yet was found in only 68.4% of child patients compared to almost 100% in adult patients [4,6-9]. Other than eating, direct contact with snails and slugs may be another risk factor for EOM in children. A report from Taiwan showed that having snails as a pet was another route of infection [12]. In conclusion, clinical features and outcomes of EOM caused by *A. cantonensis* in children were different from those in adult patients. Compared with previous data of adult patients, high proportions of fever, nausea, vomiting, hepatomegaly, neck stiffness, and cranial nerve palsies were more common in children.

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