Original Article

How to Differentiate *Angiostrongylus cantonensis* and *Gnathostoma spinigerum* as a cause of Eosinophilic Meningitis?

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Objective: The common causes of eosinophilic meningitis are *Angiostrongylus cantonensis* and *Gnathostoma spinigerum*. To differentiate both parasites can be performed by serology test. This study aimed to use clinical factors to differentiate cause of eosinophilic meningitis from *A. cantonensis* or *G. spinigerum.*

Materials and Methods: The authors retrospectively reviewed clinical factors of eosinophilic meningitis patients who were tested for *A. cantonensis* and *G. spinigerum* serology test at Srinagarind Hospital, Khon Kaen University, Thailand. Clinical factors were compared by descriptive statistics.

Results: There were 33 eosinophilic meningitis patients who were tested for both parasites by serology tests. Of those, 22 patients were positive for *A. cantonensis*, while 11 patients were positive for *G. spinigerum*. Patients with *A. cantonensis* had more headache and fever, while patients with *G. spinigerum* had more migratory swelling, radicular pain, and abnormal Babinski's sign. Regarding laboratory tests, peripheral eosinophilia, numbers of white blood cells in the cerebrospinal fluid, and numbers of eosinophils in the cerebrospinal fluid were not different between eosinophilic meningitis patients from *A. cantonensis* and *G. spinigerum.*

Conclusion: Clinical factors may be used to differentiate both parasites as a cause of eosinophilic meningitis.

Keywords: Eosinophilia, Migratory swelling, Radicular pain

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Eosinophilic meningitisis defined by presence of eosinophils in the cerebrospinal fluid, more than 10% of the total white blood cells[1]. There are several causes of eosinophilic meningitis including parasitic infection, tuberculosis, or medications[1]. The two most common causes of eosinophilic meningitis are *Angiostrongylus cantonensis* and *Gnathostoma spinigerum*[1]. The definite diagnosis of both parasitic infections is an identification of larva or a positive serology test.

The identification of larva in the cerebrospinal fluid to diagnose both parasites is rare. *A. cantonensis* larva were found in only 38 case out of 2,827 (1.34%) of eosinophilic meningitis patients in the literature[2]. While, 11% of patients with gnathostomiasis can be discovered the larva in human specimens[3]. Therefore, serology tests for both parasites are crucial diagnostic laboratory tests[4,5]. However, serology tests are not widely available even in Thailand[1]. The present study aimed to evaluate if any clinical factors can be helpful in differentiating both parasites in eosinophilic meningitis patients.

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Materials and Methods

The present study was a retrospective study and conducted at Srinagarind Hospital, Khon Kaen University. The inclusion criteria were adult patients diagnosed as eosinophilic meningitis and had been tested for both *A. cantonensis* and *G. spinigerum*.

Eosinophilic meningitis diagnosed by presence of eosinophils in the cerebrospinal fluid more than 10 cells/mm^3 or proportion of eosinophils in the cerebrospinal fluid more than 10%. Serology tests used for angiostrongyliasis and gnathostomiasis were a 29-kDaimmunotblotting test for *A. cantonensis* and a 21- or 24-kDa immunotblotting test for

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G. spinigerum. Angiostrongyliasis and gnathostomiasis were diagnosed by clinical manifestations, history of larva exposure, and positive serology test. Larva exposure for *A. cantonensis* included raw freshwater snails, shrimps, monitor lizard, frogs, and raw produce, while fish, chicken, snails, frogs, crabs, or snake containing *G. spinigerum* larva.

Clinical factors and laboratory results of all eligible patients were studied and recorded. Peripheral eosinophilia was defined if eosinophils accounted for at least 500 cells/microliter. Descriptive statistics were used to compare differences between angiostrongyliasis and gnathostomiasis group. A significant difference between groups was defined if a *p*-value less than 0.05. All statistical analysis was performed by using STATA software, version 10.0 (College Station, Texas, USA).

Results

There were 33 eosinophilic meningitis patients who had been tested for both parasites. Of those, serology test was positive for *A. cantonensis* in 22 patients (66.67%), while the other 11 patients (33.33%) had serology test positive for *G. spinigerum*. For the *A. cantonensis* group, there were six male patients (72%) with an average age of 45 years. While, male accounted for 75% (8 patients) in the gnathostomiasis group with an average age of 43 years.

Regarding clinical factors, there were five significant factors between both groups including headache, fever, migratory swelling, radicular pain, and Babinski sign (Table 1). All patients with angiostrongyliasis group had headache, while only 18.18% of patients had headache ($p<0.001$). Fever was found in 54.54% of patients with angiostrongyliasis but gnathostomiasis ($p = 0.005$). There were three clinical signs suggestive of gnathostomiasis which was not found in angiostrongylaisis group; migratory swelling (36.36%; $p = 0.008$), radicular pain (81.81%; $p<0.001$), and abnormal Babinski's sign (72.72%; $p<0.001$). There was no significant difference in laboratory tests between both groups (Table 2).

Discussion

The present study found that clinical presentations of both parasites can be differentiated mainly by presenting symptoms[1-3,6,7] and signs but not laboratory tests. Beginning with eosinophils in the cerebrospinal fluid, angiostrongyliasis causes mainly meningism, while gnathostomiasis leads to more neurological deficits. Even though both parasites are the leading causes of eosinophilic meningitis, numbers or percentage of eosinophils in the cerebrospinal fluid are comparable (Table 2).

Both parasites are tissue parasites that are neurotropic but causing different presentations due to different sizes and different preferable attack sites[1,3]. *A. cantonensis* larva are mainly located in meninges or brain, while *G. spinigerum* larva migrate randomly to brain tissue, spinal cords, nerve, eyes, or skin. *G. spinigerum* larva is shorter but wider than the *A. cantonensis* larva. The sizes for mature male worm of *G. spinigerum* and *A. cantonensis* are 9.9 to 12.5 mm x 1.0 to 1.25 mm and 20 to 25 mm x 0.32 to 0.42, respectively[7,8].

Acute meningism is the main clinical presentation of angiostrongyliasis. Almost 100% of patients with angiostrongyliasis present with headache[2]. Neck stiffness can be detected in approximately 50% of patients, while fever is quite rare in adult patients (10%), but more common in children (80%)[9-11]. Therefore, clinical meningism: fever, neck stiffness, and headache may be found only in 9% of eosinophilic meningitis caused by *A. cantonensis*[9]. History of larva exposure; eating raw freshwater snails or peripheral

Table 1. Clinical factors of eosinophilic meningitis patients categorized by serology positive for *Angiostrongylus cantonensis* and *Gnathostoma spinigerum*

Variables	Angiostrongyliasis (n = 22)	Gnathostomiasis (n = 11)	*p*-value
Headache	22 (100)	2 (18.18)	<0.001
Nausea	12 (54.54)	2 (18.18)	0.067
Fever	12 (54.54)	0	0.005
Neck stiffness	8 (36.36)	2 (18.18)	0.429
Migratory swelling	0	4 (36.36)	0.008
Radicular pain	0	9 (81.81)	<0.001
Abnormal Babinski's sign	0	8 (72.72)	<0.001

Table 2. Laboratory results of eosinophilic meningitis patients categorized by serology positive for *Angiostrongylus cantonensis* and *Gnathostoma spinigerum*

Variables	Angiostrongyliasis (n = 22)	Gnathostomiasis (n = 11)	*p*-value
Peripheral eosinophilia	12 (54.54)	9 (81.81)	0.249
CSF white blood cell count (cells/mm^3)	550 (145 to 1,600)	310 (12 to 1,080)	0.113
CSF eosinophils (%)	43 (12-84)	30 (14 to 75)	0.389

eosinophilia are main clinical clue for angiostrongyliasis. Otherwise, it will be missed or underdiagnosed as primary headache such as tension headache in clinical practice. Ocular angiostrongyliasis may or may not be accompanied by eosinophilic meningitis[12].

Gnathostomiasis has different clinical presentations from angiostrongyliasis. Due to wider size, it causes more severe neurological damage such as intracerebral hemorrhage, subdural hemorrhage, or spinal cord edema. Other than eosinophils in the cerebrospinal fluid, motor weakness or abnormal Babinski's sign are suggestive for gnathostomiasis as well as radicular pain, or migratory swelling[13,14]. However, radicular pain and migratory swelling are not quite sensitive. Approximately 30% of patients with neurognathostomiasis presented with meningitis form[8]. The most common neurological involvement of gnathostomiasis is radiculomyelitis (55%), while intracerebral/subarachnoid hemorrhage accounted for 15%.

Both parasites are tissue parasite resulting in peripheral eosinophilia. Angiostrongyliasis may have up to 80% of patients with peripheral eosinophilia[9,15]. Absolute eosinophils count over 798 cells with history of larva exposure may be suggestive for angiostrongyliasis[9]. In the present study, peripheral eosinophilia may be found more in gnathostomiasis than angiostrongyliasis (81.81% vs. 54.54%) as shown in Table 2. For eosinophils in the cerebrospinal fluid, the previous review showed that *G. spinigerum* may cause more percentage of eosinophils (74 to 100% vs. 47 to 95%) than *A. cantonensis*[7].

Another useful laboratory test to differentiate both parasites is radiological test[16]. Generally, angiostrongyliasis does not show any pathognomonic radiological abnormality of the brain or spinal cord. In contrast, neurognathostomiasis usually has significant brain findings such as subdural hemorrhage, non-traumatic subarachnoid hemorrhage, or uncommon sites of intracerebral hemorrhage; mostly track-like. Therefore, clinical presentations are still important to differentiate between both parasites.

What is already known on this topic?

An identification of larva or serology test can be used for differentiation of two important causes of eosinophilic meningitis; *Angiostrongylus cantonensis* and *Gnathostoma spinigerum*.

What this study adds?

Clinical features are helpful tool to differentiate the two important causes of eosinophilic meningitis.

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Potential conflicts of interest

The authors declare no conflict of interest.

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