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Single Case – General Neurology

Eosinophilic Meningitis due to *Angiostrongylus cantonensis* in Children

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Keywords

Angiostrongylus cantonensis · Eosinophilic meningitis · Children

Abstract

Meningoencephalitis is not a rare disease in children. However, eosinophilic meningitis due to *Angiostrongylus cantonensis* is unusual in the pediatric population. We describe the case of a 12-year-old girl from the central area of Vietnam with eosinophilic meningitis due to *A. cantonensis*. The patient lived in a rural area, where farming is widespread, and presented with fever and headache. Laboratory results showed peripheral eosinophilia, a cerebrospinal fluid white blood cell count of 730/mm³ with 65% eosinophils. Cerebrospinal fluid ELISA was positive for *A. cantonensis*, and blood ELISA was positive for *A. cantonensis*. The presentation was consistent with a diagnosis of *A. cantonensis* eosinophilic meningitis. The patient recovered fully after administration of albendazole (200 mg/day for 2 weeks), as well as intravenous dexamethasone (0.6 mg/kg/day every 8 h) and mannitol (1.5 g/kg/day every 8 h) for the first 3 days, followed by 5 days of oral prednisolone (2 mg/kg/day).

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Introduction

Angiostrongylus cantonensis (or “rat lung worm”) is responsible for most infectious cases of eosinophilic meningitis (EM) worldwide. *A. cantonensis* is endemic to Southeast Asia and the Pacific Islands, but in recent years human cases have been reported from increasingly diverse locations [1–3]. 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 [4]. The diagnosis is mostly made clinically by evidence of eosinophils in cerebrospinal fluid (CSF) constituting more than 10% of total CSF white blood cells [4, 5]. A typical presenting symptom of EM is acute severe headache without neurological deficits [6, 7]. The diagnosis may be missed because meningism signs including fever and neck stiffness are found infrequently [8]. EM in children is rarely reported in the literature. However, clinical manifestations in children may be different from those in adult patients. We hereby report a case of EM due to *A. cantonensis* in a child, who as far as we know was the first one to be diagnosed in our hospital.

Case Report

A previously healthy 12-year-old girl presented to our hospital with a headache of 3 days duration on March 23, 2019. The patient liked eating roasted seafood. Three days before hospitalization, the patient had had a fever (38–39°C), and a continuous headache with nausea but no vomiting. She had no myotonia or convulsion. She was referred to the Pediatric Neurology Unit of Hue Central Hospital with a headache of unknown cause and was examined by routine tests (as shown in Table 1). Her white blood cell (WBC) count was 5,450 cells/μL with 5.1% eosinophils. Chest radiography findings were normal, and computed tomography and magnetic resonance imaging of the brain were unremarkable. A lumbar puncture was done and revealed 468 WBCs (65% neutrophils, 35% lymphocytes) and a CSF protein level of 0.63 g/L. The patient was treated for bacterial meningitis according to the European Society for Clinical Microbiology and Infectious Diseases guideline [9] with antibiotics such as vancomycin 60 mg/kg/day (March 26 to April 4), ceftriaxone 100 mg/kg/day (March 26 to April 2), and meropenem 100 mg/kg/day (April 3 to April 4). The patient’s headache persisted, and a second lumbar puncture performed 7 days later demonstrated 750 WBCs (10% neutrophils, 90% lymphocytes), a CSF glucose level of 2.2 mmol/L, and a CSF protein level of 0.75 mg/dL. CSF culture for bacteria yielded no growth. The serum findings of an evaluation for *Entamoeba histolytica*, cysticercus, *Schistosoma* sp., *Toxocara*, *Echinococcus* sp., *Fasciola* sp., *Strongyloides stercoralis*, *Gnathostoma* sp., *Ancylostoma caninum*, *Toxoplasma gondii*, *Paragonimus* sp., *Trichinella spiralis*, and *Helicobacter pylori* were normal, and the serum ELISA tests of *E. histolytica*, cysticercus, *Schistosoma* sp., *Toxocara*, *Echinococcus* sp., *Fasciola* sp., *S. stercoralis*, *Gnathostoma* sp., *A. caninum*, *T. gondii*, *Paragonimus* sp., *T. spiralis*, and *H. pylori* were negative. Repeat lumbar puncture revealed 730 WBCs (10% lymphocytes, 5% neutrophils, and 65% eosinophils).

Given the presence of an eosinophilic pleocytosis in her spine, infection with *A. cantonensis* was suspected, and confirmation of *A. cantonensis* infection by immunodiagnosis was sought. Serum and CSF samples were sent to the Hospital for Tropical Diseases in Ho Chi Minh City (Vietnam), where Western blot analyses were done against *A. cantonensis* antigens. Both the serum and the CSF ELISA tests showed a strong reaction to *A. cantonensis*, confirming the diagnosis of angiostrongyliasis. The patient received treatment with albendazole (200 mg/day for 2 weeks), as well as intravenous dexamethasone (0.6 mg/kg/day every 8 h) and mannitol (1.5 g/kg/day every 8 h) for the first 3 days, followed by 5 days of oral prednisolone (2 mg/kg/day). After 1 week of treatment, the patient's headache was relieved and the body temperature was normal. The last lumbar puncture performed on May 9, 2020, showed normal results.

Discussion

Clinical manifestations and outcomes of EM in children were different from those in adults. According to Sawanyawisuth, children with EM revealed more systemic responses, as was apparent from the high proportion of patients with fever (78.9 vs. 10%) and nausea/vomiting (63.2 vs. 38.8%) [6]. Compared to adult patients [8], a higher proportion of children showed cranial nerve abnormalities (both cranial nerve VI and nerve 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 among child patients than among adults (68.4 vs. 9.0%). In contrast, hyperesthesia, the specific sign for angiostrongyliasis in adults, was not found in children [6]. Consistent with the clinical features described in previous reports, our patient presented with an extended prodrome of headache, fever, and vomiting [10].

Regarding laboratory results, all variables were quite comparable between children and adults, except for thrombocytosis and high CSF opening pressure [6]. These clinical features recall a report from Taiwan that showed a high proportion of fever cases (91.5%) among children with EM [11]. This may be due to systemic responses and high intracranial pressure, evidenced by higher CSF opening pressures in children than in adults [6].

Identification of *A. cantonensis* larvae occurs in only 1.9% of patients with angiostrongyliasis [12]. Therefore, immunological assays are used as tools to confirm a presumptive diagnosis, including the immunofluorescence antibody test, immunoenzyme staining test, and ELISA. With regard to imaging tests, computed tomography cannot distinguish *A. cantonensis* EM from that caused by other parasites such as gnathostomiasis or neurocysticercosis [13]. On the other hand, the use of magnetic resonance imaging to investigate *A. cantonensis* EM shows a diffuse increase in the hyperintense signal of the subcortical white matter of the bilateral cerebral and cerebellar hemispheres on T2-weighted images, probably due to the presence of granuloma as a response to the antigens released by the death of the parasite [14, 15].

The standard treatment for EM caused by *A. cantonensis* infection has been controversial [16]. Angiostrongyliasis is usually treated with albendazole. An adrenal cortical hormone combined with dehydration and neurotrophic therapy can also be used. Combined therapy with albendazole and dexamethasone has also been shown to be effective [17]. Sometimes

there was no difference in the duration or severity of illness in patients treated with analgesics alone, analgesics and glucocorticosteroids, or analgesics and antibiotics [4]. Most patients in the Hospital for Tropical Diseases (Ho Chi Minh City, Vietnam) were treated with a combination of albendazole and corticosteroids, but there is no definitive evidence for the use of anti-helminthic agents. Chotmongkol et al. [18] found no additional benefit of 14 days of albendazole plus prednisolone as compared to prednisolone alone in reducing the duration of headache in EM; however, this study did not reach the planned sample size. Adequately powered randomized controlled trials are needed to guide the optimal management of EM.

Regarding treatment outcomes, the duration of headache in children seemed to be shorter, but a higher proportion required repeated lumbar puncture. This may imply that children with EM may resolve more quickly than adults despite having more severe systemic responses, as discussed earlier. Children with EM, however, needed more frequent reduction of intracranial pressure by repeated lumbar puncture than did adult patients. Our patient was completely recovered after 1 week of treatment.

Having a history of eating raw freshwater snails is an important risk factor for angiostrongyliasis, yet was found in only 68.4% of pediatric patients compared to almost 100% of adult patients [19]. Other than eating, direct contact with snails and slugs may be another risk factor for EM in children. A report from Taiwan showed that having snails as a pet was another route of infection [6].

In conclusion, the clinical features and outcomes of EM caused by *A. cantonensis* in children were different from those in adult patients. We were able to diagnose and successfully treat a patient with EM caused by *A. cantonensis* based on clinical signs and his eating habits. The management of the patient was effective.

Statement of Ethics

This study was approved by the Ethics Committee Board of Hue Central Hospital. The authors confirm obtaining written consent from the patient's parents for publication of the manuscript.

Conflict of Interest Statement

The authors declare no financial disclosures or conflicts of interest.

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Author Contributions

H.T. Phan and H.S. Nguyen carried out and confirmed the diagnosis, provided the details of the case, and contributed to the design of the report. H.S. Nguyen drafted the manuscript. All authors read and approved the final version of the manuscript.

References

- 1 Fellner A, Hellmann MA, Kolianov V, Bishara J. A non-travel related case of *Angiostrongylus cantonensis* eosinophilic meningomyelitis acquired in Israel. *J Neurol Sci*. 2016 Nov;370:241–3.
- 2 Foster CE, Nicholson EG, Chun AC, Gharfeh M, Anvari S, Seeborg FO, et al. *Angiostrongylus cantonensis* Infection: A Cause of Fever of Unknown Origin in Pediatric Patients. *Clin Infect Dis*. 2016 Dec;63(11):1475–8.
- 3 Qvarnstrom Y, Xayavong M, da Silva AC, Park SY, Whelen AC, Calimlim PS, et al. Real-Time Polymerase Chain Reaction Detection of *Angiostrongylus cantonensis* DNA in Cerebrospinal Fluid from Patients with Eosinophilic Meningitis. *Am J Trop Med Hyg*. 2016 Jan;94(1):176–81.
- 4 Sawanyawisuth K, Sawanyawisuth K. Treatment of angiostrongyliasis. *Trans R Soc Trop Med Hyg*. 2008 Oct;102(10):990–6.
- 5 Ramirez-Avila L, Slome S, Schuster FL, Gavali S, Schantz PM, Sejvar J, et al. Eosinophilic meningitis due to *Angiostrongylus* and *Gnathostoma* species. *Clin Infect Dis*. 2009 Feb;48(3):322–7.
- 6 Sawanyawisuth K, Chindaprasirt J, Senthong V, Limpawattana P, Auvichayapat N, Tassniyom S, et al. Clinical manifestations of Eosinophilic meningitis due to infection with *Angiostrongylus cantonensis* in children. *Korean J Parasitol*. 2013 Dec;51(6):735–8.
- 7 Tseng YT, Tsai HC, Sy CL, Lee SS, Wann SR, Wang YH, et al. Clinical manifestations of eosinophilic meningitis caused by *Angiostrongylus cantonensis*: 18 years' experience in a medical center in southern Taiwan. *J Microbiol Immunol Infect*. 2011 Oct;44(5):382–9.
- 8 Sawanyawisuth K, Sawanyawisuth K, Senthong V, Limpawattana P, Intapan PM, Tiamkao S, et al. Peripheral eosinophilia as an indicator of meningitic angiostrongyliasis in exposed individuals. *Mem Inst Oswaldo Cruz*. 2010 Nov;105(7):942–4.
- 9 van de Beek D, Cabellos C, Dzupova O, Esposito S, Klein M, Kloek AT, et al. ESCMID guideline: diagnosis and treatment of acute bacterial meningitis. *Clin Microbiol Infect*. 2016 May;22 Suppl 3:S37–62.
- 10 Wang QP, Lai DH, Zhu XQ, Chen XG, Lun ZR. Human angiostrongyliasis. *Lancet Infect Dis*. 2008 Oct;8(10):621–30.
- 11 Hwang KP, Chen ER. Clinical studies on angiostrongyliasis *cantonensis* among children in Taiwan. *Southeast Asian J Trop Med Public Health*. 1991 Dec;22 Suppl:194–9.
- 12 Espírito-Santo MC, Pinto PL, Mota DJ, Gryscek RC. The first case of *Angiostrongylus cantonensis* eosinophilic meningitis diagnosed in the city of São Paulo, Brazil. *Rev Inst Med Trop São Paulo*. 2013 Mar-Apr;55(2):129–32.
- 13 Lee IC. *Angiostrongylus cantonensis* meningitis in two developmentally delayed children: findings in brain images. *Pediatr Infect Dis J*. 2010 Jan;29(1):90–1.
- 14 Jin EH, Ma Q, Ma DQ, He W, Ji AP, Yin CH. Magnetic resonance imaging of eosinophilic meningoencephalitis caused by *Angiostrongylus cantonensis* following eating freshwater snails. *Chin Med J (Engl)*. 2008 Jan;121(1):67–72.
- 15 Tsai HC, Tseng YT, Yen CM, Chen ER, Sy CL, Lee SS, et al. Brain magnetic resonance imaging abnormalities in eosinophilic meningitis caused by *Angiostrongylus cantonensis* infection. *Vector Borne Zoonotic Dis*. 2012 Feb;12(2):161–6.
- 16 Tsai HC, Lai PH, Sy CL, Lee SS, Yen CM, Wann SR, et al. Encephalitis caused by *Angiostrongylus cantonensis* after eating raw frogs mixed with wine as a health supplement. *Intern Med*. 2011;50(7):771–4.
- 17 Diao Z, Chen X, Yin C, Wang J, Qi H, Ji A. *Angiostrongylus cantonensis*: effect of combination therapy with albendazole and dexamethasone on Th cytokine gene expression in PBMC from patients with eosinophilic meningitis. *Exp Parasitol*. 2009 Sep;123(1):1–5.
- 18 Chotmongkol V, Kittimongkolma S, Niwattayakul K, Intapan PM, Thavornpitak Y. Comparison of prednisolone plus albendazole with prednisolone alone for treatment of patients with eosinophilic meningitis. *Am J Trop Med Hyg*. 2009 Sep;81(3):443–5.

- 19 Li YC, Hu XM, Tong CJ, Liu J, Li MT, Wang SQ. Investigation on serology, risk factor and awareness of *angiostrongylus cantonensis* in Hainan province [in Chinese]. *Zhongguo Ji Sheng Chong Xue Yu Ji Sheng Chong Bing Za Zhi*. 2011 Feb;29(1):74–5.

Table 1. Biochemical and cytologic analysis of the patient’s CSF and hematological analysis

Date	Biochemical and cytologic analysis of CSF						Hematological analysis			
	WBC (0–8)	Lym., % (0)	NE, % (0)	EO, % (0)	Pro., g/L (0.15–0.45)	Glu, mmol/L (2.5–4.5)	WBC, ×10 ⁹ /L (4–10)	NE, % (50–70)	Lym., % (10–50)	EO, % (0.5–5)
3/23/2019	468	35	65		0.63		5.45	55.5	29.6	5.1
4/3/2019	750	90	10		0.75	2.2	8.84	34.6	42.9	8.5
4/5/2019	739	10	5	85	0.73					
4/9/2019	361		62	15						
5/8/2019	5	60	40	0						

Values in parentheses denote normal range. CSF, cerebrospinal fluid; WBC, white blood cells; Lym., lymphocytes; NE, neutrophils; EO, eosinophils; Pro., protein; Glu, glucose.