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ORIGINAL ARTICLE

Clinical manifestations of eosinophilic meningitis caused by *Angiostrongylus cantonensis*: 18 years' experience in a medical center in southern Taiwan

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Angiostrongylus cantonensis;
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Background: With the improvement of public health, eosinophilic meningitis associated with *Angiostrongylus cantonensis* infection is now seldom reported in Taiwan. Eosinophilic meningitis typically occurred sporadically in children. This study aims to analyze the clinical manifestations and change in the contemporary epidemiology of eosinophilic meningitis in Taiwan.
Methods: This is a retrospective study of patients diagnosed with eosinophilic meningitis at Kaohsiung Veterans General Hospital, from December 1991 to September 2009. The demographic characteristics, clinical presentations, laboratory data, radiographic imaging, and treatment and clinical outcome were analyzed. A PubMed search with the keywords of eosinophilic meningitis, *A cantonensis*, and Taiwan was performed to retrieve cases of eosinophilic meningitis caused by *A cantonensis* since 1960.
Results: Thirty-seven patients were diagnosed to have eosinophilic meningitis during a period of 18 years. The median age was 32 years (range, 2–80 years). Ninety five percent (35/37) of the patients were adults. The median incubation period was 10.5 days (range, 3–80 days). Most of the patients presented with headache (29, 78%), fever (25, 68%), and 11(30%) had hyperesthesia. Patients with hyperesthesia had longer incubation period (55 *vs.* 7 days, $p = 0.004$), lower serum immunoglobulin E levels (127.5 *vs.* 1295 IU/mL, $p < 0.001$), and longer duration between symptom onset and spinal taps (14 *vs.* 5 days, $p = 0.011$). Three patients presented initially with lymphocytic meningitis, and eosinophilia only appeared on a second

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lumbar puncture. Magnetic resonance imaging of the brain disclosed leptomeningeal enhancement (17/26, 65%) and increased signal intensity (10/26, 38%) on T2-weighted and fluid-attenuated inversion recovery images. There were eight relapses and two patients died. No sequela was noted except in one 2-year-old toddler, who had weakness of both lower limbs.
Conclusions: The epidemiology of eosinophilic meningitis has changed during the past two decades in Taiwan and occurs mainly in adults in the setting of outbreaks. Hyperesthesia; repeated lumbar puncture in cases with lymphocytic meningitis of uncertain cause; and a detailed history, including food consumption, are important to establish an accurate diagnosis.

Introduction

Angiostrongylus cantonensis, the rat lungworm, is the most common infectious agent of eosinophilic meningitis worldwide.[1] Humans become infected by ingesting the intermediate hosts or a variety of paratenic hosts of *A cantonensis*, such as raw mollusks, prawns, crabs, frogs, or fish.[2,3] The major intermediate hosts in Taiwan are the African giant snail (*Achutina fulica*) and the golden apple snail (*Ampullarium canaliculatus*).[4,5] Human infections are often self-limited within weeks but may have severe headache initially.[6] Since the first human infection was reported in Taiwan in 1945,[7] there have been many cases reported and mainly in children.[8,9] Most of them were reported two to three decades ago. In 1998 and 1999, we reported two outbreaks of eosinophilic meningitis caused by *A cantonensis* infection among 17 adult male Thai laborers who had eaten raw golden apple snails.[10] Another outbreak of among family members associated with a health drink consisting of raw vegetable juice was reported in 2001.[11]

With the improvement of public health, there has been no recent large series case report in Taiwan. Therefore, this study aimed to describe the contemporary epidemiology of eosinophilic meningitis caused by *A cantonensis* in southern Taiwan during the past two decades, including the demographic characteristics, clinical manifestations, laboratory and radiological findings, and treatment and clinical outcome. A review of the literatures was performed for comparison with cases of eosinophilic meningitis because of *A cantonensis*.

Methods

Patients

We retrospectively reviewed the medical records of patients diagnosed as having eosinophilic meningitis at the Kaohsiung Veterans General Hospital, Kaohsiung, Taiwan, during a period of 18 years (from December 1991 to September 2009). The clinical definition of eosinophilic meningitis was an acute onset of headache and eosinophilia in the blood or cerebrospinal fluid (CSF) accompanied by at least of one of the following symptoms: fever, ataxia, visual disturbances, photophobia, nuchal rigidity, neck pain, hyperesthesia, or paresthesia.[12] Eosinophilic pleocytosis was defined as the presence of $\geqq$10 eosinophils/μL in the CSF or at least 10% eosinophils in the total CSF leukocyte count.[13] Peripheral blood eosinophilia was defined as an increase in the percentage of peripheral blood eosinophils to more than 10%. Data collected included sex, age, risk behaviors, incubation period, clinical manifestations, laboratory values, radiographic studies, and treatment and clinical outcomes. Eating raw snails, salads, and uncooked vegetables were considered as risk factors for eosinophilic meningitis. A definite diagnosis of eosinophilic meningitis caused by *A cantonensis* was established by detection of larvae of *A cantonensis* in the CSF. Clinical presumptive diagnosis was made by clinical symptoms of meningitis with eosinophilia; presence of risk factors, such as history of raw snail ingestion; and serological evidence of antibodies to *A cantonensis* in serum or CSF. The incubation period was defined as the duration between exposure to risk factors and the onset of symptoms (headache, fever, and so on). Relapse was defined as readmission because of recurrent headache, fever, or other associated symptoms after days of being symptom free. Every patient underwent at least one spinal tap. CSF analysis included cell counts, glucose and protein levels, Gram and acid-fast stains, India ink smear, wet mount preparations for detection of larvae, and detection of cryptococcal antigen. Cultures were obtained for bacteria, mycobacteria, fungi, and viruses. Blood tests included complete blood cells count, serum levels of creatinine, aminotransferases, creatinine phosphokinases, immunoglobulin E (IgE), and indirect hemagglutination test for amoeba. Antibodies to *A cantonensis* were detected in the serum and CSF by a micro-enzyme-linked immunosorbent assay using young-adult worm antigen, molecular weight 204 kD, purified by monoclonal antibody.[14] Stool was examined for ova, amoebic trophozoites, and parasites.

Radiographic studies included chest radiography, liver and spleen sonography, brain computed tomography, or brain magnetic resonance imaging (MRI).

A PubMed literature review with the key words of eosinophilic meningitis, *A cantonensis* with or without Taiwan was performed to retrieve the cases diagnosed to have eosinophilic meningitis caused by *A cantonensis* since 1960.

Statistical analysis

All of the continuous variables were expressed by median and range. The correlations between clinical manifestations and laboratory or CSF parameters were analyzed by Mann-Whitney *U* test. A *p* value of less than 0.05 was considered statistically significant.

Results

There were 37 patients diagnosed to have eosinophilic meningitis caused by *A cantonensis* infection during the 18-year period. These patients included two outbreaks among 17 Thai labors who had eaten golden apple snails in 1998 and 1999[10] and one outbreak among five people of the same family who had drunken raw vegetable juice in 2001.[11] Most patients were men (30/37, 81%). The median age was 32 years (range, 2—80 years). Only two patients were children, aged 2 and 3 years, respectively. Eighty-one percent (30/37) of the patients had identifiable risk factors before the onset of meningitis. The median incubation period was 10.5 days (range, 3—80 days).

Table 1 Characteristics of clinical manifestations, laboratory data, and imaging findings in our patients with eosinophilic meningitis

Variables	
Age (yr)[a]	32 (2—80)
Children (≦18-yr-old), *n* (%)	2 (5)
Adult (>18-yr-old), *n* (%)	35 (95)
Sex, *n* (%)	
Male	30 (81)
Female	7 (19)
Risk factors (*n*)	
Raw snails	22
Raw vegetable juice	7
Raw frog	1
Not identified	7
Incubation period (d)[a]	10.5 (3—80)
Clinical manifestations, *n* (%)	
Symptoms	
Headache	29 (78)
Fever	25 (68)
Neck stiffness	17 (46)
Nausea/vomiting	16 (43)
Muscle weakness	15 (41)
Orbital/retro-orbital pain	7 (19)
Abdominal pain	9 (24)
Dizziness	8 (22)
Signs	
Conscious disturbance	9 (24)
Stiff neck	15 (41)
Brudzinski's sign	12 (32)
Hyperesthesia	11 (30)
Facial palsy	1 (3)
Paralysis of the extraocular muscles	4 (11)
Laboratory data[a]	
White blood cell ($\times 10^3/\mu L$)	8.93 (4.5—25.42)
Eosinophil (%)	13.00 (0—69)
IgE (IU/mL)	1074.00 (5—6,727)
CSF white blood cell (/μL)	455.00 (0—1,660)
CSF eosinophil (%)	16.00 (0—73)
CSF eosinophil count (/μL)	60.90 (0—457)
CSF protein (mg/dL)	95.00 (27—347)
CSF/plasma glucose ratio (%)	50.00 (34—77)
MRI of brain (*n*)	26
Leptomeningeal enhancement in postcontrast studies	17
Increased signal intensity at the subcortical white matter of bilateral cerebral or cerebellar hemisphere on T2-weighted and FLAIR images	10
High signal over bilateral Globus pallidus on T1-weighted images	8
Normal	4

[a] Median (range).

CSF = cerebrospinal fluid; FLAIR = fluid-attenuated inversion recovery; IgE = immunoglobulin E; MRI = magnetic resonance imaging.

Table 2 The correlations between clinical manifestations and laboratory studies

Parameter[a]	Hyperesthesia			Brudzinski's sign		
	With ($n = 6$)	Without ($n = 13$)	p	With ($n = 7$)	Without ($n = 12$)	p
Intubation (d)	55 (7–76)	7 (3–80)	0.004[c]	7.0 (3–10)	26.5 (6–80)	<0.001[c]
White blood cell ($\times 10^3/\mu L$)	7.39 (5.14–12.67)	8.84 (5.37–25.42)	0.460	8.84 (5.14–12.13)	8.18 (5.37–25.42)	0.192
Eosinophil (%)	17 (5–21)	13 (0–69)	0.416	24 (0–40)	12 (1–69)	0.037[c]
Eosinophil ($/\mu L$)	1,341 (283–2,534)	1,340 (0–17,540)	0.398	2,246 (0–3,360)	984.5 (54–17,540)	0.048[c]
IgE (IU/mL)	127.5 (5–507)	1,295 (319–6,727)	<0.001[c]	1,295 (319–6,154)	590 (5–6,727)	0.411
Duration between onset of symptoms and spinal tap (d)	14 (3–14)	5 (2–22)	0.011[c]	3 (2–7)	13.5 (3–22)	<0.001[c]
CSF white blood cell ($/\mu L$)	620 (455–930)	210 (0–1,660)	0.312	720 (210–1,660)	307.5 (0–1,390)	0.011[c]
CSF eosinophil (%)	23 (0–73)	4 (0–50)	0.159	6 (4–50)	3 (0–73)	0.387
CSF eosinophil ($/\mu L$)	140.5 (0–383)	9.6 (0–457)	0.268	46.5 (10–457)	4.2 (0–383)	0.149
Open pressure on spinal tap (mmH_2O)	212.5 (160–250)	166 (110–270)	0.227	190 (165–270)	165.5 (110–250)	0.241
CSF protein (mg/dL)	114 (7–76)	70 (27–347)	0.606	92 (54–347)	91.5 (27–296)	0.930
CSF glucose (mg/dL)	44.5 (41–50)	59 (36–77)	0.004[c]	50 (36–77)	49 (41–75)	0.707
CSF/plasma glucose ratio (%)	43.3 (40.2–48.1)	62.5 (28.1–93.3)	0.090	46.5 (37.2–68.8)	44.2 (28.1–93.3)	0.787

Repeated spinal tap[b]			Relapse		
With ($n = 4$)	Without ($n = 15$)	p	With ($n = 2$)	Without ($n = 15$)	p
7.5 (3–10)	11 (6–80)	0.191	11.00 (3–76)	9.50 (6–80)	0.820
9.77 (7.56–12.13)	8.64 (5.14–25.42)	0.805	8.75 (5.65–13.05)	8.74 (5.14–25.42)	0.693
18.5 (0–27)	14 (1–69)	0.798	21.0 (3–40)	11.5 (0–69)	0.165
1,954 (0–3,275)	1,126 (54–17,540)	0.918	1,838 (200–3,360)	1,233 (0–17,540)	0.299
1,414.5 (428–6,154)	543 (5–6,727)	0.477	802 (52–2,241)	590 (5–6,727)	0.383
3.5 (2–7)	11 (3–22)	0.297	7 (3–14)	6 (2–22)	0.556
598.5 (210–1,660)	455 (0–1,390)	0.588	720 (0–1,390)	225 (0–1,660)	0.017[c]
7 (4–50)	5 (0–73)	0.192	30 (0–73)	4.5 (0–50)	0.112
64.2 (17–239)	9.6 (0–457)	0.411	236 (0–457)	9 (0–239)	0.005[c]
170 (165–190)	190 (110–270)	0.801	190 (160–270)	170 (110–250)	1.000
74 (54–347)	92 (27–296)	0.769	122 (27–201)	85 (36–347)	0.423
51 (45–71)	50 (36–77)	0.842	45.0 (36–70)	52.5 (41–77)	0.372
44.3 (37.2–62.5)	44.4 (28.1–93.3)	0.887	44.4 (38.3–9.33)	46.1 (28.1–78.6)	0.667

[a] Median (range).
[b] Patients who needed repeated spinal tap for symptomatic relief, such as severe headache.
[c] A p value less than 0.05.
CSF = cerebrospinal fluid; IgE = immunoglobulin E.

Clinical characteristics

The clinical manifestations are described in Table 1. Most of the patients presented with headache (29 patients, 78%) combined with a variety of other signs and symptoms. Twenty-five patients (68%) were febrile during initial presentation. Nine patients presented with altered sensorium (drowsy or comatose) and two of these patients subsequently died. Eleven patients (30%) had hyperesthesia with impaired sensation to pain and light touch. One patient had facial palsy and four patients had paralysis of the extraocular movement. The hyperesthesia, facial palsy, and extraocular muscle paralysis resolved spontaneously with time.

Laboratory manifestations

About one-half of our patients had elevated white blood cell count and most patients (25 patients, 68%) had peripheral blood eosinophilia. The CSF was cloudy with rice water appearance in seven patients. CSF eosinophilia was noted in 26 patients (70%) and elevated protein level in 32 patients (86.5%). Three patients (8%) presented with lymphocytic pleocytosis initially but repeat spinal tap disclosed an eosinophilic pleocytosis. Larvae of *A cantonensis* were found under direct examination of CSF in three patients.

The serum antibodies to *A cantonensis* were detected in 30 of 31 patients tested. The CSF antibody was positive in 17 of 30 patients. Serum IgE level were elevated in 19 (51%) patients. Increased serum levels of creatine kinase and lactate dehydrogenase were also detected in 14 and 11 patients. Hepatic enzymes (glutamic oxaloacetic transaminase and glutamic pyruvic transaminase) were mildly elevated in nine patients. Results of indirect hemagglutination for *Entamoeba histolytica*; cryptococcal antigen in CSF; and stool examination for amoeba, ova, and parasites were negative.

Radiographic studies

Chest radiography showed no specific abnormality in 23 of 31 patients. Four patients had pleural thickness over unilateral or bilateral apical area, two had increased infiltration over bilateral medial and lower lung, one had increased infiltration on the left lower lung, and one had diffused reticulonodular interstitial infiltration on both lungs. Sonography of the liver and spleen disclosed fatty liver in three patients, presence of hepatic hemangioma in one, and hepatic masses in another patient, which was later diagnosed to be hepatocellular carcinoma. No hepatic parenchymal lesions were seen in the rest of the patients. No splenomegaly was detected in all patients.

Computed tomography scan of brain was abnormal in 6 of 19 patients. One patient aged 2 years had diffuse brain swelling and bilateral cerebral hemisphere leptomeningeal contrast enhancement. Leptomeningeal contrast enhancement was also observed in two other patients. Three patients had old cerebral infarction. Mild ventricular dilation was seen in three patients and was considered to be related to aging process or brain atrophy.

MRI of brain was performed in 26 patients and described in Table 1. Leptomeningeal enhancement was the most frequent finding in MRI (17/26 patients). Increased signal intensity at the subcortical white matter of bilateral cerebral or cerebellar hemisphere on T2-weighted and fluid-attenuated inversion recovery images was seen in 10 patients.

Clinical course and response to therapy

There were 26 patients who received corticosteroid equivalent to prednisolone 0.5—1.0 mg/kg/d and the median duration was 15 days (range, 1—30 days). Twelve patients had received anthelminthic treatment. Mebendazole was administered at a dose of 100 mg twice a day in nine patients for median duration of 6 days (range, 3—12 days). The other three patients all received levamisole for 3 weeks. However, the use of corticosteroid or anthelminthic did not shorten the duration of hospitalization and illness. Neither were these treatment associated with a decreased death nor relapse rate. The median duration of illness was 20 days (range, 0—90 days). There were eight relapses because of recurrent headache. Their headaches were relieved dramatically after lumbar puncture. No sequela was noted except in one 2-year-old toddler who needed sustained rehabilitation because of weakness of both lower limbs.

Correlations between clinical manifestations and laboratory studies

Laboratory parameters were analyzed and presented in Table 2. The presence of hyperesthesia was associated with a longer incubation period, lower serum IgE levels, and longer duration between onset of symptoms and spinal tap. Those patients who presented with a positive Brudzinski's sign were likely to have shorter incubation periods, higher eosinophil counts in the peripheral blood, shorter duration between onset of symptoms and spinal tap, and higher white blood cells in the CSF. During univariable analysis, relapse was associated with higher initial white blood cells in the CSF, reflecting a more severe central nervous system infection process in those patients who experienced relapse.

Literature review

The PubMed search of English language literature or literature in Chinese with English abstract since 1960 for cases series with eosinophilic meningitis caused by *A cantonensis* was performed and included the following individual search terms: eosinophilic meningitis and *A cantonensis*. There were three large case series and described with the present study in Table 3. In Taiwan, the cases with eosinophilic meningitis caused by *A cantonensis* were children in the past three to four decades and adults in the past two decades.

Discussion

Our study showed that the epidemiology of eosinophilic meningitis caused by *A cantonensis* infection has changed during these 4 decades. Most of the reported cases and our patients were adults. We also found that an initial

Table 3 Clinical characteristics in four series of patients with eosinophilic meningitis caused by *Angiostrongylus cantonensis*

Characteristics	Taiwan			Thailand
	Yii[a],[4]	Hwang[18]	Present study	Punyagupta et al.[19]
Number of patients	125	87	37	484
Study period (A.D.)	1968–1969	1976–1991	1991–2009	1965–1968
Age group				
0–9-yr-old, *n* (%)	88 (70)	70 (80)	2 (5)	18 (4)
10–19-yr-old, *n* (%)	18 (14)	17 (20)	0 (0)	73 (15)
>20-year-old, *n* (%)	14 (11)	0 (0)	35 (95)	393 (81)
Unknown	5 (4)	0 (0)	0 (0)	0(0)
Death, *n* (%)	4 (3)	4 (5)	2 (5)	1 (<1)
Incubation period (days, mean) (range)	NR	13.0(2–45)	22.6 (3–80)	17 (2–34)
Clinical manifestations, *n* (%)				
Headache	98 (86)	51 (59)	29 (78)	477 (98)
Fever	91 (80)	80 (92)	25 (68)	177 (37)
Neck stiffness	45 (40)	69 (79)	17 (46)	312 (64)
Muscle weakness	19 (17)	19 (22)	15 (41)	4 (1)
Brudzinski's sign/Kernig's sign	50 (44)	41 (47)	12 (32)	27 (6)
Hyperesthesia/paresthesia	32 (28)	4 (5)	11 (30)	181 (37)
Facial palsy	1 (1)	9 (10)	1 (3)	20 (4)
Paralysis of the extraocular muscles	9 (8)	5 (6)	4 (11)	16 (3)
Laboratory data[b]				
Range of white blood cell ($\times 10^3/\mu L$)	5.75–35.25	NR	4.5–25.42	NR
Patients with WBC > $10.0\times 10^3/\mu L$[b]	NR	73 (84%)	17 (50%)	NR (56%)
Percentage of patients with peripheral-blood eosinophilia	100	85	68	73
Range of CSF white blood cell (/μL)	46–4,354	NR	0–1,660	500–2,000
Percentage of patients with CSF eosinophilia (criterion)	98 (>10%)	91 (>10%)	54 (≧10%)	96 (>10%)
Percentage of patients with elevated CSF protein (criterion)	NR	61 (>45 mg/dL)	89 (>45 mg/dL)	68 (>50 mg/dL)

[a] Further clinical manifestation were collected in 114 patients.
[b] Number (percent).
CSF = cerebrospinal fluid; NR = not reported.

lymphocytic pleocytosis in the CSF may turn out to be eosinophilic meningitis, and a correct diagnosis can only be made by a detailed history and a second lumbar puncture.

Eosinophilic meningitis is more common in Southeast Asia and Pacific regions than in Western countries. The most common infection is caused by *A cantonensis*, found principally in Southeast Asia and Pacific Islands but now worldwide because of ship-borne migration of rats.[15] *A cantonensis* is now capable of completing its complex life cycle almost anywhere because giant African land snails, most indigenous snail and slug species, can serve as competent intermediate hosts.[16] Other helminthic infections that can cause eosinophilic meningitis include cysticercosis, schistosomiasis, paragonimiasis, and echinococcosis. *Gnathostoma spinigerum*, another common cause of eosinophilic meningitis that has never been reported in Taiwan, causes more severe clinical presentation of eosinophilic myeloencephalitis that may result in nerve root pain, paralysis of an extremity, and subarachnoid hemorrhage associated with visceral and cutaneous larvae migrans.[17] Most of our patients (31/37) had detectable antibodies to *A cantonensis* in serum and/or CSF. Four out of the remaining six patients had a history of raw snails or uncooked vegetable intake. The last two patients were diagnosed as cases of *A cantonensis* infection according to the clinical presentation.

Previously, most cases of *A cantonensis* associated eosinophilic meningitis reported in Taiwan were in children exposed to the African giant snail (*Achutina fulica*), during playing with or by eating snails or slugs.[4,9,18] In Thailand, *A cantonensis* usually infect men in the third and fourth decades of life.[19] In contrast to the previous studies in Taiwan,[8,18] most of our patients were adults, which were similar to the cases in Thailand. The decreased case numbers in children may be related to the urbanization and improvement of public health in Taiwan in recent decades, leading to less frequent exposure of children to snails and other intermediates (Table 3).

The illness was characterized by severe headache in our patients, which were similar to the previous reports.[13,19] There were 25 patients (68%) presenting with fever, which were higher than the report from Thailand (37%)[19] but lower than previous study in Taiwan (Table 3). The rate of fever tended to higher in young patients, although not reaching statistical significance. Interestingly, paresthesia/hyperesthesia, a symptom seldom reported in bacterial, tuberculous, cryptococcal, and aseptic meningitis,

occurred in 11 of our patients (30%). The exact mechanism was unclear and may be associated with an immune reaction to or neuron root invasion of *A cantonensis*. An association of hyperesthesia with longer incubation periods and duration between symptom onset and spinal tap (Table 2) was noted. One possible explanation for this finding is that prolonged inflammation of the neural root may be required for hyperesthesia to develop. A positive Brudzinski's sign was associated with higher peripheral blood eosinophils and pleocytosis and shorter incubation period (Table 2). This implies more severe central nervous system inflammation, resulting in meningeal irritation and a shorter incubation time. However, further studies in animals and humans are needed to confirm this hypothesis.

A cantonensis eosinophilic meningitis usually resolves spontaneously and is rarely fatal. There were two fatal cases in our study and both presented with drowsiness initially. The case mortality rate was 5% in our series, which was similar to the previous studies in Taiwan (Table 3). The disease is much more serious in children.[4,18] It is possible that higher worm load is relative to body size. The mortality rate was lower in Thailand (<1%).[19] However, all the cases may not be caused by *A cantonensis*.

Eosinophilic pleocytosis in the CSF was the typical laboratory abnormality but not always present initially. Three patients presented with lymphocytic pleocytosis, which became eosinophilic on a second lumbar puncture. Therefore, the absence of initial eosinophilic pleocytosis cannot rule out the possibility of eosinophilic meningitis. A detailed history of risk factors and a second lumbar puncture of lymphocytic meningitis of uncertain cause is crucial for an accurate diagnosis.

Imaging of the brain may aid to distinguish *A cantonensis* eosinophilic meningitis from other parasitic eosinophilic meningitis, such as gnathostomiasis or neurocysticercosis. Similar to previous studies[20–24], MRI studies revealed diffuse leptomeningeal enhancement (17/26, 65%) and hyperintense signal intensity at the subcortical white matter of bilateral cerebral or cerebellar hemisphere on T2-weighted and fluid-attenuated inversion recovery image (10/26, 38%). It was likely that the hyperintense signal intensity at the subcortical white matter was caused by the granulomatous response to the dead worms.[25] In our study, hyperintense basal ganglia abnormalities on T1-weighted MRI were seen in 8 patients.[10] This finding is relatively nonspecific[26] and not been reported in past literature.

The role of treatment with anthelminthic agents and corticosteroids remains controversial. In our study, the use of corticosteroid alone or with anthelminthic agents did not decrease the duration of illness. It was believed that corticosteroid therapy was able to decrease duration of headache in the randomized double-blind placebo-controlled studies in Thailand.[27] In another study, Sawanyawisuth et al.[28] and others showed a shorter course (one week) of corticosteroid had the same beneficial effect in relieving headaches as a 2-week course. Anthelminthic agents were not recommended because of possibility of exacerbating symptoms resulting from inflammatory responses because of the death of larvae in isolated reports or experimental infection studies.[29–31] In the other hand, a recent randomized trial showed that albendazole alone can reduce the duration of headache.[32] An observational clinical study in Taiwan also showed good results with albendazole and levamisole in the treatment of children with eosinophilic meningitis.[9,18] *A cantonensis* eosinophilic meningitis responds well to conservative treatment, such as repeated lumbar puncture or analgesics, in most patients.[33]

The limitations of our study included a small sample size and the retrospective study design. Most of our patients (22/37, 59%) were from outbreaks that may result in selective bias. All the cases of eosinophilic meningitis reported in Thailand[19] may not be caused by *A cantonensis*, however. Relapse was limited to readmission cases and some of the cases might not detectable after discharge.

In summary, *A cantonensis* eosinophilic meningitis was a self-limited disease and responded well to conservative treatment. The epidemiology of eosinophilic meningitis in Taiwan has changed over the past two decades, possibly related to improved public health and urbanization. Eosinophilic meningitis cannot be excluded despite the initial absence of eosinophilia in the CSF. A detailed history of food consumption, laboratory tests, and a second lumbar puncture are important to establish an accurate diagnosis.

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