Eosinophilic Meningitis
Due to *Angiostrongylus cantonensis*
in a Returned Traveler: Case Report
and Review of the Literature

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**Angiostrongylus cantonensis**, the rat lungworm, is the prin-
cipal cause of eosinophilic meningitis worldwide, and the
increase in world travel and shipborne dispersal of infected
rat vectors has extended this parasite to regions outside of
its traditional geographic boundaries. We report a case of
eosinophilic meningitis due to *A. cantonensis* in a patient
who recently returned from a trip in the Pacific.

Eosinophilic pleocytosis in the CSF is an uncommon finding
that most often results from helminthic infection of the CNS
[1]. *Angiostrongylus cantonensis*, the nematode lungworm in
rats, is the principal cause of eosinophilic meningitis worldwide
[2]. It occurs predominantly in Southeast Asia and throughout
the Pacific basin [3]. However, with the increase in world travel
and the shipborne dispersal of infected rats, the parasite has
been extending its range [4]. Cases of *A. cantonensis* infection
have been reported in Australia [5] and, more recently, in North
America [6]. Although the parasite has begun to garner atten-
tion as an emerging infectious disease, clinical awareness re-
mains low. The diagnosis should always be considered for a
patient with subacute meningitis, particularly if there is CSF
eosinophilia or if the patient has traveled to an area of endem-
icity. We report a case of eosinophilic meningitis due to *A.
cantonensis* in a traveler who had recently returned from a trip
to the Pacific basin.

**Case report.** A 37-year-old woman presented to our hos-
pital with a 4-week history of severe headaches, paresthesias,
and diminished hearing in her left ear. The patient was pre-
viously healthy and had spent the past 5 years sailing around
the Pacific basin, traveling between islands in the Tongan ar-
chipelago. She initially developed a severe headache associated
with photophobia and migratory, burning paresthesias over
much of her body. One week into her illness, she lost hearing
in her left ear.

The patient originally presented to an Auckland hospital in
New Zealand after 11 days of these symptoms. She was nontox-
emic in appearance and afebrile, with a blood pressure of 155/
75 mm Hg and a pulse of 70 beats/min. No nuchal rigidity was
noted. There was sensorineural hearing loss in her left ear, but
there were no other focal neurological deficits. Her WBC count
was 7100 cells/μL with 8% eosinophils. Chest radiograph findings
were normal and CT and MRI of the brain were unremarkable.
A lumbar puncture was done and revealed an opening pressure
of 21 cm H2O, 246 WBCs (1% neutrophils, 79% lymphocytes,
17% monocytes, 3% eosinophils), 2 RBCs, a CSF protein level
of 100 mg/dL, and a CSF glucose level of 36 mg/dL.

The patient's headache persisted, and a second lumbar punc-
ture performed 5 days later demonstrated an opening pressure
of 26 cm H2O, 302 WBCs (9% neutrophils, 66% lymphocytes,
9% monocytes, 16% eosinophils), and 2 RBCs. CSF culture for
bacteria yielded no growth. The findings of an evaluation for
cryptococci, mycobacteria, herpes simplex virus, and varicella-
zoster virus were normal, and the results of cytologic testing
were negative. ELISA for HIV yielded negative results. She was
discharged 8 days after presentation with a severe persistent
headache that was treated with oral tramadol, morphine, and
amitriptyline.

The patient returned to the United States and presented to
our hospital 4 weeks after her symptoms began, continuing to
complain of a severe headache. Her hearing had fully returned
in her left ear, but she had residual migratory paresthesias. The
findings of a physical examination were unremarkable, with the
exception of some limited flexion of her neck. The findings of
a second MRI of the brain were unremarkable. Repeat lumbar
puncture revealed 13 WBCs (96% lymphocytes, 2% monocytes,
2% eosinophils), 12 RBCs, a CSF glucose level of 45 mg/dL,
and a CSF protein level of 43 mg/dL.

When questioned about her activities while traveling in the
Pacific, the patient recalled that, 5 days before the onset of her
symptoms, she had eaten fresh lettuce on Tonga. Given the
presence of an eosinophilic pleocytosis in her spinal fluid and
her recent travel to an area of endemcity, infection with *A.
cantonensis* was suspected. Because no parasites were identified
in the CSF specimens, confirmation of *A. cantonensis* infection

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specimens tested negative for confirming the diagnosis of *Angiostrongylus cantonensis* and *Gnathostoma spinigerum* antigens. The initial serum sample showed little reaction to *A. cantonensis*, but the convalescent sample showed many more strongly reactive bands and demonstrated a specific band reactive to a 31-kDa antigen, confirming the diagnosis of angiostrongyliasis (figure 1). Both specimens tested negative for *G. spinigerum*, which is also endemic in this area. The patient did not receive treatment with corticosteroids or antiparasitic agents. The headache was quite persistent but gradually abated over several months. Three months after the onset of the illness, occasional paresthesias continued to be noted.

**Discussion.** *A. cantonensis*, a natural parasite of rats, is the most common cause of eosinophilic meningitis. The parasite was first described in 1935 by Chen [7], who identified the organism in rat lungs in Canton, China. It was reported to cause human disease in 1945 by Nomura and Lin [8]. *Angiostrongylus* infection occurs principally in Southeast Asia (Thailand and Malaysia, in particular) and throughout the Pacific basin, including Hawaii, Indonesia, The Philippines, Japan, and Papua New Guinea [4]. Because of shipborne intercontinental migration of rats, further dissemination of the parasite has occurred outside of these areas. *A. cantonensis* adult worms have been recovered from the pulmonary arteries of rats in New Orleans [9]. The first case of human infection in North America was reported in 1995 in a child who had eaten a raw snail [6].

*A. cantonensis* is a zoonosis that affects rats as the primary hosts [10, 11]. Sexually mature male and female worms reside in the pulmonary arteries of rats, where they lay their eggs. First-stage larvae hatch and migrate into rat feces via the trachea and the gastrointestinal tract. Snails and slugs that feed on rodent excrement serve as intermediate hosts. After ingestion by these mollusks, first-stage larvae undergo 2 molts to form infective third-stage larvae. Rats and humans become infected by consuming raw snails, vegetables contaminated with mollusk slime, or carrier hosts, such as land crabs or freshwater shrimp, that have themselves eaten infected mollusks [12]. In humans, third-stage larvae are hematogenously transported to the CNS, burrowing into neural tissue and inciting an inflammatory response [2]. The nematode does not complete its life cycle in humans and usually dies in the CNS [13]. In the rat, third-stage larvae undergo 2 further molts to become adult worms capable of reproduction. These can force their way back into the systemic venous system through the cerebral veins and settle as adult worms in the pulmonary circulation, where they lay eggs.

The signs and symptoms observed in our patient were similar to those of other proven cases. Clinical manifestations in humans usually develop ~2 to 35 days after ingestion of larvae by immunodiagnosis was sought. Acute and convalescent serum samples were sent to Bangkok (Dr. Wanpen Chaicumpa, Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand), where Western blot analyses were done against *A. cantonensis* and *G. spinigerum* antigens. The initial serum sample showed little reaction to *A. cantonensis*, but the convalescent sample showed many more strongly reactive bands and demonstrated a specific band reactive to a 31-kDa antigen, confirming the diagnosis of angiostrongyliasis (figure 1). Both specimens tested negative for *G. spinigerum*, which is also endemic in this area. The patient did not receive treatment with corticosteroids or antiparasitic agents. The headache was quite persistent but gradually abated over several months. Three months after the onset of the illness, occasional paresthesias continued to be noted.

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Concomitant peripheral blood eosinophilia (elevated, and the CSF glucose level is usually normal [14, 15]. was seen in our patient. CSF protein levels are often slightly dominant cellular element, especially during convalescence, as the range of 20%–70% [15]. Lymphocytes are the other predominant cellular element, especially during convalescence, as was seen in our patient. CSF protein levels are often slightly elevated, and the CSF glucose level is usually normal [14, 15]. Concomitant peripheral blood eosinophilia (≥3%) is found in at least two-thirds of patients [18]. The absence of focal lesions on CT or MRI of the brain helps distinguish A. cantonensis meningitis from other CNS helminthic infections [2].

Definitive diagnosis is obtained by the demonstration of worms in the CSF or other tissues [10]. Larvae are infrequently seen in CSF specimens [19]. Brain biopsies are rarely necessary, and most patients improve completely, so identifying the larvae in necropsy specimens is very uncommon. Because the detection of worms is so unusual, immunologic techniques have been developed to confirm a presumptive diagnosis. Several serological tests based on the ELISA have been used, although none are commercially available [20, 21]. This method requires A. cantonensis antigens prepared from larvae or young adults. The detection of serum antibody has been found to be more sensitive than detection of CSF antibody [21]. Western blot analysis has also been used to detect antibodies to A. cantonensis. Nuamtanong [22] found that the reaction of serum antibodies to the 31-kDa antigen of A. cantonensis provided a more specific immunodiagnosis of angiostrongyliasis, and this was the technique used for confirming infection in our patient. The application of monoclonal antibody technology has recently been proposed for the detection of specific A. cantonensis antigens in serum and CSF specimens [23]. Further studies need to be done to confirm the suitability of this method in the identification of A. cantonensis infection.

There is no proven specific therapy for angiostrongyliasis in humans. Treatment consists primarily of supportive measures aimed at reducing headaches and preventing volume depletion. There are several reports in which repeated lumbar puncture provided symptomatic relief for patients with persistent headaches caused by increased intracranial pressure [24, 25]. Our patient benefited from this intervention. Punyagupta et al. [14] compared the use of analgesics, prednisone (30–60 mg per day for 5 days), and antibiotics (parenteral penicillin, 2.4–3.6 million units per day, or tetracycline, 2 g per day) in the treatment of acute A. cantonensis infections. None of these therapies was found to be clinically effective, although steroids were not continued beyond the initial 5-day study period. In cases of chronic infection, Pien and Pien [18] recommend 40–60 mg of prednisone per day, tapered over weeks to months, to alleviate the symptoms of increased intracranial pressure and reduce the allergic reaction to infective larvae.

No anthelminthic agent has been formally evaluated for efficacy in treating angiostrongyliasis. Thiabendazole, albendazole, mebendazole, and ivermectin have not been shown to provide clinical benefit, and many patients have worsened while being treated with these therapies because of the inflammatory reaction to antigens released by dying worms [18].

Most patients with A. cantonensis eosinophilic meningitis have a self-limited course and recover completely [13]. Migrating larvae eventually die in the CNS, and the accompanying inflammation subsides. Typically there is progressive improvement during a period of 3 to 6 weeks, and only a minority of patients have manifestations that persist for months [2]. In rare cases, paresthesias, weakness, and cognitive deficits may be present, representing a chronic form of this disease [25]. Fatalities are uncommon. Unfortunately, there is no evidence that a single attack of cerebral angiostrongyliasis confers immunity, and re-infection has been reported [3].

In cases of eosinophilic meningitis, the diagnosis of A. cantonensis infection should be considered and the appropriate exposure history obtained. It is important for clinicians to consider A. cantonensis when evaluating a patient with an eosinophilic meningitis, even in regions outside of its traditional geographic boundaries. This case also highlights the new immunologic techniques being used to confirm the diagnosis of angiostrongyliasis.

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References