Eosinophilic meningitis is defined by the presence of 10 or more eosinophils per microliter in the cerebrospinal fluid (CSF) or eosinophilia of at least 10% of the total CSF leucocyte count. It is rare in Western countries, where it is sometimes seen in association with tuberculosis, syphilis, and coccidioidomycosis. Worldwide, the most common cause of eosinophilic meningitis is invasion of the central nervous system by helminthic parasites, in particular *Angiostrongylus cantonensis* and *Gnathostoma spinigerum*. Most cases occur in Southeast Asia and throughout the Pacific basin. International travel has increased the possibility of exposure to these parasites and has led to further dissemination via ship-borne dispersal of infected rat vectors. In this article, we report a case of eosinophilic meningitis due to *A. cantonensis* in a Singaporean woman.

**Case Report**

A 48-year-old Singaporean Chinese, female, coffee shop assistant presented with a 2-day history of severe headache in October 2001. The headache started in the right occipital area, rapidly increased in intensity, and became generalized. It was associated with one episode of vomiting. The patient did not complain of paresthesias. Her past medical, family, and social histories were unremarkable, but she had traveled to South Korea in May 2001, 5 months prior to the onset of these symptoms. She had no dietary preferences, but claimed that she does not eat raw fish or raw meat; however, she does like to consume raw vegetable salads.

Clinical examination was unremarkable. She was afebrile. Neurologic examination was normal; in particular, there was no nuchal rigidity and no papilledema seen upon fundoscopy. The complete blood count was normal, except for a mildly raised eosinophil count of 4.1% and a raised total white cell count of $11.6 \times 10^9/L$ (polymorphs 70.6%, lymphocytes 21.5%, monocytes 3.3%, basophils 0.5%). The renal and liver function tests were normal. Findings on chest radiographs were normal. A non-enhanced computed tomography scan of the head revealed a mildly dilated ventricle. A magnetic resonance image of her brain showed no abnormal leptomeningeal enhancement, but there were some nonspecific white matter changes. Upon lumbar puncture, the opening pressure was 28 cm H₂O and the CSF appeared clear and colorless. The white cell count was 2,250/uL, glucose was 2.3 mmol/L, and total protein was 134 mg/dL. The differential cell count showed 50% eosinophils, 32% monocytes, and 3% lymphocytes. The CSF cytology was negative for malignant cells. The Gram stain and the acid-fast stain of the CSF were negative. CSF aerobic and anaerobic cultures and cultures for *Mycobacterium tuberculosis* were all negative.

We suspected parasitic eosinophilic meningitis and started empiric treatment with albendazole and prednisolone. Serum samples taken 1 week after admission were sent to a reference laboratory in Bangkok (Department of Parasitology, Mahidol University, Bangkok, Thailand), where Western blot analysis revealed antibodies against the 31 kDa antigen specific for *A. cantonensis*. The serum samples tested negative for antibodies against *G. spinigerum*.

The patient had a rapid recovery, with most of her symptoms resolved about 24 hours after the commencement of treatment. A repeat lumbar puncture was done 7 days after the first lumbar puncture. The CSF eosinophilia had disappeared, the total white cell count decreased to 88 cells per microliter (90% lymphocytes, 10% polymorphs), and protein and glucose levels were normal.

The patient was discharged well from the hospital and completed 3 weeks of albendazole with a tapering dose of prednisolone. At the last follow-up visit in February 2002, she remained asymptomatic.

**Discussion**

*A. cantonensis* is a zoonosis that affects rats as the primary hosts. Sexually mature male and female worms reside in the pulmonary arteries and right side of the heart.
of various rodents, including *Rattus rattus*, the black rat, and *Rattus norvegicus*, the brown rat, both of which have worldwide distribution. The gravid female lays eggs in the pulmonary circulation of the rats. The first-stage larvae migrate to the pharynx, are swallowed, and pass in the feces. Snails (eg, *Achatina fulica*—the giant African land snail, and *Pila ampullacea*) and slugs that feed on the rodent excrement serve as the intermediate hosts. After two molts, the third-stage larvae are produced, which are infective to mammalian hosts. Humans become infected by consuming raw snails or slugs, contaminated with the molluscs’ slime, or carrier (transport) hosts such as land crabs and freshwater shrimps that have eaten infected molluscs.

In humans, larvae penetrate the intestinal mucosa and migrate to the central nervous system, burrowing into the neural tissue and inciting an inflammatory response. The nematode does not complete its life cycle in humans and usually dies in the central nervous system.

The correspondent clinical manifestations of angiostrongyliasis are predominantly signs and symptoms relating to the central nervous system. Acute severe headache is the most significant symptom and is most likely due to elevated intracranial pressure. Neurologic findings are absent in half the cases. Other symptoms include nausea, vomiting, somnolence, lethargy, fever, malaise, anorexia, constipation, and abdominal pain. Clinical signs include nuchal rigidity, a positive Kernig’s sign, abnormal deep tendon reflexes, extracocular muscle palsies, and hepatomegaly. Paresthesias are the most distinctive neurologic findings in adults with angiostrongyliasis. Infective larvae can migrate to the eye, causing retinal detachment and hemorrhage leading to blindness. The prognosis is usually very good, with a case mortality ratio of less than 0.5%. Since migrating larvae eventually die in the central nervous system, the accompanying inflammation subsides and the disease is self-limiting. Progressive improvement during a period of 3 to 6 weeks is typical, with rare cases having persistent minor deficits (paresthesia, persistent headache, cognitive deficits). Anthelmintics are not effective and may even worsen symptoms. Although the use of corticosteroids does not improve mortality rates, a 2-week course of prednisolone has been shown to relieve headaches. There is no evidence that a single attack of cerebral angiostrongyliasis confers immunity, and reinfection has been reported.

The diagnosis of angiostrongyliasis is often clinical—as serologic tests are not commercially available—and is based on an appropriate epidemiologic history combined with the characteristic clinical symptomatology and CSF findings. CSF eosinophilia typically exceeds 10% in 95% of cases and is usually in the range of 20 to 70%. Blood eosinophilia occurs in two-thirds of cases. CSF protein levels are often slightly elevated, and the CSF glucose level is usually normal.

The main differential diagnosis of angiostrongyliasis is eosinophilic meningoencephalitis due to *G. spinigerum*, which is also endemic in Southeast Asia. However, the clinical presentation of cerebral gnathostomiasis is more fulminant than that of angiostrongyliasis. The most distinctive clinical manifestations are radiculitis, paralysis, and myelitis, bloody or xanthochromic CSF, and sudden impairment of the sensorium caused by cerebral hemorrhage. The absence of focal lesions on computed tomographic scans or magnetic resonance imaging of the brain distinguishes *A. cantonensis* meningitis from other helminthic infections of the central nervous system.

Trichinosis, trichuriasis, and opisthorchiasis can cross-react against the 31 kDa component of the test. Although we did not perform serology to exclude these diseases, they are highly unlikely because of their lack of compatibility with the clinical picture.

Our patient presented with the typical history of acute progressively worsening headache. She was afebrile and had no neurologic signs or deficits. The clinical manifestations and her CSF findings were in accordance with the typical picture of angiostrongyliasis, albeit being on the milder aspect of the clinical spectrum of this disease. She recovered rapidly and uneventfully, which was most likely due to the corticosteroids rather than the anthelmintic therapy. The reasons for her relatively mild and benign course are unclear. Infection with a lower parasitic inoculum is possible, or perhaps variations in the strain of *A. cantonensis* were involved. Presumably vegetables contaminated with molluscs’ secretions were the source of transmission because the patient indicated that she ate salads and raw vegetables frequently. However, in Singapore angiostrongyliasis has not been reported, except for one case in an Indonesian boy in 1990, and that case was most likely imported. The incubation period is reported to be between 2 and 35 days. *A. cantonensis* is endemic in Korea and the consumption of raw food is common; the interval of 5 months between her visit to Korea and the onset of her symptoms makes it unlikely, yet not impossible, that the source of her infection was in Korea. If the source of infection was indeed in Singapore, then this would be the first reported case of angiostrongyliasis acquired in Singapore. Singapore imports large quantities of vegetables and salads from the region; therefore, diligent washing and preparation of salads and raw vegetables is paramount.

*A. cantonensis* infection occurs principally in Southeast Asia and throughout the Pacific basin. However, because of the ship-borne international migration of rats, dissemination of the parasite has occurred to further destinations, including Australia and North America. Cases of angiostrongyliasis have been reported in Western tourists returning from the Pacific Islands and the
Caribbean Islands. An outbreak occurred amongst Thai laborers in Taiwan after the consumption of raw snails. Raw snails are a delicacy in southern Vietnam and are often eaten at celebrations; raw seafood minced with Thai spices and herbs are a delicacy in North Eastern Thailand. In Western countries the consumption of raw food in the form of Japanese sushi is increasing. However, the apparent increase of fish-borne parasitoses, such as anisakiasis, other than angiostrongyliasis has been reported to be related more to advances in diagnostic abilities than to the commercialization of sushi. Well-designed studies are needed to determine whether the consumption of sushi is indeed associated with a higher risk of acquiring angiostrongyliasis and other parasitoses.

Although parasitosis is slowly gaining attention as an emerging infectious disease, clinical awareness remains low. Travel medicine practitioners, physicians, and public health officials should be well informed about this condition. Headache, elevated intracranial pressure, and eosinophilia in the CSF of the patients from endemic areas should suggest the possibility of A. cantonensis infection. For disease prevention, travelers should be informed to avoid eating unwashed vegetables and undercooked or raw foods, in particular, snails and other molluscs, when traveling in an endemic area.

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References