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Eosinophilic Meningitis Caused by *Angiostrongylus cantonensis*

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ABSTRACT: Rat lungworm, *Angiostrongylus cantonensis*, is one major cause of human eosinophilic meningitis. This helminth is endemic in Southeast Asia, Pacific Islands, and the Caribbean and has recently expanded to South America. The infection is characterized by an elevated eosinophil count in cerebrospinal fluid. Common symptoms and signs include headache, neck stiffness, paresthesia and nausea/vomiting. The unique history of eating freshwater and land snails or slugs within 2 weeks before onset is helpful for diagnosis. Antihelminthic agents have not shown efficacy in human infection; treatment involves supportive care with management of inflammation and intracranial pressure.

KEYWORDS: *Eosinophilic meningitis, Angiostrongylus cantonensis, rat lungworm*

Recently nine confirmed cases of *Angiostrongylus cantonensis* infection were reported in the state of Hawaii. To date, more than 100 local infection cases were documented on the islands, which accounts for around 90% of cases in the United States. Of note, the autopsy findings of the first cases in Hawaii during 1959−1960 helped to establish *A. cantonensis* as an etiology of eosinophilic meningitis for the first time.

A. cantonensis, known as the rat lungworm (Figure 1), is a parasitic nematode that completes its lifecycle between definitive host rats and intermediate host snails or slugs. It was first isolated from rat pulmonary arteries in China 1933, while the first case in humans, which are incidental hosts, was reported in 1945. Humans acquire infection through consumption of mollusks harboring infective third-stage larvae (Figure 2). Epidemiological evidence also suggests that prawns, frogs, and lizards, as well as contaminated vegetables, could be sources of infection. Cases of *A. cantonensis* infection in humans have been reported most often in Southeast Asia. However, this disease emerged in the Pacific soon after the Second World War, followed by the Caribbean, and most recently South America.[1] The rapid growth of global shipping, accompanied by the invasion of ship rats (*Rattus rattus* and *R. norvegicus*) and some mollusks (e.g., African giant snail, *Achatina fulica*), may explain the global spread of this parasite. To date, several thousand cases have been reported around the world.[2]

Figure 1. Young adult worm isolated from rat brain.

Figure 2. Third-stage larvae in snail.

A. cantonensis is one of the major causes of human eosinophilic meningitis. The larvae invade the blood and lymph vessels in the digestive tract and migrate to organs within circulation. The larvae of *A. cantonensis* are neurotropic; they exclusively present in brain and spine several days to weeks postinfection, where they develop to young immature adults. Unlike in the permissive definitive host (rats), the worms rarely further travel to the pulmonary arteries in humans. Therefore, the main symptoms are associated with inflammation in the central nervous system (CNS). Although the expression of cytokines and chemokines in brain tissue significantly alters during *A. cantonensis* infection, the detailed mechanism of larval killing is unclear. Interleukin 5 was the first factor identified in the killing mechanism.[3] This cytokine facilitates the generation

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and activation of eosinophils. The latter kill the larvae and induce additional inflammation. Therefore, an elevated eosinophil count in cerebrospinal fluid (CSF) is an important marker suggestive of *A. cantonensis* infection.

The most common symptoms and signs of eosinophilic meningitis caused by *A. cantonensis* infection include headache, neck stiffness, nausea, vomiting, and paresthesia. Ocular cases with or without meningitis have also been reported. In such cases, motile worms may be observed in eye chambers. The symptoms and signs of eosinophilic mentingitis and ocular angiostrongyliasis are often mild or moderate. However, fatal outcomes can occur in the setting of heavy infections and among young children. Autopsies in such cases often reveal encephalitis and lung involvement.

Diagnosis of *A. cantonensis* infection relies predominantly on clinical signs and symptoms, as well as exposure history. Discovery of larvae from CSF confirms the diagnosis, but the discovery rate is very low, depending on the worm burden.[4] The unique history of ingesting raw snails, slugs, frogs, lizards, or other potentially contaminated foods within 2 weeks before the onset of symptoms may be supportive of a diagnosis. Immunological and molecular detection provide more definitive evidence, but such tests are not available in many settings.[5] Although *A. cantonensis* infection accounts for the majority of reported eosinophilic meningitis cases, other helminth infections can cause a similar syndrome. Infection with *Gnathostoma* spp. should be considered in the differential diagnosis. This infection is acquired by eating undercooked or raw freshwater fish. CNS involvement usually presents as eosinophilic radiculomyelitis and encephalitis with symptoms of headache, motor weakness, and nerve root pains. Subarachnoid hemorrhage is frequently observed. *Baylisascaris procyonis*, caused by the raccoon roundworm, is a rare cause of severe eosinophilic meningitis in children, usually associated with a history of consuming dirt. Prognosis for these infections is worse than *A. cantonensis* infection. Other infectious (e.g., *Coccidioides spp.*) and noninfectious etiologies (allergic reaction, malignancies) may cause a compatible syndrome of eosinophilic meningitis.

Eosinophilic meningitis caused by *A. cantonensis* is usually self-limiting. Mild infection needs no special treatment. Anthelmintic drugs (e.g., albendazole and mebendazole) have been used to treat patients by killing the worms in CNS, but a randomized trial demonstrated no benefit to their use. The rapid degradation of larvae killed by drugs may in fact exacerbate the inflammatory reaction, causing more severe symptoms. Corticosteroids can alleviate inflammation and were shown in one trial to reduce headache persistence and the need for lumbar puncture to relieve intracranial pressure.

Angiostrongyliasis is an important emerging pathogen that is growing in geographic reach as a result of global transport networks.[6] Surveillance for eosinophilic meningitis and monitoring for infection among consumable snails may provide local risk estimates and inform prevention measures for this serious disease.

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Notes

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