FATAL AUTOCHTHONOUS EOSINOPHILIC MENINGITIS IN A JAMAICAN CHILD CAUSED BY ANGIOSTRONGYLUS CANTONENSIS


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Abstract. A fatal case of infection with Angiostrongylus cantonensis is reported in a 14-month-old Jamaican boy. Although infection with Angiostrongylus was not considered initially, sections of multiple worms were observed in the brain and lungs at autopsy and confirmed the infection. This is the first reported fatality due to this infection in the Western Hemisphere, and follows shortly after an outbreak of eosinophilic meningitis among a group of travelers to Jamaica. The source of infection in this case could not be determined.

INTRODUCTION

Angiostrongylus cantonensis is the most common cause of eosinophilic meningitis worldwide. The rat is the definitive host of the parasite and humans are infected by ingesting third-stage larvae, which develop in a molluscan intermediate host. Routes of infection include ingestion of snails, crabs, freshwater prawns, or vegetables contaminated with infective larvae. The infection is common throughout Southeast Asia and the Pacific Basin, but has also been reported from several foci in the Western Hemisphere, including the United States, Puerto Rico, Cuba, the Dominican Republic, and Jamaica. A single human infection was reported from the United States following intentional ingestion of a snail, a series of five cases was reported from Cuba, and an outbreak of 11 cases from Jamaica, which apparently resulted from ingestion of contaminated vegetables. There were no deaths in any of these cases. We report the first fatal case of infection with A. cantonensis in the Western Hemisphere.

CASE REPORT

A 14-month-old boy was admitted to the Bustamante Hospital for Children in Kingston, Jamaica with a four-day history of anorexia, constipation, and abdominal distension. His mother had a normal pregnancy and he had been previously well, was fully immunized for his age, and had normal developmental milestones.

On examination, he weighed 11.6 kg, was afebrile with pink mucous membranes, and the only abnormal finding was abdominal distension with generalized tenderness. His hemoglobin level was 12.4 g/dL and his white blood cell (WBC) count was 15.8 × 10⁹/L with a normal platelet count. His abdominal signs settled over the next two days, but on day 5 post-admission, he was febrile (temperature = 39°C), had poor head control, truncal ataxia, generalized hypotonia, and intermittent flexor movements at both ankle joints. Reflexes were normal in both upper limbs, but absent in both lower limbs symmetrically. There was grade III-IV power in the left upper limb but no active movements in the other limbs, and there was a generalized diminished response to painful stimuli. His blood pressure was persistently elevated (140/110 mm of Hg).

The differential diagnoses included viral encephalitis/meningitis, Guillain-Barré syndrome, and lead encephalopathy. Following a normal computed axial tomography scan, a lumbar puncture showed clear cerebrospinal fluid (CSF) with 20 red blood cells and 30 WBCs (98% neutrophils), and normal proteins and glucose.

He was treated for bacterial meningitis with crystalline penicillin and chloramphenicol following initial doses of dexamethasone and his elevated blood pressure was managed with hydralazine. He subsequently developed seizures (controlled with phenytoin and diazepam) and hyponatremia (serum sodium = 111 mmol/L, normal range = 135–145 mmol/L), and his generalized loss of sensation and grade 0 power in the lower limbs persisted. Hyponatremia persisted despite attempts at correction and the possibility of syndrome of inappropriate antidiuretic hormone (SIADH) was contemplated. Edema, peripheral at first then progressing to generalized, developed on day 12 post-admission. The following day he developed aspiration pneumonia and was admitted to the intensive care unit (ICU), intubated with an endotracheal tube, and placed on a T-piece. Repeat lumbar puncture showed 130 WBCs (84% neutrophils and 16% lymphocytes) and normal protein and glucose levels. Results of human immunodeficiency virus and other viral studies were negative and his blood lead levels were normal (1.8 mg/dL). Peripheral blood eosinophilia of up to 13% was documented. The pediatric neurologist noted pinpoint pupils, Doll’s eyes movement, absent gag reflex, generalized flaccid tone, areflexia, and absence of response to deep pain.

His stay in the ICU was characterized by persistent hypothermia. On the seventh day in the ICU, he had respiratory arrest with bradycardia and was placed on a ventilator. His overall condition remained poor and he died on day 34 post-admission.

Necropsy revealed an edematous, hemorrhagic brain (1,127 grams), solid, hemorrhagic lungs, and marked congestive hepatosplenomegaly. Microscopy showed meningeal infiltration by eosinophils, macrophages, and lymphocytes, which was most marked in the cerebral hemispheres. Portions of worms identified as A. cantonensis were present within the meninges and the brain parenchyma (Figures 1 and 2), and the latter showed microthrombi associated with dense perivascular chronic inflammatory cell exudation rich in eosinophils. The lungs showed extensive, confluent, organizing bronchopneumonia, with focal microinfarcts, and degenerating and viable worms were noted in blood vessels and in the parenchyma (Figures 3 and 4).

Immunoblot analysis on an acute serum sample that was conducted after the child died was negative for A. cantonensis. No follow-up serology was possible.
DISCUSSION

This is the first report of fatal *A. cantonensis* infection in the Western Hemisphere. It follows the report of an outbreak of eosinophilic meningitis among a group of adult travelers to Jamaica and the presence of established foci of infection among rats and snails on the island. The infection must be considered autochthonous since the child had never traveled outside of Jamaica.

Adult *A. cantonensis* worms are found in branches of the pulmonary artery and sometimes in the right ventricle of rats. Eggs are carried to the lung capillaries where they hatch and first-stage larvae enter the alveoli, ascend the trachea, are swallowed, and passed in the feces. A number of snail and slug species ingest the first-stage larvae and there are two molts to the infective, third-stage larva. Humans become infected by ingesting raw or undercooked snails or slugs or vegetable matter contaminated with third-stage larvae. In addition, freshwater prawns, crabs, and toads may act as sources of infection to humans. Third-stage larvae released from host tissues penetrate the intestinal tissues of humans and are carried by the blood to the liver, heart, lungs, and ultimately to the central nervous system (CNS). While in the CNS, the larvae continue to develop to the fourth and fifth stage. In humans, there is rarely migration to, and further development in, the lungs.

At age 14 months the child may have ingested infective larvae from a variety of sources. Snails and slugs are not a normal part of the Jamaican diet and it is highly unlikely that he was fed undercooked portions of these animals intentionally. However, the snail and slug fauna of Jamaica is very rich in diversity and abundance, and it is possible that he could have ingested (accidentally or intentionally) an infected intermediate host in the garden, or may have been fed vegetables or fruits that were unwashed and contaminated by snails or slugs. The parasite is well established in rats across much of Jamaica, including Kingston, where the child lived. Crabs and freshwater prawns are thoroughly cooked before they are consumed in Jamaica and are therefore unlikely sources of infection for the child. He lived with two young siblings, who showed no signs of infection nor were there any other suspected cases from his neighborhood.

**FIGURE 1.** Immature *Angiostrongylus cantonensis* in the brain. Section contains the intestine but no reproductive tubes. Dome-shaped lateral chords are evident. Scale bar = 50 μm.

**FIGURE 3.** Low-power image of sections through a coiled *Angiostrongylus cantonensis* lying in a thrombosed, occluded blood vessel in the lung. Intense inflammation is evident, and the worm is undergoing degeneration. Scale bar = 200 μm.

**FIGURE 2.** Section through an immature female *Angiostrongylus cantonensis* in the brain, showing a section through the intestine (larger tube to the bottom) and two reproductive tubes. The nature of the gut, including numerous nuclei and granules lining the lumen border is evident. Scale bar = 50 μm.

**FIGURE 4.** Cross section through a small vessel in the lungs containing three sections of a male *Angiostrongylus cantonensis*. Little reaction to the parasite is evident. The intestine, composed of few cells with prominent nuclei, the sublateral chords, and the testis are all evident. Scale bar = 100 μm.
The most consistent clinical finding among young children infected with *A. cantonensis* is a persistent fever with encephalitis. The case under discussion was brought to medical attention because of anorexia, constipation, urine retention, and itching in the lower limbs. Although his mother reported that the child had been febrile for four days prior to being seen at Bustamante Hospital for Children, he was afebrile on admission. However, he developed fever five days afterwards, but did not remain febrile throughout the course of his illness.

Abnormalities of motor function including paraplegia and weakness of the upper limbs were a feature of our patient’s clinical course. Similar findings were seen in other affected children. Fever and failure to bear weight on the legs were reported in a 10-month-old Samoan boy with eosinophilic meningitis associated with *A. cantonensis*. As the clinical course progressed, he also lost strength in his upper extremities. Similarly, an 11-month-old boy developed flaccid quadriplegia after infection with *A. cantonensis*. The presence of worms in the brain of young children results in a progressive deterioration of CNS function as seen in the current case and in several others reported elsewhere.

Findings in the CSF were significant for a neutrophilic pleocytosis with lymphocytes, which has not been previously reported in these cases, and this finding may represent non-specific neutrophilic exudation in the early phase of meningeal inflammation. Central nervous system eosinophilic pleocytosis is known to peak between 25 and 30 days post-infection and is therefore not seen in many patients in the early stages of infection. In a previous fatal case, eosinophils were not detected in the CSF despite peripheral blood eosinophilia. In fact, nearly 30% of 17 cases of eosinophilic meningitis did not exhibit CSF eosinophilia. The CSF findings may have been affected by a delay in examining the sample after collection even though the Bustamante Hospital for Children protocol requires that all CSF samples are examined immediately upon collection. We could not ascertain whether there was a delay in the examination of the CSF of the current case. Peripheral blood eosinophilia of 13% was noted late in the clinical course of our patient. The absence of these clear findings led to the initial diagnoses of acute flaccid paralysis, encephalitis, Guillain-Barré syndrome, and SIADH. Serologic testing post mortem did not detect a response to the parasite. However, the test used is not likely to show positive results on samples taken during the acute phase of the infection.

Infection with *A. cantonensis* is generally self-limiting, and recovery usually occurs within about four weeks. The case fatality rate, when determined for large cohort studies, is generally low; one of 484 cases in Thailand and four of 114 cases in Taiwan. Conversely, in a report of three related cases, two of the three persons died. There may be several reasons that some cases progress to death, including the level of medical care, underlying medical conditions, the age of the patient, and, an apparent high infecting dose. In the present case and many other fatal cases, numerous worms were seen in the brain and lungs post mortem.

Thiabendazole and levamisole have been used to treat eosinophilic meningitis due to *A. cantonensis*, although their efficacy is doubtful and symptoms may worsen during treatment. This is attributed to the presence of dead worms in the CSF. Corticosteroids, repeated lumbar punctures, and analgesics may alleviate some symptoms of increased intracranial pressure, reduce allergic reactions, and relieve headaches.

Cases of eosinophilic meningitis are not often seen in Jamaica, and, prior to this case there was only a single case in an adult reported in the literature. The etiology of that case was never confirmed and there was no history of snail consumption. A history of ingesting snails or paratenic hosts by the child may have assisted the diagnosis.


