Encephalitis Caused by *Angiostrongylus cantonensis* after Eating Raw Frogs Mixed with Wine as a Health Supplement

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**Abstract**

*Angiostrongylus cantonensis* also known as the rat lungworm, is prevalent in the Pacific Islands and southeast Asia and is the most common cause of eosinophilic meningitis in humans. Although frogs and toads are known as paratenic hosts of *A. cantonensis*, they are rarely reported as the infectious source of human angiostrongyliasis. We report a case of encephalitis caused by *Angiostrongylus cantonensis* after eating raw frogs mixed with wine as a health supplement. Prednisolone at a dose of 1 mg/kg/day was prescribed for 14 days successfully. We advise that travelers and residents of endemic areas should avoid eating raw frogs and a public caution on the danger of eating raw wild animal products or the whole animal is recommended to alleviate such accidental infection.

**Key words:** *Angiostrongylus cantonensis*, eosinophilic meningitis, encephalitis

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**Introduction**

*Angiostrongylus cantonensis*, also known as the rat lungworm, is prevalent in the Pacific Islands and southeast Asia and is the most common cause of eosinophilic meningitis in humans in areas endemic for this parasite (1-3). Rats serve as the definitive host of the nematode. Humans are infected by ingestion of freshwater and terrestrial snails and slugs, or transport hosts, such as freshwater prawns, frogs, fish, and planarians (4-6). Infection can be acquired by the consumption of fresh produce, such as lettuce, contaminated with these intermediate or transport hosts (7, 8). The major intermediate hosts in Taiwan are the African giant snail (*Achutina fulica*) and the golden apple snail (*Ampullarium canaliculatus*). Field studies in southern Taiwan have shown that 14-31% of *Ampullarium canaliculatus* contain third-stage larvae of *A. cantonensis* (9). To date, Taiwan has recorded hundreds of cases of eosinophilic meningitis with reports coming from nearly all parts of the island. Most of the cases occurred among children and were recorded before the 1970s (3). There was usually a history of eating or playing with snails or slugs. Only three scattered outbreaks were found to have occurred during the past two decades caused by eating raw golden apple snails and drinking raw vegetable juice (10, 11). Frogs and toads are known as paratenic hosts of *A. cantonensis* (12). Ingestion of raw liver of a toad containing infective larvae leading to *A. cantonensis* infection was reported in previous studies decades ago (13). Herein, we report a case of encephalitis caused by *A. cantonensis* after ingestion of raw frog mixed with wine as a health promotion medicine.

**Case Report**

A 74-year-old woman was admitted to the Infectious Diseases Division of Kaohsiung Veterans General Hospital, Taiwan, in July 2009 after 2 days of dizziness, weakness of...
lower legs, unsteady gait and change in sensorium. At presentation, she had a body temperature of 37.3°C, respiration rate of 18 beats/minute, a heart rate of 98 beats/minute, and a blood pressure of 161/96 mm of Hg. Results of a physical examination were unremarkable except for an impaired tandem gait and a positive Romberg’s test. She was drowsy without meningeal signs. Laboratory tests showed a white blood cell count of 25,420/μL (19% neutrophils, 10% lymphocytes, 69% eosinophils, and 2% monocytes). Results of renal and liver function tests were normal, and levels of electrolytes were all within normal limits. Creatine kinase was elevated at 253 U/L (normal 24-120 U/L). Computed tomography of the brain did not show any parenchymal lesions, atrophy or hydrocephalus. Lumbar puncture was performed smoothly. The opening pressure was 20 cm of H2O. Results of cerebrospinal fluid (CSF) examination showed a white blood cell count of 4/cm³, a red blood cell count of 42/cm³, a protein level of 36 mg/dL, and a glucose level of 50 mg/dL (serum glucose level 115 mg/dL). Results of CSF cryptococcus antigen as well as cultures for bacteria, mycobacteria, fungi and virus were negative. Parasites were not seen during stool examination. The patient was also negative for HIV by ELISA method. Magnetic resonance imaging scans of the brain showed the presence of multiple small high signal intensities on both cerebellar hemispheres with bilateral fronto-temporo-parieto-occipital cortical and subcortical regions and bilateral central white matter region on T2 WI, FLAIR and DWI imaging (Fig. 1). A diagnosis of *A. cantonensis* infection was made by a positive microenzyme-linked immunosorbent assay (ELISA), using young-adult worm antigen molecular weight 204 kD, purified by monoclonal antibody (14).

The patient had ingested raw frogs (*Rana plancyi*) approximately 3 weeks prior to admission. She caught 4-5 frogs that were approximately 7-8 cm in size and without removing the viscera and the intestines, she seasoned them with wine and ingested them raw with wine. The patient denied eating any other raw food or fish in the past year.

On the basis of the history, clinical presentation, antibody results and imaging findings, *A. cantonensis* infestation associated with encephalitis was suspected. Treatment was mainly symptomatic. Prednisolone at a dose of 1 mg/kg/day was prescribed for 14 days and additional lumbar punctures were performed 2 weeks after hospitalization. After 2 weeks, the patient’s general condition improved markedly; however, minor symptoms such as diminished concentration, and unsteady gait persisted. She was regularly followed up in the outpatient department. Magnetic resonance imaging scans of the brain 7 months later revealed complete resolution of the previous intracranial high signal intensities (Fig. 1). Levels of serum antibody to *A. cantonensis* [positive control >1.2 optical density (OD), negative control < 0.12 OD] decreased from 1.3 OD (43 days after the ingestion of frogs to examination) to 0.28 OD (425 days from in-
gestion of frogs to examination). She was free of unsteady gait and was conscious.

**Discussion**

Ingestion of raw frogs causing *A. cantonensis* infection has been documented in previous studies (13). Ottsu et al studied definitive, intermediate, and paratenic hosts of *A. cantonensis* in the southwestern islands of Japan and Taiwan 3 decades ago and found that larvae were present in many species of frogs, including *Rana plancyi* (6 of 28, 21.4%) (15). Lai et al identified a case of eosinophilic meningitis caused by *A. cantonensis* probably associated with ingestion of raw frog muscles and bones seasoned with soy sauce (16). It is likely that our patient was infected due to ingestion of the whole raw frogs, since the larvae of *A. cantonensis* are most frequently found in the frog’s stomach, intestinal wall, mesentery, liver and muscle (12).

Brain MRI abnormalities in eosinophilic meningitis caused by *A. cantonensis* infection is relatively common. Multiple enhancing nodules in the brain and linear enhancement in the leptomeninges, accompanied by stick-shaped enhancement are the characteristic signs of the disease on Gd-DTPA-enhanced T1-weighted images (17). Also there is a significant correlation between the severity of headache, cerebrospinal fluid (CSF) pleocytosis, and CSF and blood eosinophilia with MRI signal intensity in T1-weighted imaging (18). In addition, lepto-meningeal enhancement, ventriculomegaly and abnormal enhancement within the cerebral and cerebellar hemisphere is found on the T2WI and FLAIR imaging. In contrast to these reports, the present patient had multiple small high signal intensities over the bilateral cerebellar hemisphere, central whiter matter and bilateral fronto-temporo-parieto-occipital cortical and subcortical regions. Though a normal CSF finding was noted at the initial presentation, the resolution of the brain MRI lesions 7 months after treatment, accompanied by a history of ingestion of raw frogs, positive serological antibody and the disappearance of unsteady gait all supported the clinical diagnosis of encephalitis associated with *A. cantonensis* infection.

The brain pathological findings in patients infected with *A. cantonensis* includes meningitis with a predominance of eosinophils and plasma cells, tortuous tracks of various sizes in the brain and spinal cord surrounded by an inflammatory reaction and degenerating neurons, granulomatous response to the dead parasites, and nonspecific vascular reactions including thrombosis, rupture of vessels, arteritis, and aneurysm formation (19). Animal studies in mice have shown that plasmigen activators and matrix metalloproteinase -9 proteolytic cascade may be associated with blood-CNS barrier disruption in eosinophilic meningitis caused by *A. cantonensis* (20). Albendazole and dexamethasone co-therapy was reported to significantly decrease plasmigen activators after treatment on day 5 post-inoculation (21).

The standard treatment for eosinophilic meningitis caused by *A. cantonensis* infection remains controversial. Punyagupta et al (2) found no difference in the duration or severity of illness in patients treated with analgesics alone, analgesics and glucocorticosteroids, or analgesics and antibiotics. Hwang et al (22, 23) reported good results with albendazole or levamisole in uncontrolled studies of children. Chotmongkol et al (24) found that a 2-week course of prednisolone helped relieve the headache, shortened the median time until resolution of headache, and reduced the need for repeated lumbar puncture. They did not find a better treatment effect when combination therapy with prednisolone and albendazole was compared to prednisolone alone (25). We treated the present patient with a 2-week duration of prednisolone and the outcome was good.

In summary, frogs, previously recognized as paratenic hosts of *A. cantonensis*, may cause human angiostrongyliasis if they are eaten raw. Travelers and residents of endemic areas should avoid eating raw foods, such as frogs.

**The authors state that they have no Conflict of Interest (COI).**

**References**

probably caused by the swallowing of fresh liver of a toad (*Bufo asiaticus*). 46th Annual Meeting, Okinawaken Igakkai 7-8, 1975.


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