Harry L. Arnold Jr. MD Case of the Month

Eosinophilic Meningitis / Angiostrongyliasis From Eating Aquaculture-raised Snails: A Case Report

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A 68-year-old recently-retired Chinese-American telephone switchman developed a headache and a short-lived papular rash about one week after eating home-cooked ("Chinese style"; stir-fried) fresh snails, a gift from his neighbor, a home aquaculturist. He developed worsening confusion and hallucinations, fell twice at home, and was admitted to the hospital. His medical history was remarkable for mild hypertension and gout. Routine medications were nadolol, colchicine, and probenecid.

Examination revealed that he was alert and oriented to month and year, but not to day or date; he was unable to perform "serial sevens" or "serial fives." Vital signs and general examination were unremarkable. Fever and meningismus were absent. Laboratory tests were normal except for serum sodium of 118 meq/dL. Several normal serum sodium levels had been documented during the years prior to this illness. MRI scan of the brain was normal.

After hospitalization and IV fluid administration hyponatremia was corrected, but his condition worsened. He began to hallucinate, seeing imaginary people and objects in his room. Agitation, and acute urinary retention developed. Lumbar puncture revealed cerebrospinal fluid (CSF) white blood cell count 1,300, with 73% eosinophils; glucose was 31 mg/dL, protein was slightly elevated. All cultures and stains were negative. He was treated supportively for a diagnosis of eosinophilic meningitis. Empiric therapy for tuberculous meningitis was administered for one week.

Repeat lumbar puncture two weeks later revealed moderate improvement in the CSF eosinophilia. However, he remained delirious and delusional, with hallucinosis. Transfer to a care home for six weeks was required before his family was again able to care for him. Bladder catheterization was successfully discontinued shortly thereafter. Mental function improved slowly, although twelve months following onset of illness, he remained unable to perform "serial sevens" calculations.

Serology specimens were sent to the Faculty of Tropical Medicine in Thailand.[10] Results revealed Angiostrongylus cantonensis antibody titers of 1:3200 by ELISA; Gnathostoma spinigerum antibody by Western blot was "weakly positive". There may be considerable cross-reaction among helminthic antigens within these tests.

Gnathostomiasis[1,6] typically causes painless migratory subcutaneous swellings lasting several days, and subsiding spontaneously ("larva migrans"). Immature worms can cause eosinophilic meningitis when they migrate to the CNS. The usual presenting symptom is sharp, agonizing cranial nerve root pain, or sudden impairment of sensorium due to cerebral hemorrhage. CSF is usually bloody or xanthochromic. Snails are not a known host of Gnathostoma spinigerum.

Although presenting some unusual features, the clinical diagnosis of eosinophilic meningitis due to Angiostrongylus cantonensis is unequivocally established in this case based upon CSF results, serology, ingestion of snails, and the clinical course of the illness.

Discussion

Almost all cases of eosinophilic meningitis are caused by *Angiostrongylus cantonensis*, the nematode lungworm of rats. Other parasitic helminths (e.g. *Taenia solium, Paragonimus westermani, Gnathostoma spinigerum)* may rarely cause CSF eosinophilia, but usually as part of distinctive illnesses (cerebral cysticercosis, etc.) readily distinguished clinically from *Angiostrongylus cantonensis*. The first human case of eosinophilic meningitis was reported in Taiwan in 1944, followed by thousands of cases in Southeast Asia and the Pacific basin over the ensuing fifteen years. *Angiostrongylus cantonensis* was first etiologically linked to eosinophilic meningitis in Hawaii and Tahiti in 1962.[1,4] The first case from mainland China was reported in 1984,[2] and the first case in North America in 1995[3].

Angiostrongylus cantonensis is a zoonosis affecting rats as the primary hosts. Several land mollusks (over 40 species of snails and slugs) are the intermediate hosts. A number of land planaria, freshwater prawns and crabs, frogs, and occasionally swine and cattle may serve as paratenic, or "carrier" hosts, but do not directly participate in the life cycle of *Angiostrongylus cantonensis.*[4] *Achatina fulica*, the giant African land snail, was introduced progressively across the Pacific, both willfully and unintentionally, during the 1940's and 1950's, and has played a major role as an intermediate host in the dissemination of *Angiostrongylus cantonensis.*[5] Rats infected with *Angiostrongylus cantonensis* have been found in all areas reporting eosinophilic meningitis.

Human infections are usually acquired by accidental or purposeful ingestion of raw or partially cooked terrestrial mollusks, planaria, and freshwater crustaceans containing infective larvae. Ingestion of contaminated water or vegetables are other possible sources of infection. The incubation period is about one week. Clinical manifestations typically consist of severe headache, paresthesias, occasionally meningismus and cranial nerve palsies, and rarely

fever. The eye may become involved, occasionally with permanent visual impairment. The majority of cases are self-limiting, with acute symptoms lasting for one to two weeks. Rare residual neurological symptoms (diplopia, ataxia) usually resolve within several months. Incomplete neurological recovery is probably seen in less than one percent of cases.

Exceptionally severe cases, and chronic cases, have occasionally been reported. Pathogenesis of eosinophilic meningitis involves migration of third stage larvae via the systemic circulation to the brain (and spinal cord), where they die, causing an intense inflammatory, eosinophilic reaction. In the primary host, the rat, the larvae migrate within the brain, eventually reaching the subarachnoid space.[6] Several autopsy studies of fatal human eosinophilic meningitis have found parasites, and oval worm tracks, throughout the white matter of the brain and spinal cord.[1] Characteristic abnormalities on brain CT have been reported. No pathological studies of completely recovered cases of eosinophilic meningitis were found in this literature review.

Diagnosis is based almost entirely on the clinical presentation, the marked CSF eosinophilia (and occasionally demonstration of larvae in the CSF or anterior chamber of the eye), and a history of exposure to (ingestion of) an intermediate or paratenic host. About 60% of cases have peripheral eosinophilia; all have CSF eosinophilia of greater than 20% of total CSF white blood cells, at some time during the course of illness. Patchy lung infiltrates and other abnormalities on chest X-ray have been described, primarily in children.[7] Presentation can rarely resemble bacterial meningitis with meningismus and fever. Urinary incontinence, ataxia, and cranial nerve palsies are symptoms which demand consideration of alternative diagnoses (tuberculous meningitis, syphilis, etc.) when present. Our patient was treated with antitubercular antibiotics for about one week until tuberculosis was confidently ruled out.

Several serological tests for *Angiostrongylus cantonensis* have been evaluated. The only test with promise is an enzyme-linked immunosorbent assay (ELISA) test.[8] The detection of *serum* antibody is much more sensitive than that of *CSF* antibody; sensitivity for IgG antibody is greater than for other antibody classes.[9]

There is no specific effective treatment for eosinophilic meningitis. Several antihelminthic agents (primarily thiabendazole, anecdotally ivermectin etc.) have been evaluated, with inconclusive and inconsistent results. It is thought that live larvae may be less antigenic to the brain than dying or dead larvae, so that antihelminthic

treatment could exacerbate symptoms.[1] The vast majority of cases recover fully with supportive care. Severe symptoms appear to be often due to increased intracranial pressure, and repeated lumbar puncture has occasionally caused marked improvement. Corticosteroids have not been found to be of any value, although several anecdotal cases of improvement with corticosteroids in patients with presumed increased intracranial pressure, were found in a literature review[1] However, as this case demonstrates, eosinophilic meningitis is a disabling and sometimes prolonged illness, often requiring hospitalization, expensive diagnostic testing, and occasionally prolonged post-hospital institutional care.

Presentation with acute delirium and hallucinations, the severe hyponatremia, and the prolonged duration of dementia (three months) seen in this case are all somewhat unusual for eosinophilic meningitis. No previously published cases of eosinophilic meningitis presenting with severe hyponatremia were found in this literature review. Published case studies of eosinophilic meningitis, reporting a preponderance of complete neurological recovery, do not specify the extent of follow-up neurological examination. Detailed mental status examinations, or evaluations of cognitive performance, may not have been done. Since parasites invade and damage brain parenchyma (to some degree) in man prior to their death, it seems surprising that complete neuropsychological recovery would be the common outcome. Our patient has persistent, moderately severe acalculia. Although this was not tested prior to his illness, he had very recently retired from a job requiring an understanding of mathematics, and had successfully conducted a small catering business for many years.

Our patient's aquaculturist neighbor reportedly sells most of his produce to local hotels and restaurants for preparation of "escargots." Since *Angiostrongylus cantonensis* is well-established in Hawaii, it is not surprising that fresh water aquaculture of one of its intermediate hosts would be susceptible to infestation. Presumably, pharmacological antihelminthic treatment for *Angiostrongylus cantonensis* would not be possible in such an environment, without also damaging the snails.

Telephone contact, on several occasions during the course of this case, to the Hawaii Department of Health, disclosed that eosinophilic meningitis is not a "reportable disease" in the United States or Hawaii, and therefore, not under the purview of the Department, or of any other state regulatory agency that they were aware of, even though the aquacultured snails are being sold commercially. However, the Centers for Disease Control in Atlanta, Georgia, would be interested in hearing about any further cases, particularly from an aquaculture source (personal communication).

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