Eosinophilic Meningitis due to *Angiostrongylus cantonensis* in Germany

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DOI: 10.1111/j.1708-8305.2009.00337.x

We report a case of eosinophilic meningitis due to *Angiostrongylus cantonensis* in a patient who returned from Thailand. The presence of a compatible epidemiologic history and eosinophilia in cerebrospinal fluid (CSF) lead to the diagnosis, which was confirmed by detection of specific antibodies. After treatment with albendazole and corticosteroids he recovered completely.

Eosinophilic meningitis is a rare condition. It is associated with parasitic and bacterial infections, drugs, and malignancies. The most common cause of eosinophilic meningitis in South East Asia and throughout the Pacific basin is *Angiostrongylus cantonensis*. Adults of this nematode parasite reside and lay their eggs in the pulmonary arteries of rats and other rodents. After hatching, first-stage larvae migrate up the respiratory tract, are swallowed and excreted with the feces via the gastrointestinal tract. They develop into second- and third-stage larvae within molluscs such as snails and slugs that serve as natural intermediate hosts. Humans become infected with third-stage larvae by consuming raw snails, vegetables contaminated by mollusc slime, or carrier hosts such as freshwater shrimps and terrestrial crabs that have themselves eaten infected molluscs. After either moving actively or being hematogenously transported to the central nervous system, third-stage larvae cause an inflammatory reaction. Larvae cannot complete their life cycle and eventually die after reaching the human central nervous system. We describe a case of eosinophilic meningitis due to *A. cantonensis* in a patient who returned from a trip to Thailand.

Case Report

A previously healthy 32-year-old Asian male presented with a 10-day history of ongoing moderate bitemporal treatment-resistant headache. He had visited Thailand 6 months ago and recalled eating raw fish, clams, vegetables, and salad during this trip.

On examination the patient was afebrile, fully conscious and orientated. The patient suffered from general mild lassitude, but neither neck stiffness nor focal neurological deficits were noted.

His blood leukocyte count was 8,500 cells/μL with a blood eosinophilia of 15.7% and elevated serum levels of immunoglobulin E of 5,748 IE/mL. Chest radiograph findings were normal, as were computed tomography (CT) of the brain and magnetic resonance imaging (MRI) of the brain and spinal cord. Electroencephalography showed normal alpha rhythm in absence of pathological patterns.

A lumbar puncture revealed an opening pressure of 23 cm H2O, 699 white blood cells (WBCs)/μL compared to the first lumbar puncture, a CSF protein level of 40 mg/dL, a CSF glucose level of 61 mg/dL, and a CSF lactate level of 1.73 mmol/L (Figure 1).

As the patient’s headache persisted, a second lumbar puncture was performed demonstrating an opening pressure of 25 cm H2O, an eosinophilic pleocytosis with an increase to 1,109 WBCs/μL compared to the first lumbar puncture, a CSF protein level of 40 mg/dL, a CSF glucose level of 61 mg/dL, and a CSF lactate level of 1.73 mmol/L.
Figure 1 (A) Eosinophilic granulocytes in May-Grünwald-Giemsa stained CSF. (B) Western blot analysis for *Angiostrongylus cantonensis* with specific antigenic 29 kDa and 31 kDa bands.

of 1.54 mmol/L. CSF culture for bacteria yielded no growth. Gram stain and Ziehl-Neelsen stain of CSF were negative.

Serologic tests for *Treponema pallidum*, *Borrelia burgdorferia*, *Leptospira, Mycoplasma pneumoniae*, *Chlamydia pneunoniae*, and *Brucella* were negative as well as tests for human immunodeficiency virus (HIV), herpes simplex virus (HSV), cytomegalovirus (CMV), and varicella zoster virus (VZV).

Serum and CSF samples were sent to the Diagnostic Centre, Swiss Tropical Institute in Basel, Switzerland. Western blot analysis using soluble antigen from young adult worms revealed antibodies against *Angiostrongylus* spp. in serum but not in CSF (Figure 1). Furthermore, the serum and CSF samples tested negative for antibodies against *Gnathostoma spinigerum*, which is also endemic in this area and a major differential diagnosis. The positive serology of strongyloides in the absence of gastrointestinal symptoms and in the absence of strongyloides larvae in the feces is more likely due to a cross-reaction than a coinfection with strongyloides.

Repeated lumbar puncture did not provide symptomatic relief of headaches in contrast to previous reports in literature. The patient received an antiparasitic treatment with albendazole (800 mg per day) in combination with corticosteroids. Dexamethasone was administered at a dosage of 12 mg per day during the first week and 6 mg per day on Days 8 to 21. Under this treatment regime the patient’s condition improved, his headaches ceased over the following weeks, and he became completely asymptomatic after 2 months.

**Discussion**

*Angiostrongylus cantonensis* is the most frequent cause of eosinophilic meningitis in travelers returning from endemic regions like South East Asia. Eosinophilic meningitis may well be underreported as eosinophilia of the CSF and can easily be missed. Clinical manifestations in humans usually develop between 2 to 35 days after the ingestion of larvae of *A cantonensis*. Main complaints are insidious or abrupt excruciating frontal, occipital, or bitemporal headache. Neck stiffness, nausea, and vomiting are also common findings. Paresthesias and hyperesthesias of the extremities, trunk, or face are distinctive neurological findings, which may persist for several weeks even after other symptoms have resolved. Cranial nerve involvement, seizures, and paralysis are rarely reported. Fever is generally absent or of low grade. CSF usually discloses an elevated opening pressure, a WBC count between 150 and 2,000/μL, and an eosinophilic pleocytosis, generally >20%. Thus, it is essential to perform a May-Grünwald-Giemsa stain of the CSF. The CSF protein level is typically increased, whereas the CSF glucose level remains normal. The peripheral WBC count is normal or slightly increased and the eosinophilia is less pronounced than in the CSF.

The diagnosis of *A cantonensis* meningitis is suggested by the triad of typical clinical presentation, eosinophilic
pleocytosis of the CSF, and a history of consumption of food likely to contain infective larvae in endemic areas.

The gold standard for diagnosis is the recovery of larvae from CSF, but this is rarely accomplished. Therefore, serological tests [enzyme immunoassays (EIA), Western blot] are used to confirm the diagnosis. Usually Western blot analysis reveals over ten antigenic bands with sera of patients with angiostrongyliasis. However, only five antigen bands (29 kDa, 31 kDa, 55 kDa, 85–99 kDa, 200–204 kDa) are specific for the diagnosis. Two of these antigen bands (29 kDa and 31 kDa) were clearly visible in our patient (Figure 1).

The most important differential diagnosis is eosinophilic meningitis due to the parasite G. spinigerum. It can be distinguished from angiostrongyliasis by involvement of nerve roots, xanthochromic or bloody CSF, and cerebral hemorrhage. The subspecies Angiostrongylus costaricensis found in Central America has a similar capacity to cause CSF eosinophilia. Other conditions associated with eosinophilic meningitis include cerebral schistosomiasis, cerebral toxocariasis, neurocysticercosis, neurotrichinosis, coccidioidomycosis, lymphoma, and intraventricular antibiotics.3

The treatment of angiostrongyliasis consists principally of supportive measures. Repeated lumbar punctures may provide symptomatic relief of headache by reducing intracranial pressure. One randomized double-blind study favored the use of 60 mg prednisolone per day for 2 weeks with regard to persistence of headache and the need for repeated lumbar punctures for symptomatic relief.4 Albendazole in the dosage of 15 mg/kg per day for 2 weeks reduced the duration of headaches significantly.5 Albendazole may induce an exacerbation of meningitis, possibly due to an inflammatory response following parasite death.6 Therefore a combination of corticosteroids and albendazole or mebendazole has been proposed.5,7

The prognosis of angiostrongyliasis is generally good. Most patients have a self-limited course and recover completely. Fatal courses are uncommon with a reported mortality rate of less than 0.5%.5 Unfortunately, there is no evidence that a single episode of angiostrongyliasis confers immunity, and reinfection has been reported.8

The diagnosis of angiostrongyliasis is extremely rare in Europe.3,9,10 Nevertheless, increasing intercontinental travel, immigration as well as importation of food from South East Asian countries demand greater awareness of this parasitic infection in the western hemisphere, which should be suspected in cases of eosinophilic meningitis with appropriate exposure history. The diagnosis is confirmed by detection of specific antibodies against A. cantonensis by Western blot. Although the combination therapy of albendazole and corticosteroids needs to be confirmed by further studies, we recommend it to travelers with eosinophilic meningitis due to A. cantonensis based on the experience with our patient.

Declaration of Interests
The authors state that they have no conflicts of interest.

References