Eosinophilic meningoencephalitis caused by *Angiostrongylus*, the parasitic 'rat lungworm': a case report

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Case report

A 73-year-old Nepalese woman was admitted to the medical ward of Ruttonjee Hospital on 13 June 2020. She enjoyed good past health and worked as a street cleaner. She presented with a 3-day history of fever, headache, and nausea. On admission, she was conscious and alert, and physical examination was unremarkable. Computed tomography (CT) of the brain was likewise unremarkable. Leukocytosis (white cell count 12.73×10^9/L) with raised neutrophils (absolute neutrophil count 7.43×10^9/L) and raised eosinophils (1.91×10^9/L) was noted.

Lumbar puncture yielded clear cerebrospinal fluid (CSF) with raised opening pressure of 29 cm H_2O. Cerebrospinal fluid showed leukocytosis (CSF white cell count 510/mm^3, lymphocytes: 76%), low glucose (CSF: 2.1 mmol/L; serum: 5.9 mmol/L) and high protein levels (1.24 g/L) but tested negative for bacteria, virus, acid-fast bacilli smear, fungal smear, and cryptococcus antigen. Empirical treatment for tuberculous meningitis including isoniazid, rifampicin, ethambutol, pyrazinamide, and dexamethasone was commenced. She responded quickly with resolution of fever and headache.

Nonetheless her condition deteriorated 5 days later with recurrence of fever, new-onset confusion, vomiting, and urinary incontinence. Alanine aminotransferase increased to 368 IU/L. In view of her deranged liver function, tuberculosis treatment was stopped. Serial eosinophil count rose from 1.91×10^9/L to 4.97×10^9/L. Plain and contrast brain CT were unremarkable with normal ventricle sizes. Magnetic resonance imaging of the brain showed inflammatory changes in bilateral cerebral and cerebellar sulcal spaces and the leptomeningeal region.

Due to new-onset confusion, incontinence and fever, a second lumbar puncture was performed and revealed a high opening pressure of 21 cm H_2O, turbid CSF with a rising white cell count of 920/mm^3 (lymphocytes: 60%, polymorphs: 40%), low glucose (CSF: 2.3 mmol/L; serum: 6.0 mmol/L) and high protein levels (0.71 g/L). Eosinophilic meningoencephalitis was suspected and a pathologist was consulted for eosinophil screening of her CSF. Eosinophils were found. The patient had no rash, diarrhoea, drug history or allergy that could account for eosinophilia. Stool analysis for parasites, ova and cysts was negative. Autoimmune markers including antineutrophil cytoplasmic antibody were negative. Cerebrospinal fluid did not reveal malignant cells. Cerebrospinal fluid was sent for polymerase chain reaction testing for parasites and was found to be positive for *Angiostrongylus* spp.

A further food history was explored. The patient had ingested raw snails from an unknown source 2 weeks prior to admission. She had a habit of consuming raw snails to boost bone health, a Nepalese custom.

She was prescribed prednisolone at a dose of 40 mg daily for 2 weeks then tapered off. Peripheral eosinophilia resolved within 5 days. She made a full neurological recovery and was discharged home.

Discussion

Angiostrongylus cantonensis is a parasitic helminth. It was first described in 'Canton' Guangzhou, China in 1935. Rats are the primary hosts. Eggs hatch in the rats' lungs, and first-stage larvae (L1) are passed in their faeces. Snails and slugs that feed on rat faeces act as intermediate hosts (L2). Larvae reach the third stage (L3) in the intermediate host and can infect humans when they consume slugs, snails or contaminated vegetables.[1]

Following human host ingestion, larvae (L3) are released in the gastrointestinal tract where they enter the bloodstream. They penetrate the liver, brain and spinal cord where they moult to mature stages (L4 and L5). Most cease to develop and die within the central nervous system. Nonetheless the presence of larvae alone attracts lymphocytes, plasma cells and eosinophils, generating an inflammatory response.

Since *Angiostrongylus* was first reported in 1945, over 2000 cases have been reported worldwide, mostly in Asia (Thailand: 47%; China: 27%), while four cases have been reported in Hong Kong.[2] It is the most common parasitic cause of eosinophilic meningitis. Symptoms are often mild or moderate and include headache, vomiting, photophobia, and neck stiffness. Fever is uncommon. In severe cases, heavy infestation can lead to coma and death.[3]

Angiostrongylus meningitis infection typically gives a CSF finding of leukocytosis with eosinophilia, and raised protein level with normal to low glucose level.[1] With the exception of eosinophilia in CSF, this mimics tuberculous meningitis.

The degree and evolution of eosinophilia can be variable. A study of infected travellers to Jamaica observed that although all their patients developed eosinophilia at some point, fewer than half had peripheral eosinophilia on their initial blood test. Eosinophil level did not peak until 2 weeks later. Only half of affected patients had eosinophils in their CSF at the time of their first lumbar puncture.[4] In our patient, eosinophils were not found in the first lumbar puncture although the peripheral eosinophil count continued to rise and did not peak for 13 days.

Causes of eosinophils in CSF include parasites (angiostrongyliasis, gnathostomiasis, and baylisascariasis), other infectious agents (bacteria, fungal, and virus), haematological malignancy, and adverse drug reactions. Diagnosis is often difficult. Larvae occur in only a number in the CSF and are hard to identify. Serological methods such as enzyme-linked immunosorbent assay and immunoblotting are not often available and are limited by cross-reactivity with other helminths.[3] Polymerase chain reaction of *Angiostrongylus cantonensis* DNA in the CSF is the most accurate way to confirm a diagnosis with 70% to 80% sensitivity and 99% specificity.[3]

Choice of anthelmintic drugs is controversial as there have been few clinical trials. They are more effective when started early, preferably within 2 weeks of infection, as they work better against younger larvae. By the time patients seek medical attention, larvae in the central nervous system have reached maturation, rendering treatment ineffective. Another concern is that worm death caused by anthelmintic drugs may trigger a severe inflammatory reaction and aggravate neurological symptoms.[5]

Prednisolone has been shown to be superior to placebo in reducing headache duration. Corticosteroids may reduce intracranial pressure and blunt the inflammatory reaction to dying worms.[6] Lumbar punctures are also reported to be effective in reducing intracranial pressure and relieving headache.[3]

There was a seemingly stable period after our patient's first lumbar puncture and the commencement of tuberculous meningitis treatment, with subsidence of fever and headache. Her transient improvement may have been due to the use of dexamethasone (as part of tuberculous meningitis treatment) and the relief of intracranial pressure by lumbar puncture.

The present case demonstrates that clinicians should be aware of the differential diagnosis of *Angiostrongylus* meningoencephalitis, especially in the context of eosinophilia, snail ingestion or travel to endemic areas. Timely confirmation by polymerase chain reaction testing of CSF is important. Supportive therapy with corticosteroids may provide symptom relief.

Author contributions

Both authors contributed to the concept of study, acquisition and analysis of data, drafting of the manuscript, and critical revision of the manuscript for important intellectual content. Both authors had full access to the data, contributed to the study, approved the final version for publication, and take responsibility for its accuracy and integrity.

Conflicts of interest

Both authors have disclosed no conflicts of interest.

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Ethics approval

The patient was treated in accordance with the Declaration of Helsinki and verbally agreed to publication of this anonymous case report.

References

1. Ansdell V, Wattanagoon Y. *Angiostrongylus cantonensis* in travelers: clinical manifestations, diagnosis, and treatment. Curr Opin Infect Dis 2018;31:399-408.
2. Wang QP, Lai DH, Zhu XQ, Chen XG, Lun ZR. Human angiostrongyliasis. Lancet Infect Dis 2008;8:621-30.
3. Murphy GS, Johnson S. Clinical aspects of eosinophilic meningitis and meningoencephalitis caused by *Angiostrongylus cantonensis*, the rat lungworm. Hawaii J Med Public Health 2013;72(6 Suppl 2):35-40.
4. Slom TJ, Cortese MM, Gerber SI, et al. An outbreak of eosinophilic meningitis caused by *Angiostrongylus cantonensis* in travelers returning from the Caribbean. N Engl J Med 2002;346:668-75.
5. Hidelaratchi MD, Riffsy MT, Wijesekera JC. A case of eosinophilic meningitis following monitor lizard meat consumption, exacerbated by anthelminthics. Ceylon Med J 2005;50:84-6.
6. Chotmongkol V, Sawanyawisuth K, Thavornpitak Y. Corticosteroid treatment of eosinophilic meningitis. Clin Infect Dis 2000;31:660-2.