

Eosinophilic Meningitis due to *Angiostrongylus Cantonensis*: First Reported Case in the UK

Angiostrongylus cantonensis, the rat lungworm, is the commonest cause of eosinophilic meningitis worldwide.¹ The organism is endemic in Southeast Asia and the Caribbean, although an increase in world travel has seen cases occurring outside of these areas. Cases have been documented in the USA,² Switzerland,³ Australia,⁴ and New Zealand.⁵ There are no previous reported cases of angiostrongyliasis in the UK. Eosinophilic meningitis is rare in the UK and awareness of parasitosis as an emergent cause of infectious disease remains relatively low. We report a case of *A. cantonensis* infection in a female patient returning to the UK from Thailand.

Case report

A thirty-year-old Thai woman, living in the UK, attended her local district general hospital with five days of worsening headache and meningism. The patient had been a resident of the UK for two years but had visited Thailand recently, returning ten days prior to her presentation to hospital. On her admission she was pyrexial with a temperature of 38°C. She had nuchal rigidity and photophobia, but no focal neurological deficits. A CT brain scan was reported as normal and lumbar puncture revealed slightly turbid CSF with 626 WBC per mm³ (90% lymphocytes, 10% polymorphs). CSF protein was 0.55g/L (normal 0.15-0.45). No organisms were seen on Gram stain and there was no growth on bacterial culture. The patient was treated symptomatically with a presumptive diagnosis of viral meningitis and discharged after seven days. At home, the patient's headache worsened and she developed diplopia and hyperaesthesia of the right lower limb. She was readmitted to her district general hospital nine days later and underwent further lumbar puncture. This revealed slightly turbid CSF with 483 WBC per mm³ (70% lymphocytes, 30% polymorphs). CSF protein was 0.75g/L. She was commenced on intravenous Aciclovir and an MRI of the brain ordered. MR scanning revealed multiple hyperintense white matter lesions and the patient was then transferred

to the regional neurology centre.

On arrival, the patient was pyrexial (38°C) with signs of nuchal rigidity and photophobia. She had a right sixth cranial nerve palsy and a patch of altered sensation over the lateral border of her right lower limb. No other abnormalities were evident on neurological examination. Review of her MRI scans revealed multiple white matter hyperintense lesions in the deep cerebral white matter, periventricular regions and in the corpus callosum, which did not enhance with gadolinium contrast (Figures 1 and 2). There was no enhancement of the pachymeninges. Lumbar puncture was repeated and revealed an opening pressure of 28cm of water, 361 WBC per mm³ (70% lymphocytes), protein of 0.73g/L, glucose of 2.61mmol/L (serum glucose 5.3mmol/L) and was negative for AAFB.

Further questioning revealed that whilst recently in Thailand she had visited Bangkok and the Northern region of Isaan. She had eaten snails, which she believed to be cooked, as part of a salad in the village from where she originally came. She had no specific risk factors for HIV infection and said she had tested negative six months prior to this illness. Review of her blood results from the original hospital admission revealed an eosinophilia of 1.35*10⁹/L (total white cell count 10.1*10⁹/L), which had persisted into her second admission. This prompted re-examination of the original CSF samples for eosinophils. Cytological analysis revealed a significant eosinophilia (Figure 3). In light of this, a parasitic infection was considered likely, in particular 'rat lungworm' meningitis caused by *Angiostrongylus cantonensis*.

While further microbiological investigations were being performed, the patient was treated with isoniazid, rifampicin, pyrazinamide and ethambutol with dexamethasone to cover the possibility of tuberculous meningitis. We discussed the case with the Department of Parasitology at the Hospital for tropical diseases in London, who arranged to send the patients serum and CSF samples to Bangkok to test for *Angiostrongylus cantonensis* and *Gnathostomia spinigerum* antibodies.



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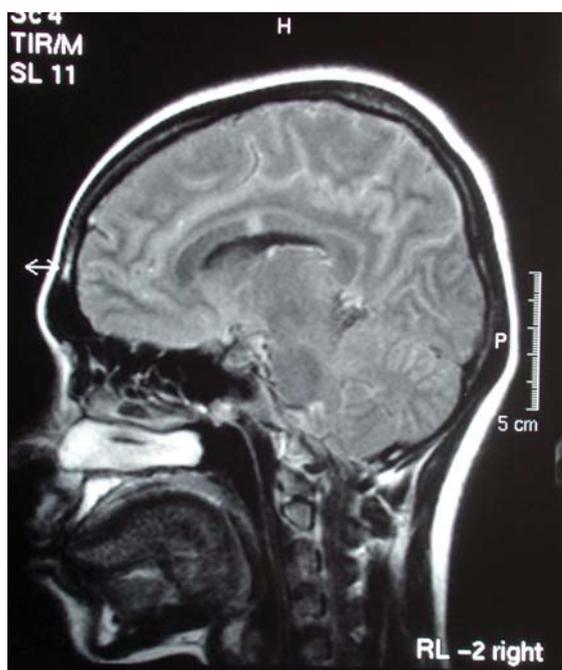


Figure 1: MR scan of the brain showing high signal lesion on the corpus callosum on T1 weighted images.

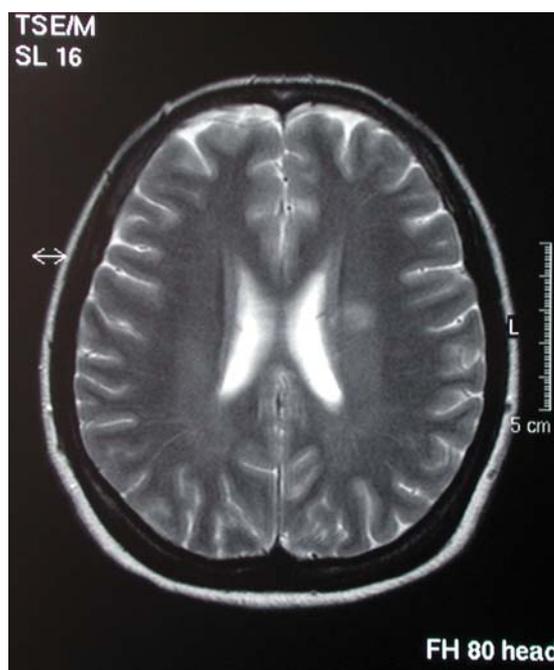


Figure 2: High signal lesion in the deep white matter on T2 weighted images.

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Polymerase Chain Reaction (PCR) for herpes simplex virus, varicella zoster virus, enterovirus and parechovirus nucleic acids were negative in the CSF. PCR for *Mycobacterium tuberculosis* was also negative. Serum HIV test was negative and cryptococcal antigen was not detected in the CSF. Stool and urine were negative for ova, cysts and parasites. As she was originally from an endemic area for *Strongyloides stercoralis* and was receiving steroids as part of the anti-tuberculosis treatment, she was treated with Ivermectin to prevent strongyloides hyperinfection. ELISA testing for *Strongyloides* was positive. Her symptoms however, were not thought to be attributable to *Strongyloides* infection.

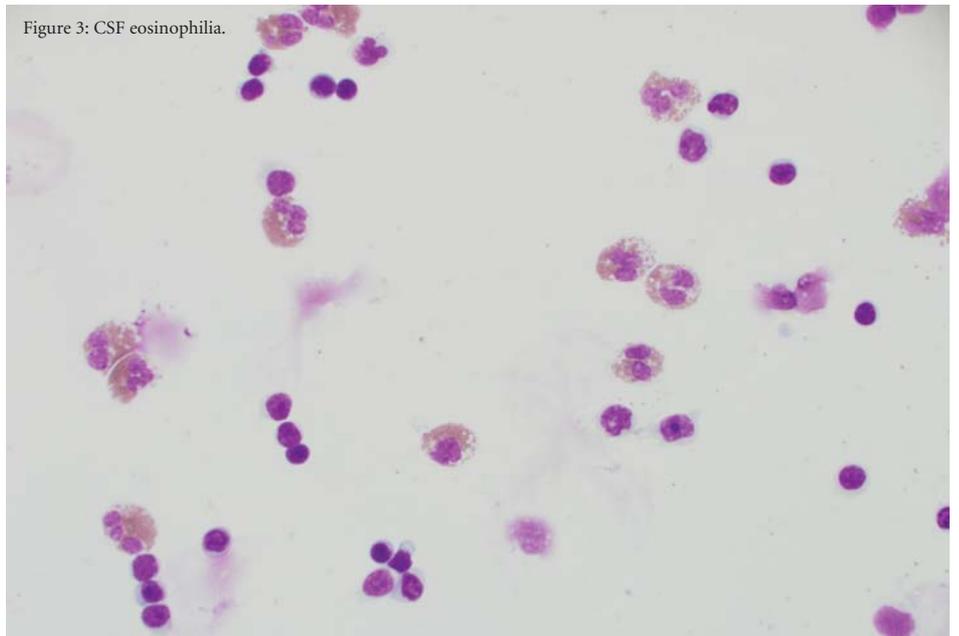
The patient's symptoms improved with reduction in severity of headache, resolution of meningism and improvement in diplopia. Repeat MRI scan of the brain showed almost complete resolution of the white matter lesions seen on the initial scan. Thirteen days after admission she was discharged home. Upon review seventeen days later her headache had considerably improved and she had no diplopia. Neurological examination was normal. Repeat lumbar puncture showed 170 WBC, predominantly lymphocytes.

Serum and CSF results confirmed infection with *Angiostrongylus cantonensis*. Anti tuberculosis chemotherapy was stopped and the dexamethasone tapered at a rate of 1mg per week until stopped. One month later she returned complaining of increasing headache and neck stiffness. Repeat LP revealed 506 WBC per mm³ (80% eosinophils). She was then treated with a further reducing course of dexamethasone. The patient's symptoms improved and her CSF WBC returned to normal.

Discussion

Angiostrongylus cantonensis is the most common cause of eosinophilic meningitis worldwide. This helminth is endemic in Southeast Asia and the Caribbean, and the disease is well recognised in these areas. The rat is the primary host of *A. cantonensis*. First stage larvae hatch in the lungs of rats and migrate into rat faeces via the trachea and gut. Molluscs that feed on rat excrement become intermediate hosts and within these organisms the first stage larvae moult twice to become the infective third stage larvae. Humans who eat the snails may then become infected. Vegetables contaminated with mollusc slime can also be a source of infection, as can transport hosts such as freshwater prawns, fish or crabs. In humans, larvae migrate via the bloodstream to the CNS where they cause an inflammatory response. Man is

Figure 3: CSF eosinophilia.



an accidental end stage host in which the larvae are unable to complete their life cycle and eventually die.^{1,6}

Symptoms occur 4-23 days after infection.⁷ The illness is characterised by headache and meningism.² Hyperaesthesia and paraesthesia are well described.¹ Other symptoms may include visual disturbance, fever, fatigue and cognitive impairment.^{7,8} On examination there may be photophobia, nuchal rigidity, sensory disturbance, encephalopathy, and cranial nerve, including abducens and facial nerve, palsy.^{2,7}

In this case, finding a peripheral eosinophilia prompted the search for parasitic causes and necessitated re-examination of the CSF for eosinophils. If parasitosis is clinically suspected the CSF should be specifically examined for eosinophils. It may be possible to visualise the worms on direct microscopy. The diagnosis can be confirmed by serological tests on serum and CSF.

The MRI scan in the patient described above demonstrated high signal lesions in deep white matter and corpus callosum, reminiscent of demyelination. A wide variety of MRI abnormalities have been reported in *Angiostrongyliasis*. High T2 signal intensity lesions, contrast enhancing lesions, meningeal enhancement and high signal intensity in the globus pallidus have all been reported.^{9,10,11}

We gave our patient no specific treatment for *A. cantonensis* infection. Treatment is primarily supportive, with repeated lumbar puncture thought to relieve symptoms of persistent

headache due to raised intracranial pressure. Anthelmintics can theoretically worsen symptoms due to an inflammatory reaction to dying worms. One randomised, double blind, placebo controlled trial has assessed the use of corticosteroids in eosinophilic meningitis.¹² This trial concluded that a two week course of prednisolone, 60mg per day, significantly reduced headache and the need for repeat lumbar puncture. No adverse effects were reported. In our patient, we believe that the initial improvement in symptoms and CSF findings was due to dexamethasone which she received as part of anti-tuberculous treatment. Her symptoms recurred and CSF eosinophilia worsened after discontinuing the steroids, but a further, more prolonged, course of steroids had a beneficial effect.

In cases of meningitis in travellers returning from endemic areas, it is vital to specifically look for eosinophils in the CSF. *A. cantonensis* is the commonest cause of eosinophilic meningitis worldwide, and subacute meningitis with associated hyperaesthesia and paraesthesia should alert the clinician to this organism. MRI scan appearances in this condition can be normal or widely variable. The hyperintense T2 signal lesions can appear demyelinating in character and location. This is, to our knowledge, the first reported case of *A. cantonensis* meningitis in the UK. With increasing international travel, it is likely that cases will be encountered more frequently in the future.

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