First report of human angiostrongyliasis acquired in Sydney

Clinical record

In 2001, a young man was admitted to hospital with a 3-day history of gradual-onset headache, nausea, vomiting, neck stiffness and photophobia. Three weeks earlier he had experienced a gastrointestinal illness (nausea, abdominal cramps, diarrhoea, myalgia and fever) that persisted for 1 week.

On examination, he had a low-grade fever and meningism. A cerebral computed tomography scan showed no abnormality. Peripheral blood eosinophilia (1.6 x 10⁹/L; reference range [RR], <0.44 x 10⁹/L) was noted, and examination of cerebrospinal fluid (CSF) showed 530 x 10⁶/L monocytes (RR, <5 x 10⁶/L), 22 x 10⁶/L red cells (RR, <1 x 10⁶/L), no eosinophils on routine staining, a raised protein level of 1.07 g/L (RR, <0.45 g/L) and a normal glucose level. He was treated with intravenous aciclovir for 6 days. A CSF polymerase chain reaction test for herpes simplex virus-1 (HSV-1) and HSV-2 subsequently gave negative results. Serological tests for Strongyloides and Angiostrongylus were negative. CSF and blood cultures showed no growth. Twelve days after admission, he was discharged from hospital with resolving meningism.

Five days later, increasing headache and drowsiness prompted his admission to another hospital. He was afebrile, drowsy and irritable, with gross bilateral papilloedema. He described mild paraesthesiae in both hands. He had peripheral blood eosinophilia (3.1 x 10⁹/L). Magnetic resonance imaging of the brain with gadolinium contrast showed multiple focal enhancing lesions in the deep white matter of both cerebral hemispheres, including the corpus callosum (Figure A). CSF from cisternal puncture was cloudy, under high pressure and, on routine toluidine blue staining, had 1008 x 10⁶/L polymorphonuclear cells (reference range, <5 x 10⁶/L), 186 x 10⁶/L monocytes and 21 x 10⁶/L red cells. Further staining to detect eosinophils was requested, and 90% of the polymorphonuclear cells were found to be eosinophilic (Figure B). His CSF protein level was elevated at 0.8 g/L and glucose level 2.6 mmol/L (50% serum glucose). India ink, Ziehl–Neelsen and Gram stains were negative.

Repeated questioning revealed that the patient had ingested, 5 weeks earlier, for a dare, two slugs from a garden in a Sydney suburb. Repeat Angiostrongylus immunoglobulin G (IgG) enzyme-linked immunosorbent assay (ELISA), tested in parallel with the first specimen, was positive, confirming seroconversion. Several leopard slugs, Limax maximus (Figure C), taken from the Sydney garden were dissected without finding larvae (Figure D), but no rats from the vicinity were examined for this infection.

Treatment comprised measures to reduce intracranial pressure with repeated CSF drainage, acetazolamide and dexamethasone, initially given intravenously, and then orally. CSF drainage consisted of one cisterna magna puncture and two lumbar punctures. Specific anthelmintic agents were not given. No ocular larvae were seen on regular formal ophthalmological review. He improved gradually and, after 17 days in hospital, was discharged with instructions to take a reducing dose of dexamethasone over 4 weeks. His final lumbar puncture 1 month after admission showed an almost normal CSF protein level (0.5 g/L) and a reduction in CSF white cell count (107 x 10⁶/L; 8% eosinophils). After 5 months, he successfully returned to full-time studies and competitive sport.

A: Magnetic resonance image of the brain, showing multiple focal enhancing lesions in the deep white matter (arrows).
B: Spun-down cerebrospinal fluid cells (Romanowsky stain: original magnification x400).
C: Limax maximus, the leopard slug, an intermediate host for Angiostrongylus cantonensis.
D: Adult female Angiostrongylus cantonensis from the lungs of Rattus norvegicus.

The lifecycle of the parasite from the adult stage in the definitive rat host through the intermediate mollusc host has been described previously. Humans become accidental hosts when they ingest the larval stage in raw or under-cooked molluscs or crustaceans or in fresh vegetables contaminated by infected molluscs. The diagnosis of angiostrongyliasis in a patient with acute eosinophilic meningoencephalitis is supported by a history of mollusc ingestion, but eliciting this may require specific questioning.

Symptoms occur 2–45 days after ingestion. The most common symptom is headache. Paraesthesiae are frequently reported. In our patient, the acute febrile gastrointestinal illness 6 days after consuming the slugs may have been caused by invasion of the parasite through the intestinal wall. Initial entry into the meninges, and subsequent migration through brain parenchyma, caused the clinical picture of meningitis followed by encephalitis. Seizures or other
Lessons from practice

- *Angiostrongylus cantonensis* should be considered as a cause of aseptic meningitis in patients with paraesthesiae and peripheral eosinophilia, and a history of exposure to undercooked molluscs or crustaceans.

- It is important to specifically request tests for eosinophils in cerebrospinal fluid (CSF) when their presence is suspected, particularly if there is peripheral eosinophilia.

- Eosinophilia in peripheral blood and CSF supports a diagnosis of *Angiostrongylus* meningoencephalitis, but absence of eosinophilia does not exclude it, particularly early in the course of the illness.

focal neurological symptoms may occur. Peripheral blood and CSF eosinophilia strongly support a diagnosis of *Angiostrongylus* meningoencephalitis, but may appear only later in the course of the illness, or, in a minority of cases, not at all.4,7,8

It is important to emphasise that eosinophils may not easily be differentiated from neutrophils on routine microbiological staining, such as with toluidine blue wet films. In aseptic meningitis, particularly associated with peripheral eosinophilia, specific Romanowsky stains, such as May–Grünwald–Giemsa or Wright stains, should be performed. An ELISA measuring total IgG can be diagnostic. The ELISA used to demonstrate seroconversion in this case utilised somatic antigens from adult *A. cantonensis*. The ELISA can be performed on serum or CSF. The Institute for Clinical Pathology and Medical Research at Westmead Hospital is the only centre in New South Wales performing the assay. As parasitologically proven cases are rare, it is difficult to determine the sensitivity and specificity of this assay.

*Angiostrongylus* meningitis is usually mild and resolves spontaneously over 6 weeks. Occasionally, cases are severe and may have chronic sequelae.2,5,6,8 No randomised controlled studies have assessed optimal management, but repeated CSF drainage may give symptomatic relief.8,9 Steroid treatment appears to be beneficial, presumably reducing CSF pressure and inflammatory response. Regimens reportedly of benefit include prednisolone 30–60 mg/day for 5 days,8 prednisolone 40–60 mg/day with weaning over a few weeks,9and prednisolone 60 mg/day for 2 weeks.10 The use of anthelmintic agents is controversial. Generally, avoidance of anthelmintic agents has been recommended on the (theoretical) basis of their potential for harm owing to the inflammatory response provoked by antigen release after parasite death.4,8

*A. cantonensis* should be considered as a cause of aseptic meningitis in patients with paraesthesiae and peripheral eosinophilia, and a history of exposure to undercooked molluscs or crustaceans. This report highlights the wider distribution of this parasite in Australia and, in particular, its close proximity to urban populations.

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