Case Report: Thoracic Myelopathy due to Gnathostomiasis Acquired in New Zealand

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Abstract. Gnathostomiasis is a zoonotic disease endemic in Asia. It most commonly manifests as gastrointestinal and cutaneous disease. Central nervous system involvement is a rare but feared complication, often leaving patients with permanent neurologic deficits. Clinicians outside of Asia and Latin America may have little experience with this illness, causing delays in diagnosis and treatment. We describe a 40-year-old woman who developed a progressive myelopathy over 18 months. She had never traveled outside of New Zealand. Cerebrospinal fluid (CSF) showed marked eosinophilia and *Gnathostoma* serology was positive in both serum and CSF. This is the first report of gnathostomiasis acquired in New Zealand, and the first case of neurognathostomiasis reported outside Asia. Clinicians should include neurognathostomiasis in the differential diagnosis of myelopathy and CSF eosinophilia, even if there is no history of travel to endemic areas.

CASE REPORT

A 40-year-old New Zealand Maori woman complained of right lower limb numbness and weakness and constipation over 2 months. Her symptoms started with numbness in the neck and severe “electric shock” pain down both arms, and down her spine on neck flexion. There were no changes in bladder function. She experienced intermittent itching on her abdomen. She was otherwise well and taking no medications. Examination at initial presentation showed a T4 sensory level to pinprick on the right side but no change in tone or power in the limbs. Cranial nerve examination was normal. Magnetic resonance imaging (MRI) of the spine showed patchy T2 hyperintensity extending from T1 to T12 associated with mild cord swelling (Figure 1). MRI of the brain was normal.

Cerebrospinal fluid (CSF) examination showed eosinophilic pleocytosis (white cells $80 \times 10^6/L$ [43% eosinophils, 57% lymphocytes], protein 0.93 g/L [normal 0.15–0.45 g/L]). CSF oligoclonal bands were present. Full blood count, routine serum chemistries, thyroid function, rheumatoid factor, antinuclear antibodies, serum complement, vitamin B12, folate, serum copper, human immunodeficiency virus, human T-lymphotropic viruses 1 and 2, cryptococcal serology, *Strongyloides* serology, and neuromyelitis optica IgG antibodies were all normal or negative. Total serum IgE was elevated at 524 kIU/L (normal 0–100 kIU/L) but specific IgE levels against *Dermatophagoides pteronyssinus* (house dust mite) were normal. Skin prick allergy testing to dust mites was also normal. Lactate dehydrogenase and JAK2 mutation analyses were unrevealing and three CSF cytologies showed no malignant cells. Computed tomography of chest, abdomen, and pelvis was normal. *Toxocara* serology showed a *Toxocara* IgG ratio of 3.01 (normal < 1) consistent with previous exposure. Given that she had never traveled outside of New Zealand, further parasitic testing was not requested. She was treated for presumed *Toxocara* myelitis with 15 days of mebendazole 200 mg daily and prednisone 60 mg daily.

After an initial mild improvement, her symptoms worsened. By 4 months, she required sticks to mobilize and had moderate lower limb weakness, extensor plantar responses,

and a T10 sensory level. By 10 months, she had developed spastic paraparesis. By 14 months, she was wheelchair bound and needed to self-catheterize. Repeat MRI of the spinal cord showed T2 hyperintensity and cord swelling at T8/T9 with patchy contrast enhancement (Figure 2). Further questioning revealed a high intake of raw fish, marinated fish, and seafood. Particular favorites included locally fished mullet, kahawai, paua, and sea snails. Often, the origin of the marinated fish was not known. Despite her lack of travel history, parasitic testing (performed in the Department of Helminthology of the Faculty of Tropical Medicine at Mahidol University in Bangkok) was undertaken on both serum and CSF. *Gnathostoma* testing (by detection of antibodies to *Gnathostoma spinigerum* 24-kDa antigen by immunoblot analysis) in both serum and CSF samples was positive, suggesting a diagnosis of central nervous system (CNS) gnathostomiasis. Immunoblot testing for angiostrongyliasis, fascioliasis, filariasis, paragonimiasis, toxocariasis, and trichinellosis as well as enzyme-linked immunosorbent assay (ELISA) testing for strongyloidiasis were all negative. She was treated with 3 weeks of albendazole 400 mg twice daily and 5 weeks of prednisone. Her neurological findings have stabilized but not improved.

DISCUSSION

The *Gnathostoma* nematode, first discovered in the stomach wall of a tiger in London zoo in 1836, is a zoonotic parasite most commonly encountered in southeast Asia, particularly Thailand.^{1,2} In recent years, increases in international travel mean that physicians outside endemic areas are increasingly confronted with this disease in returned travelers.^{2,3} In addition, an increasing number of countries are reporting locally acquired disease, with cases acquired in Africa, the Americas, and Australia appearing in the literature.^{2,4–8} Of the six *Gnathostoma* species that cause human disease, the most common is *G. spinigerum*, whose definitive hosts are vertebrates such as dogs and cats.⁴

The *Gnathostoma* life cycle requires three hosts. Initially, *Gnathostoma* eggs are shed in the feces of definitive animal hosts.^{2,4} Once in fresh water, they embryonate and become first-stage larvae (L1). These larvae are ingested by copepods, and further mature into second-stage larvae (L2).^{2,4} Hosts that feed on such crustaceans (fish, eels, snakes, and frogs) acquire L2, which mature in their intestines to third-stage

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FIGURE 1. T2 weighted sagittal (left image) and axial (right image) magnetic resonance imaging of the thoracic spine at initial presentation showing patchy T2 hyperintensity and cord swelling within the thoracic cord. Axial images taken at the level of the T8/9 intervertebral disc.

larvae (L3) and encyst in their tissues.^{2,4} Humans are accidental hosts, becoming infected through consumption of muscle-encysted L3 larvae in undercooked freshwater fish, frogs, or snakes.^{2,4} Infection may also occur through consumption of contaminated water or from direct skin penetration from L3 in infected meat. Most cases acquired in

endemic countries are due to ingestion of raw or undercooked freshwater fish in cheap eateries (more up-market establishments generally serve salt-water fish in their ceviche or sashimi, which tend not to harbor parasites).^{2,4}

Tissue damage in affected organs results from direct larval migration, release of destructive proteases by the parasite

FIGURE 2. Sagittal T2 (right image) and axial T1 post-contrast (left image) magnetic resonance imaging of the spinal cord after 14 months showing T2 hyperintensity and patchy contrast enhancement at the T8/9 spinal level (red arrow).

and the host's immune response.³ The clinical symptoms of gnathostomiasis reflect the nematode's migration through the human body. Once ingested, the parasite penetrates the intestinal wall and migrates via the portal system to the liver.²⁻⁴ During this phase, which is often misdiagnosed as gastroenteritis or food poisoning, patients may report abdominal discomfort, nausea, vomiting, and general malaise.²⁻⁴ Serum eosinophilia often develops at this stage.² Larvae often remain dormant here for a number of months, sometimes years (especially in cases without cutaneous involvement), but may later progress to involve other tissues.⁴ Any tissues can be involved, but some, such as the skin, are classic.²⁻⁴ The most common presentation of gnathostomiasis is cutaneous, with migratory, pruritic skin swellings.⁴ The eye, lungs, gastrointestinal, genitourinary, and central nervous systems can all be affected.^{2,4}

CNS involvement with gnathostomiasis is an uncommon but potentially devastating complication of disease. To date, it has only been reported in cases arising in the Asian continent, and only as a result of *G. spinigerum* infection.³ Many of the "classic" *Gnathostoma* manifestations, such as cutaneous disease, may be absent in neurognathostomiasis.³ The initial manifestation is often, as in our case, one of severe radicular pain, which represents larval migration via peripheral nerves into the CNS.^{2,3} Once in the CNS, larvae measuring an average of 3 mm in length burrow through nervous tissue, producing characteristic linear hemorrhagic tracts on brain imaging.^{2,3} Burrowing through vessels can result in hemorrhagic complications (subdural and subarachnoid hemorrhage).³

CNS involvement can produce a myelopathy, encephalopathy, meningitis, or intracranial hemorrhagic disease. *Gnathostoma* myelopathy is the most common form of neurognathostomiasis and classically begins with a radiculitis as the parasite invades the spinal cord through nerve roots, followed by progressive spastic paraparesis with loss of bowel and bladder control and a spinal sensory level, usually in the thoracic region.³ Spinal MRI shows longitudinally extensive T2 hyperintense cord lesions with cord swelling.^{3,9} Gadolinium enhancement, if present, is usually slight or ill defined.^{3,9}

Cerebral gnathostomiasis may present with a decreased level of consciousness, headaches, and cranial nerve (most commonly palsies).^{3,10} Hemorrhagic complications may also occur, usually resulting in sudden neurological decline and focal neurological signs.^{3,10} Magnetic brain imaging in these cases may show hemorrhagic tracts, which if present are a strong pointer to the diagnosis of neurognathostomiasis.^{3,10} Meningitis presents with typical symptoms of meningeal irritation (headache, photophobia, neck stiffness).

CSF examination may be helpful, due to the marked eosinophilic pleocytosis seen in this disease.^{3,10} The presence of red cells in the CSF is also considered characteristic, probably as a result of microhemorrhages resulting from the mechanisms described above.³ In endemic areas, the main differential for CSF eosinophilia is *Angiostrongylus* infection, but this is usually easily differentiated by the absence of radicular pain, hemorrhagic brain lesions, and red cells in CSF examination.³

Immunodiagnostic techniques looking for antibodies to *Gnathostoma* species in the serum and CSF are the mainstay of diagnosis. The screening tests usually use ELISA techniques, with confirmation via Western blot.³

There is no accepted treatment regimen for neurognathostomiasis. Most reported cases have been treated with albendazole for 3–4 weeks, usually with corticosteroids to minimize cord inflammation and paradoxical worsening in symptoms induced by parasite death.³ Despite treatment, neurologic disability is common and likely related to the delay in treatment from the time of initial presentation.^{2,3}

This is the first case of gnathostomiasis acquired in New Zealand, and is the first case of neurognathostomiasis reported outside of the Asian continent. How our patient acquired the nematode is unclear, but the most plausible explanation is the consumption of imported fish infected with *Gnathostoma* cysts. *Gnathostoma* is exotoxic to New Zealand, and among potential intermediate hosts only goldfish would be likely to survive. The likelihood of it perpetuating its life cycle in New Zealand is therefore remote.¹¹ For this reason, consumption of native fish infected with the parasite seems a less likely explanation.

Physicians should consider gnathostomiasis in the differential diagnosis of eosinophilic myelitis not only in travelers returning from endemic areas but also in patients who have not visited these countries, especially if they have a history of raw fish consumption.

Received April 11, 2016. Accepted for publication May 27, 2016.

Published online July 11, 2016.

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