# Cutaneous and Medullar Gnathostomiasis in Travelers to Mexico and Thailand

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Gnathostomiasis is a rare nematode disease acquired by travelers to endemic areas. The most common clinical presentations are cutaneous forms; however, neurologic involvement can also occur. We present two cases of gnathostomiasis, one of them with severe neurologic complications, in Spanish travelers to Thailand and Mexico, who consumed local food and became infected.

## Case Report 1

A 31-year-old Spanish male traveler spent 20 days touring Thailand, staying for most of the time in Bangkok. During this time, he experienced an episode of epigastric pain with nausea, vomiting and fever, which he could not attribute to a single meal because he ate all sorts of local food, including raw fish and crab salads. He was treated with loperamide, and recovered after 4 days. A week later, back in Spain, he noticed a slightly reddish and tender lesion on the skin of his right groin. It was associated with a dysesthesic sensation characterized by painful hypersensitivity, initially located on the right side of the chest, and extending to the abdomen and the lumbar region on both sides. A few days later, he noticed weakness and paresthesia in both legs and feet. The next day, he developed pain in the lower abdomen and urinary retention.

Physical examination was unremarkable, except for the neurologic findings. Sensation was altered in the D5–D6 dermatomes. Light touch was perceived as uncomfortable, and pinprick as excessively painful. There was also bilateral hyperreflexia, bilateral Babinski's sign and a distended urinary bladder. Motor power was 5/6 in both legs. Apart from these findings, neurologic examination was normal.

Blood cell counts, total eosinophils and erythrocyte sedimentation rate were within normal ranges. Biochemical measurements were normal, except for elevated serum creatinine (1.7 mg/dL) and cholesterol (263 mg/dL). Urinalysis was normal. A spinal tap was performed, and showed a colorless fluid with a normal initial pressure, 10 cells/mm$^3$ (90% mononucleated) and normal glucose and protein content. Conventional culture of the cerebrospinal fluid (CSF) was negative, and serologic studies of the CSF for syphilis, *Borrelia burgdorferi*, varicella-zoster, herpes, picornavirus, measles and mumps were negative. Magnetic resonance imaging of the brain and dorsal spinal cord was normal. An anti-HIV antibody test was negative. Anti-DNA, autoantibody and antinuclear antibody titers were all negative. Serologic studies in serum for syphilis, toxoplasmosis, varicella-zoster, *Rickettsia conorii* IgG, mumps, measles, herpes simplex 1 and 2 IgG and *Borrelia burgdorferi* were all negative. Serology for enterovirus Echo-Coxsackie was positive at a titer of 1 : 128. *Angiostrongylus* serology could not be performed.

On the grounds of clinical suspicion based on the epidemiologic and cutaneous findings, the patient received treatment with albendazole (400 mg b.i.d.) for 1 month, together with dexamethasone and vitamin B complex. Initial *Gnathostoma* serology (enzyme-linked immunosorbent assay, crude antigen preparation of *Gnathostoma spinigerum* from Thailand, in-house test of Robert Koch Institute, Berlin, Germany, provided by Professor K. Janitschke) was negative. Follow-up serology on the 21st day after initiation of treatment yielded a positive result for *Gnathostoma*. All other antibody tests showed no significant titer movements compared to the first set of samples.

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There was complete recovery of all the neurologic defects during the first 4 weeks of therapy, and after 6 months of follow-up the patient remains well.

## Case Report 2

A 40-year-old Spanish woman attended the outpatient department complaining of a 14-month history of lumps in both arms and legs. She had no relevant past medical history. On examination, there were multiple and slightly tender purple subcutaneous nodules, 1 to 4 cm in diameter, in all four limbs. The patient reported that the nodules appeared and disappeared spontaneously in a waxing-and-waning pattern over 2- to 3-day periods, without any associated symptoms except for light pain. She had experienced many similar episodes, the last one 20 days before consultation. The lesions had been biopsied three times. The histologic changes were present mainly in the subcutaneous layers, with mechanical disruption of the connective and fat tissues with small areas of hemorrhage, edema and focal inflammatory infiltrates composed mainly of eosinophils (Fig. 1). The periodic acid–Schiff (PAS) reaction for fungi was negative. Parasites were not seen in the first two biopsies, but in the third one a section of a larval worm was observed in the subcutaneous tissue (Fig. 2). On physical examination, no abnormalities were detected. Full blood count and white cell count differential were within normal ranges. Serologic tests for *Echinococcus granulosus*, *Fasciola hepatica*, lymphatic filaria and *Onchocerca volvulus* were negative.

The patient had traveled to different countries during the previous 9 years, including Mexico, Guatemala, Honduras, Costa Rica, northern India, Indonesia, Pakistan, China, Namibia and Botswana. She had eaten "ceviche" while in Mexico. As gnathostomiasis is endemic in many of them, we performed serologic testing for this parasite. The serology test was positive for *Gnathostoma spinigerum*. The patient was treated with 800 mg of oral albendazole once a day for 3 weeks. The episodes of subcutaneous nodules decreased in frequency and intensity over the next 12 months, but relapsed on two more occasions after albendazole therapy.

## Discussion

*G. spinigerum*, *G. hispidum, G. nipponicum* and *G. doloresi* are nematode worms that live in tumor-like lesions formed in the stomach walls of dogs, cats and other carnivores. Eggs are passed via the feces into water, where they undergo embryologic development and hatch. There are two intermediate hosts: a crustacean, *Cyclops*, which ingests the larvae, and a second intermediate host that eats the *Cyclops*: fish, frogs, snakes, birds and small mammals.[1] Larvae develop into the third stage in the flesh of these animals. *Gnathostoma* infects humans following ingestion of third-stage larvae in undercooked fish, such as "ceviche" – marinated raw fish – consumed in Mexico and Peru,[2] fermented fish (which is a Thai delicacy), raw snakes, frogs, crustaceans, amphibians or other animal flesh such as undercooked chicken. Although rare, prenatal transmission from mother to fetus and transcutaneous infection have been described.[1] The infection is found mainly in Southeast Asia, namely in Thailand, Vietnam, Philippines, Malaysia, Myanmar, Bangladesh, Cambodia, Laos and Indonesia. It has also been documented in China, India, Japan, Central America (Mexico),[2,3] South America (Ecuador), and East Africa,[4] and is increasingly being reported as an imported disease in nonendemic countries.[5] In humans, larvae are unable to fully develop, and they wander through the tissues causing migratory swellings, often in the subcutaneous tissues (cutaneous gnathostomiasis). Sometimes the larva burrows deep into the internal tissues, such as muscles, retina, liver, lungs, gastrointestinal tract and genitourinary system; central nervous system (CNS) involvement can have a potentially fatal outcome.[1] Two main types of cutaneous lesions have been described. The most common is an intermittent migratory erythematous edema, which may be highly

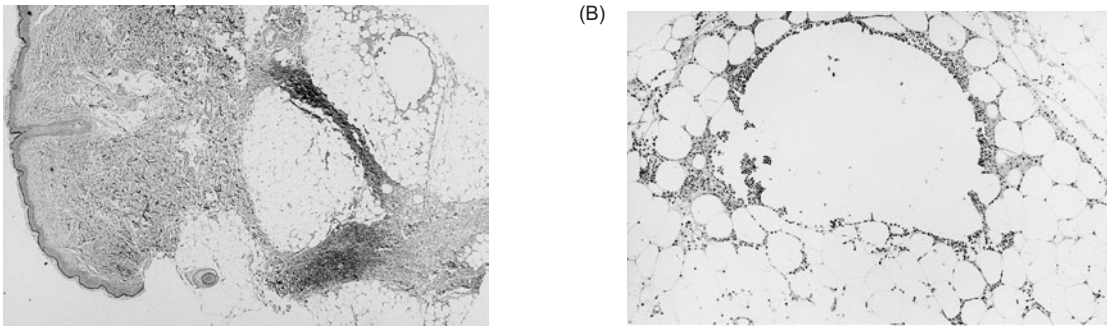
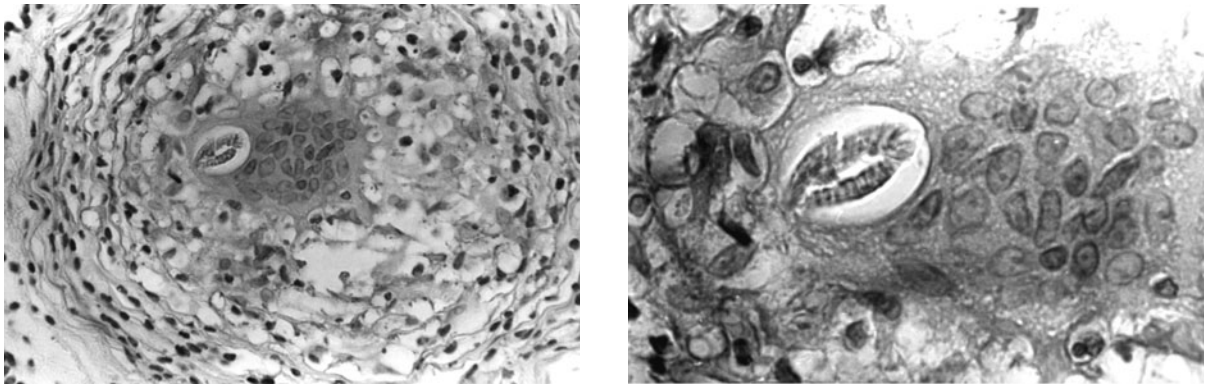



**Figure 1** (A) Subcutaneous tissue: focal mechanical disruption of collagen and fat lobule, with an inflammatory reaction composed of eosinophils, lymphocytes and histiocytes. (B) The hollow produced after larval migration.



(A) (B)

**Figure 2** (A) Inflammatory reaction around a section of a larval worm in the subcutaneous tissue. (B) A closer view of the parasite section. Hematoxylin and eosin, ×100.

pruritic and painful. It usually lasts for a few hours to a few days, and then migrates to other areas. It occurs in an episodic fashion. Episodes tend to become less intense and of shorter duration after time. Another less frequent presentation is that of a serpiginous pruritic cord (creeping eruption), from which the larvae can be recovered. Occasionally, microabscesses or nodular lesions can be seen.[6] Histopathologically, gross mechanical disruption can be observed along the track of a migrating larva. In its wake, the parasite leaves edema and small hemorrhage, moderate to large numbers of eosinophils, lymphocytes and plasma cells, and a few neutrophils dispersed in edema fluid.[6] A stationary parasite can elicit an intense inflammatory reaction, with many eosinophils and karyorrhectic debris. A fibrogranulomatous response develops around the periphery.

Radiculomyelopathy is the commonest neurologic presentation of the disease. However, myeloencephalitis, subarachnoid hemorrhage and isolated eosinophilic meningitis are also observed.[7–9] Radiculomyelitis cases are characterized by severe and burning root pain, paraplegia, tetraplegia or monoplegia, sensory defects and associated sphincter involvement causing urinary retention. Paroxysmal crisis of bilateral excruciating pain has been attributed to the penetration of larvae through the spinal roots. Occasionally, pure medullar forms without complete recovery after treatment have been reported.[10] In our case, it is possible that prompt therapy with albendazole and corticosteroids averted a more severe disease course, leading to complete recovery of the neurologic deficits. When larvae penetrate the CSF and the brain, the migratory movement of the parasite within the tissues can cause neurologic defects due to local hemorrhages and furrows.[11,12] The CSF shows eosinophilic pleiocytosis in most cases, but peripheral eosinophilia may not be present. In different series of CNS gnathostomiasis, mortality varied from 7.7% to 25%.[8,9] Definitive diagnosis is established by direct demonstration of larvae. Indirect diagnosis by means of serology using crude antigen is the most commonly used diagnostic method.[1]

Treatment options for gnathostomiasis include albendazole (400 mg b.i.d. or 800 mg once a day) for 3 or 4 weeks, with cure rates as high as 94%.[10,13] Refractory cases have been successfully treated with ivermectin (220 μg/kg/day) for 2 consecutive days.[14] In cutaneous forms, parasites might emerge from under the skin, and can be removed.[5] Dexamethasone can be used in cases with neurologic involvement.

In the present cases, we could not confirm the diagnosis of gnathostomiasis by direct visualization of the parasite, but seroconversions for *G. spinigerum*, consistent clinical presentations, epidemiologic evidence (food consumed and geographic locale), resolution of symptoms following treatment and absence of plausible differential diagnoses point at the correct diagnosis in both cases.

In conclusion, physicians should advise travelers to gnathostomiasis-endemic areas to avoid undercooked fish, and they should be alerted to the cutaneous and neurologic manifestations associated with this disease, as early treatment may prevent serious complications.

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Mahaballipuram, a rock temple, Tamil Nadu, India. Submitted by Dr. Davidson H. Hamer.