

Migratory Nodules in a Traveler

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A 41-year-old man presented to a dermatology clinic in the United States with a migratory subcutaneous nodule overlying the left upper chest that initially developed 12 months prior and continued to migrate along the trunk and proximal aspect of the arms. The patient had spent the last 3 years residing in Peru. He never observed more than 1 nodule at a time and denied associated fever, headache, visual changes, chest pain, cough, abdominal pain, and diarrhea. Laboratory studies including a blood eosinophil count and serum *Strongyloides* immunoglobulins were within reference range. An excisional biopsy was performed.

WHAT'S YOUR DIAGNOSIS?

- a. cutaneous larva migrans
- b. erythema nodosum
- c. gnathostomiasis
- d. larva currens
- e. loiasis

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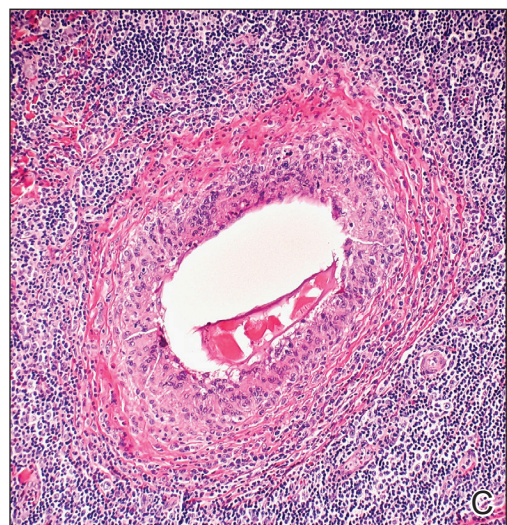
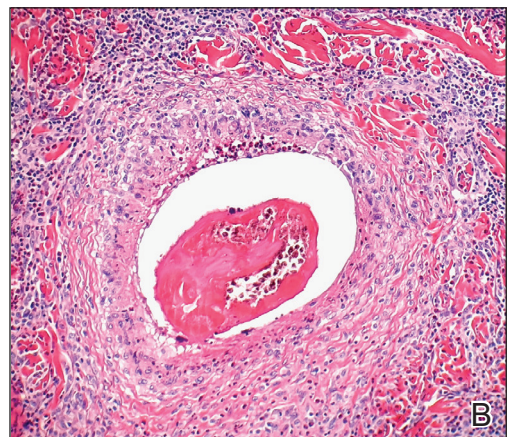
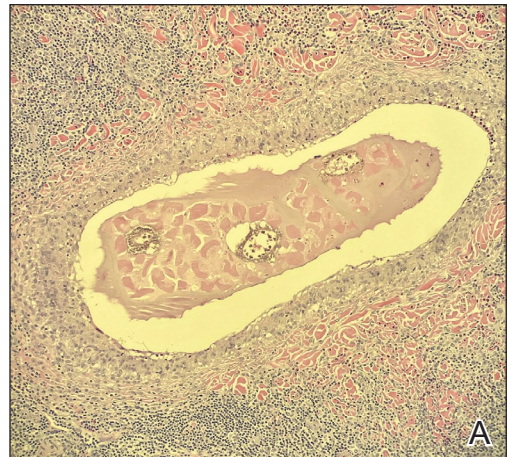
THE DIAGNOSIS: Gnathostomiasis

The biopsy demonstrated a dense, eosinophilic, granulomatous infiltrate surrounding sections of a parasite with skeletal muscle bundles and intestines containing a brush border and luminal debris (Figure), which was consistent with a diagnosis of gnathostomiasis. Upon further questioning, he revealed that while in Peru he frequently consumed ceviche, which is a dish typically made from fresh raw fish cured in lemon or lime juice. He subsequently was treated with oral ivermectin 0.2 mg/kg once daily for 2 days with no evidence of recurrence 12 months later.

Cutaneous gnathostomiasis is the most common manifestation of infection caused by the third-stage larvae of the genus *Gnathostoma*. The nematode is endemic to tropical and subtropical regions of Japan and Southeast Asia, particularly Thailand. The disease has been increasingly observed in Central and South America. Humans can become infected through ingestion of undercooked meats, particularly freshwater fish but also poultry, snakes, or frogs. Few cases have been reported in North America and Europe presumably due to more stringent regulations governing the sourcing and storage of fish for consumption.¹⁻³ Restaurants in endemic regions also may use cheaper local freshwater or brackish fish compared to restaurants in the West, which use more expensive saltwater fish that do not harbor *Gnathostoma* species.¹ There is a false belief among restauranteurs and consumers that the larvae can be reliably killed by marinating meat in citrus juice or with concurrent consumption of alcohol or hot spices.² Adequately cooking or freezing meat to 20 °C for 3 to 5 days are the only effective ways to ensure that the larvae are killed.¹⁻³

The parasite requires its natural definitive hosts—fish-eating mammals such as pigs, cats, and dogs—to complete its life cycle and reproduce. Humans are accidental hosts in whom the parasite fails to reach sexual maturity.¹⁻³ Consequently, symptoms commonly are due to the migration of only 1 larva, but occasionally infection with 2 or more has been observed.^{1,4}

Human infection initially may result in malaise, fever, anorexia, abdominal pain, nausea, vomiting, and diarrhea as the parasite migrates through the stomach, intestines, and liver. After 2 to 4 weeks, larvae may reach the skin where they most commonly create ill-defined, erythematous, indurated, round or oval plaques or nodules described as nodular migratory panniculitis. These lesions tend to develop on the trunk or arms and correspond to the location of the migrating worm.^{1,3,5} The larvae have been observed to migrate at 1 cm/h.⁶ Symptoms often wax and wane, with individual nodules lasting approximately 1 to 2 weeks. Uniquely, larval migration can result in a trail of subcutaneous hemorrhage that is considered



A–C, Histopathology showed a dense eosinophilic and granulomatous infiltrate surrounding a transected parasite with visible skeletal muscle bundles and bowels (H&E, original magnifications $\times 40$).

pathognomonic and helps to differentiate gnathostomiasis from other forms of parasitosis such as strongyloidiasis and sparganosis.^{1,3} Larvae are highly motile and invasive, and they are capable of producing a wide range of symptoms affecting virtually any part of the body.^{1,2} Depending on the anatomic location of the migrating worm, infection also may result in neurologic, gastrointestinal, pulmonary, or ocular symptoms.^{1-3,7} Eosinophilia is common but can subside in the chronic stage, as seen in our patient.¹

The classic triad of intermittent migratory nodules, eosinophilia, and a history of travel to Southeast Asia or another endemic region should raise suspicion for gnathostomiasis.^{1-3,5,7} Unfortunately, confirmatory testing such as *Gnathostoma* serology is not readily available in the United States, and available serologic tests demonstrate frequent false positives and incomplete cross-reactivity.^{1,2,8} Accordingly, the diagnosis most commonly is solidified by combining cardinal clinical features with histologic findings of a dense eosinophilic inflammatory infiltrate involving the dermis and hypodermis.^{2,5} In one study, the larva itself was only found in 12 of 66 (18%) skin biopsy specimens from patients with gnathostomiasis.⁵ If the larva is detected within the sections, it ranges from 2.5 to 12.5 mm in length and 0.4 to 1.2 mm in width and can exhibit cuticular spines, intestinal cells, and characteristic large lateral chords.^{1,5}

The treatment of choice is surgical removal of the worm. Oral albendazole (400–800 mg/d for 21 days) also is considered a first-line treatment and results in clinical cure in approximately 90% of cases. Two doses of oral ivermectin (0.2 mg/kg) spaced 24 to 48 hours apart is an acceptable alternative with comparable efficacy.¹⁻³ Care should be taken if involvement of the central nervous system is suspected, as antihelminthic treatment theoretically could be deleterious due to an inflammatory response to the dying larvae.^{1,2,9}

In the differential diagnosis, loiasis can resemble gnathostomiasis, but the former is endemic to Africa.³

Cutaneous larva migrans most frequently is caused by hookworms from the genus *Ancylostoma*, which classically leads to superficial serpiginous linear plaques that migrate at a rate of several millimeters per day. However, the larvae are believed to lack the collagenase enzyme required to penetrate the epidermal basement membrane and thus are not capable of producing deep-seated nodules or visceral symptoms.³ Strongyloidiasis (larva currens) generally exhibits a more linear morphology, and infection would result in positive *Strongyloides* serology.⁷ Erythema nodosum is a septal panniculitis that can be triggered by infection, pregnancy, medications, connective tissue diseases, inflammatory conditions, and underlying malignancy.¹⁰

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