CASE REPORT: GNATHOSTOMIASIS IN TWO TRAVELERS TO ZAMBIA

DEVON C. HALE, LUCILLE BLUMBERG, AND JOHN FREAN

Department of Medicine, Division of Infectious Diseases University of Utah, Salt Lake City, Utah; Department of Clinical Microbiology and Infectious Diseases, University of the Witwatersrand and the National Health Laboratory Service, Johannesburg, South Africa

Abstract. Gnathostomiasis is a systemic infection caused by migrating nematode larvae of the genus Gnathostoma. It is a zoonosis involving a wide variety of animals as intermediate and definitive hosts, and consumption of raw fish is the main risk factor. The condition is most commonly seen in southeastern Asia, but has been described in a number of other countries, all outside Africa. We report the infection in two travelers returning from southcentral Africa, who presented with non-specific symptoms and marked eosinophilia, and in whom schistosomiasis was initially suspected. The typical migratory skin lesions of gnathostomiasis appeared later. The infections responded well to albendazole. The patients acquired the infection in western Zambia; this region of Africa appears to be a newly identified risk area for gnathostomiasis in tourists who indulge in eating raw freshwater fish.

CASE REPORT

Gnathostoma species are tissue nematodes that should be considered in the differential diagnosis when a traveler from an endemic area presents with eosinophilia, especially when there is an associated migratory skin rash. Much of our knowledge regarding this organism has emerged from Southeast Asia, but reports from Mexico, Equador, and Japan show that infection with this parasite is widespread. The medical literature has not previously considered Africa to be a risk region for gnathostomiasis, although a cluster of three cases was diagnosed in 1994 (Wolfe MD, unpublished data).

This is a report of a single-source infection of two men who fished on the Zambezi River in western Zambia from August 4 to August 8, 1998. The pair, a father and son, ate fresh, raw bream marinated in lemon juice. Each returned to his respective home where symptoms developed about 12–14 days later.

Case 1. The father was a 70-year-old man who developed fever, chills, headache, myalgias, and arthralgias on August 19, 1998. The symptoms lasted several days, resolved, and then recurred on August 25. He was seen on August 28 at the University of Utah/Salt Lake County International Travel Clinic and asked if he might have malaria. The results of his physical examination were normal and his malaria blood smear was negative, but his white blood cell count (WBC) was 15,900 × 10^9/L with 25% eosinophils (normal ranges: WBC = 3–11.2 × 10^9/L, eosinophils = 0–6%). On August 31 he was treated presumptively with praziquantel for schistosomiasis. Serologic test results for schistosomiasis and strongyloidiasis were negative. He seemed to improve but returned on September 15 with a rash on his entire right anterior chest wall extending over the deltoid area of his shoulder. The rash was erythematous, hot to the touch, indurated, and resembled a streptococcal cellulitis. The ampicillin/sulbactam that had been prescribed one day earlier by his primary care doctor was continued, but prednisone, which had been started at the same time, was discontinued. His absolute eosinophil count remained elevated at 1,470 × 10^9/L. Serologic test results for filariasis, toxocariasis, and trichinosis were negative. A return visit on September 17 showed that the skin rash had almost completely resolved, leaving a 2 × 3 mm, slightly raised, firm nodule on the shoulder. He was seen on an emergency basis in the evening because the nodule had migrated 4 cm toward his scapula, leaving a broad-based (1–2 cm) erythematous, indurated track (Figure 1). Gnathostomiasis was suspected and he was then treated with albendazole (400 mg twice a day). Two separate biopsies were performed and did not detect any organism. A Western blot assay for gnathostomiasis done at the Mahidol University Applied and Technological Service Center in Bangkok, Thailand was reported on October 1 as giving a positive result. The patient’s symptoms resolved within four days of starting treatment with albendazole.

Case 2. The son was a 45-year-old man living in South Africa who was assessed initially by his general practitioner and referred to the South African Institute for Medical Research on September 5, 1998. His presenting symptoms were muscle pain, intermittent low-grade fever, nausea, abdominal pain, sweating, chills, chest pain, shortness of breath, and fatigue. He had a WBC count of 19,970 × 10^9/L with 55.5% eosinophils. He was treated empirically with praziquantel for schistosomiasis. Results of tests for schistosomal-specific IgM, IgG, and IgA antibodies done on September 5 and 14 were subsequently reported as negative. His work up included three malaria smears, two Plasmodium falciparum histidine-rich protein 2 blood antigen rapid tests, serologic analysis for amebiasis, abdominal ultrasound, and a chest radiograph, all of which were non-diagnostic.

One week after initial presentation, he was seen with a 10-cm cutaneous swelling of the left buttock that was slightly hot to the touch, erythematous, and slightly pruritic, with a white center. He was given amoxicillin-clavulanate and the rash resolved in eight hours. One week later, the original lesion reappeared accompanied by a similar lesion 20 cm down the posterior thigh. These lesions were indurated, erythematous, and non-fluctuant with poorly defined edges. No skin tracks were seen.

On September 18 his WBC was 15,600 × 10^9/L with 55.9% eosinophils. A serum specimen for antibodies to Gnathostoma was reported as positive on October 1. He was then treated with albendazole (400 mg twice a day). A biopsy of a migratory skin lesion of his left thigh done on October 7 showed eosinophilic vasculitis and folliculitis, but no larva. His symptoms and eosinophilia resolved with three weeks of treatment.

DISCUSSION

Gnathostomiasis was previously diagnosed clinically and serologically in a group of three individuals who ate raw catfish caught on the Rufiji River in southeastern Tanzania in
of mistranslation of the French in the original report. G. spinigerum
have also been found in animals in Zimbabwe. 5
slightly elevated erythematous track that is left as the larva migrates
from the shoulder across the upper back.

1991 and diagnosed three years later in 1994 (Wolfe MS, unpublished data). These cases were presented at the American Society of Tropical Medicine and Hygiene meeting in 1995, but we are not aware of other published reports of human cases from Africa. The geographic origin of a Cambodian case was erroneously listed as being from Cameroon1 because of mistranslation of the French in the original report.4 Gnathostomes have also been found in animals in Zimbabwe.5

The genus Gnathostoma includes at least 12 species, of which G. spinigerum is the most common cause of human disease. The definitive host range includes a number of carnivorous mammals such as cats, tigers, leopards, lions, dogs, raccoons, opossums, and pigs. The adult gnathostomes live in tumor-like masses in the stomach wall of the definitive host and eggs are passed fecally. Eggs hatch in water to release first-stage larvae, which develop into second-stage larvae after being ingested by small copepods (Cyclops species) that are the first intermediate hosts. The second intermediate hosts are freshwater fish, frogs, eels, snakes, birds, and some mammals, which become infected when they swallow the infected copepod. The third-stage larvae then develop and encyst in their flesh. The life cycle is completed when a definitive host ingests a second intermediate host infected with mature third-stage larvae.1,5

Humans usually acquire infections by ingesting raw or undercooked infected second intermediate hosts. Most cases of gnathostomiasis have been associated with eating raw freshwater fish. Alternatively, it has been postulated that humans could become second intermediate hosts by ingesting infected copepods or that the third-stage larva from infected meat could penetrate the skin of food handlers without being ingested.1 Humans represent a dead-end host since the female gnathostome fails to mature to the adult stage.5

The systemic symptoms of gnathostomiasis may include fever, arthralgias, myalgias, malaise, anorexia, nausea, vomiting, diarrhea, and epigastric pain. These symptoms are reported to occur as soon as 24–48 hours after ingestion of the larvae. Our patients’ symptoms began later.

Cutaneous gnathostomiasis represented by a migratory swelling is the most common and helpful physical sign of this infection. However, cutaneous larva migrans caused by animal hookworm and Strongyloides species must also be considered in the differential diagnosis. Once the first patient developed the classic broad-based migratory rash, gnathostomiasis became the most likely cause of symptoms. The second patient’s skin lesions were not obviously migratory, making the diagnosis of gnathostomiasis more difficult. Of 300 patients reported in Mexico, 235 (78.2%) had cutaneous manifestations described as intermittent migratory swelling and indurated erythematous plaques.5 Without treatment, intermittent cutaneous lesions have continued for up to 10–12 years after infection.

Visceral gnathostomiasis occurs when the larvae migrate through internal organ systems. Infection of the pulmonary system, gastrointestinal tract, genitourinary tract, eye, ear, nose, throat, and the central nervous system have all been reported, with symptoms depending on the organ system involved. Central nervous system gnathostomiasis is more often associated with morbidity and mortality.1

Eosinophilia is a clue to the diagnosis, but unless cutaneous lesions develop, it may be an indicator of a number of diseases. In patients returning from Africa with water contact, schistosomiasis would be the most likely cause of eosinophilia, and both patients were treated independently with praziquantel for this infection. The incubation time of 12–14 days seen in the Salt Lake City patient would be considered unusually short for schistosomiasis. Sixty-nine percent of 240 patients with gnathostomiasis in Mexico had an eosinophilia greater than 5%. The large percent of controls with eosinophilia (46.1%) makes this data more difficult to interpret.2 Early in the illness, 50% eosinophilia is common, as experienced by the South African patient.

Biopsy of a skin lesion or a visceral eosinophilic mass found at surgery can be helpful diagnostically, and be curative if the larva is removed. Biopsies of migrating lesions frequently miss the larvae and are helpful only in demonstrating an eosinophilic infiltration, as seen in both of our patients. Only 12 of 35 skin biopsies done in Mexico detected the larva.2

A number of serologic tests have been developed to help in the diagnosis of gnathostomiasis, but the Western blot used to confirm the diagnosis in our cases has a reported sensitivity and specificity of 100%.6 The Division of Parasitic Diseases of the Centers for Disease Control and Prevention was helpful in facilitating transport of specimens to Thailand and the results of the Western blot were returned quickly by e-mail. The enzyme-linked immunosorbent assay testing from Mexico reported 279 of 300 (sensitivity = 93%) infected patients positive and 5 of 150 controls positive (specificity = 96.7%).2

Albendazole is the treatment of choice for this infection, and this proved to be the case in this study. A study by Kraivichian and others3 reported a 93.9% cure rate for high dose albendazole (400 mg twice a day) and a cure rate of 94.1% for an intermediate dose (400 mg per day) given for 21 days, while 12 patients followed for six months on placebo continued to show evidence of disease. Surgical resection has also proved to be an effective treatment.

Preventive measures include avoiding eating fresh meat from second intermediate hosts, particularly raw fish, from infected waterways. The larva appear to be killed by freezing infected meat to -20°C for 3–5 days. Marinating infected meat in various substances is of limited effectiveness, with vinegar killing the organism in about 6 hours, soy sauce in 12 hours,
and lime juice being regarded as not effective after 5 days at room temperature and after 30 days at 4°C.\(^1\)

With the large variety of animals that are susceptible to infection as definitive and intermediate hosts, it is not surprising to find gnathostomiasis present in Africa. The high incidence of infection in Southeast Asia and Central and South America most likely represents the frequency of eating fresh water fish as part of the culinary tastes: sushi and sashimi in Japan, sum-fale in Thailand, and ceviche in Central and South America. The paucity of reports from Africa may reflect different dietary habits of the African population, or may be due to a lack of awareness of gnathostomiasis.

Gnathostomiasis should be considered as a possible diagnosis of migratory skin lesions and eosinophilia in individuals living in, or recently returning from, endemic areas. South-central Africa should now be regarded as a potential area of risk.

Received June 3, 2002. Accepted for publication March 3, 2003.

Authors' addresses: DeVon C. Hale, Department of Medicine, Division of Infectious Diseases, University of Utah, 30 North 1900 East, Room 4B319, Salt Lake City, UT 84132-2405, Telephone: 801-585-9573, Fax: 801-581-4873, E-mail: devon.hale@hsc.utah.edu. Lucille Blumberg, Department of Clinical Microbiology and Infectious Diseases, University of the Witwatersrand and the National Health Laboratory Service, PO Box 1038, Johannesburg, South Africa, Telephone: 27-11-321-4241, Fax: 27-11-882-3741, E-mail: lucilleb@niv.ac.za. John Frean, Department of Clinical Microbiology and Infectious Diseases, University of the Witwatersrand and the National Health Laboratory Service, P.O. Box 1038 Johannesburg, South Africa, Telephone: 27-11-489-9345, Fax: 27-11-489-9357, E-mail: johnf@mail.saimr.wits.ac.za.

Reprint requests: DeVon C. Hale, Department of Medicine, Division of Infectious Diseases, University of Utah, 30 North 1900 East, Room 4B319, Salt Lake City, UT 84132-2405.

REFERENCES