A Case of Human Gnathostomiasis Successfully Treated with Ivermectin

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Cutaneous gnathostomiasis has also been called larva migrans profundus and nodular migratory eosinophilic panniculitis. Human gnathostomiasis is caused mainly by the nematode Gnathostoma spinigerum. It causes migratory cutaneous, erythematous, indurated plaques and serious visceral sequelae. Medical treatment with mebendazole, albendazole, and ivermectin has been disappointing. Surgical excision of the parasite is the treatment of choice when possible. (Ann Dermatol (Seoul) 18(1) 33～36, 2006)

Key Words: Gnathostomiasis, Ivermectin

INTRODUCTION

Human gnathostomiasis is caused by migrating nematode, larvae of the genus Gnathostoma, particularly Gnathostoma spinigerum[1], and is acquired by ingestion of raw freshwater fish. It is endemic in much of Asia such as Thailand, Japan, China, and the Philippines, but reports from the United States, Mexico, Israel, and Europe show that infection with this parasite is widespread[1-3]. With the recent increase of travel to Southeast Asia, an increased incidence of human gnathostomiasis can be also expected in Korea.

The Gnathostoma species most frequently affects the skin and subcutaneous tissue, but larvae can migrate to the vital organs, including the central nervous system, lungs, and eyes, and the disease can be fatal. Therefore, early diagnosis is important for preventing serious sequelae.

Treatment with all kinds of antiparasitic drugs has been disappointing.

We describe a case of gnathostomiasis on the face of a Korean traveler, who had eaten raw saltwater fish and cuttlefish in Sri Lanka. He was treated with albendazole and ivermectin, and showed clinical and laboratory improvement during 7 months of follow up.

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CASE REPORT

A 44-year-old Korean man visited our hospital for evaluation of a migratory, erythematous, subcutaneous swelling on his face. The lesion was an oval shape, approximately 3-5 cm in size, and was painful but not pruritic. It had first appeared on the left forehead 1 month before the visit, and had migrated to the right eyelid two weeks later (Fig. 1A). After another 2 weeks, the subcutaneous swelling migrated down to the lower lip (Fig. 1B). The patient had eaten raw saltwater fish and cuttlefish at seaside restaurants two or three times during his trip to Sri Lanka 6 weeks before the visit. However, he denied having nausea, fever or diarrhea during his stay in Sri Lanka. The symptom of a migratory subcutaneous swelling (Fig. 2) and his food-intake history in Sri Lanka clinically suggested deep larva migrans, also known as gnathostomiasis or nodular migratory eosinophilic panniculitis. White blood cell count was normal, 8800 cells/$\mu\ell$, but eosinophilia has been detected with 7% eosinophils. Histologic examination of the lower lip showed interstitial and perivascular infiltrate of eosinophils, involving subcutaneous

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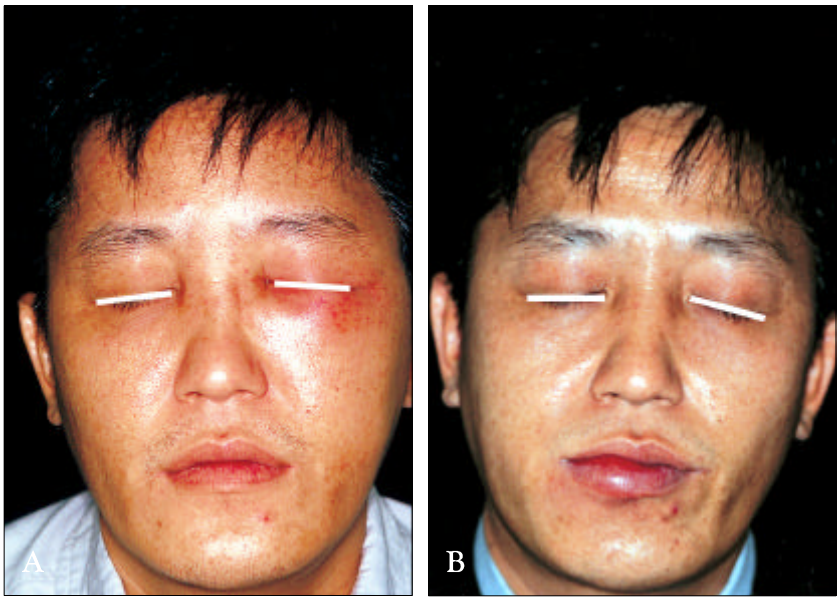

Fig. 1. (A) Erythematous subcutaneous swelling on the right eyelid at first visit. (B) Migration of the lesion to the lower lip, 2 weeks later.

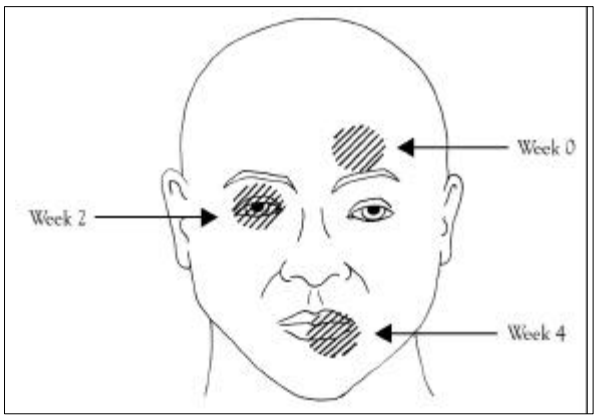

Fig. 2. Migration of the subcutaneous swelling on the face.

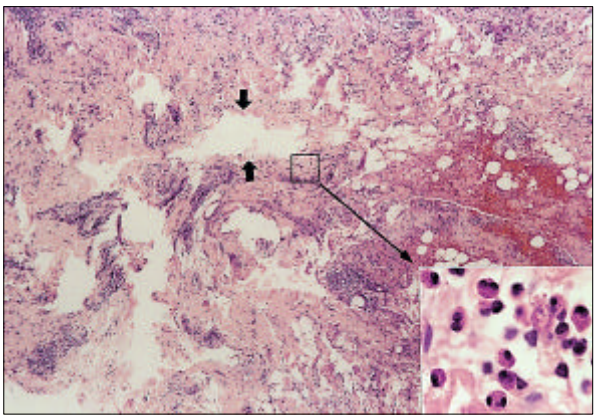

Fig. 3. Histologic examination of the swelling of the lower lip shows interstitial infiltration of numerous eosinophils, and a few burrows, involving the dermis and subcutaneous tissue (H & E, ×40; inlet: × 400).

tissue and a few burrows in the dermis (Fig. 3). However, the parasite was not found in the histopathologic slide. In the serum of the patient, enzyme-linked immunosorbent assay (ELISA) using Gnathostoma doloresi antigen was positive, with a value of 0.417 (normal value < 0.30). The symptoms remained after oral albendazole treatment, 400 mg twice daily for 21 days, therefore, 12 mg (200 μg/kg) of ivermectin was given once for 4 days after the completion of the albendazole treatment. The lesion disappeared without side effects 1 week after ivermectin treatment, and did not relapse during 7 months of follow-up. Antibody titers against G. doloresi decreased dramatically from 0.417 to 0.183, although they did not fully drop below the negative standard value (Fig. 4).

DISCUSSION

Gnathostoma species are found in the stomach or esophageal wall of definite hosts such as cats, dogs and wild felines that consume raw fish. Eggs discharged with host's feces hatch in water and are ingested by a species of Cyclops, a small fresh water crustacean, in which they develop to second stage

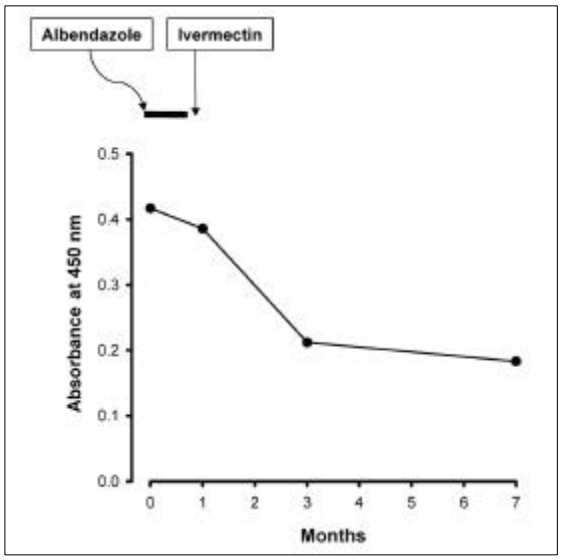

Fig. 4. Changes to the absorbance of antibody against Gnathostoma dolores antigen by ELISA after treatment with albendazole and ivermectin.

of larvae. When Cyclops is ingested by the second intermediate (and/or paratenic) host such as frogs, snakes, and fish, the larvae develop to the third stage, which are in turn eaten by the definitive host, thus completing the life cycle. Dogs, various felines, and wild mammals serve as the definitive hosts in the life cycle of the nematode.

Humans are accidental or paratenic hosts; and they acquire infection generally by ingestion of Cyclops in water, or of inadequately cooked or raw flesh of the intermediate host[4,5]. After being ingested, the third stage of larvae of Gnathostoma species penetrate the wall of the gastrointestinal tract and may migrate to any tissue, including the dermis and any viscera[5]. The patient in our case was suspected of being infected with the Gnathostoma species due to ingestion of inadequately processed marine fish and cuttlefish. However, it is also possible that he may have become infected by drinking water contaminated by infested Cyclops.

The most common manifestation of human gnathostomiasis is intermittent migratory swelling of the skin and subcutaneous tissue with localized erythema, which may be associated with pruritus or pain at the affected sites. The parasite may be spontaneously extruded, or may randomly migrate intermittently for years[5]. The disease may be fatal if the larvae migrate to the vital organs, such as the central nervous system, lungs, and eyes. Serious complications, including eosinophilic encephalomyelitis, subarachnoid hemorrhaging or a stroke may occur. Blindness may be caused by migration of larvae into the vitreous[6]. Early treatment of worms on the face is therefore important to prevent ocular involvement. The current patient had migratory erythematous swelling limited to the face and transient periorbital swelling, but did not show any neurologic or ocular symptoms such as headache, conjunctival erythema or changes to visual acuity.

Eosinophlia is a clue to the diagnosis, but unless cutaneous lesions develop, it may be an indicator of a number of diseases. Sixty-nine percent of 240 patients with gnathostomiasis in Mexico had an eosinophilia greater than 5%[7]. ELISA is important for the confirmation of the diagnosis as well as for the treatment response. ELISA testing to confirm the diagnosis in our case had a reported sensitivity of 93.0% and specificity of 96.7%[7]. Biopsy of a skin lesion can be helpful diagnostically, and be curative if the larva is removed. However, biopsies of migrating lesions frequently miss the larvae and are helpful only in demonstrating an eosinophilic infiltration, as seen in our patient.

Surgical excision is the treatment of choice for this infection. However, surgical removal is complicated by the large size of the lesions and rapid migration of the organism. Gnathostomiasis has responded poorly to traditional antihelminthic drugs. Recently Kraivichian et al. reported a 94% cure rate with albendazole, 400 mg once or twice a day, for 21 days[8]. Another study, which compared a single dose of 200 μg/kg of ivermectin with 400 mg of albendazole once a day for 21 days, did not reveal a significant difference of cure rate in the treatment of gnathostomiasis between the two drugs[9]. In our patient, the cutaneous symptom after albendazole treatment was thought to be related to the presence of the migrating larvae, but we couldn't rule out the possibility that it was related to a local reaction caused by the death of the parasite. The skin lesion disappeared and did not relapse after a single dose of ivermectin, and an antibody titer also showed a decreasing tendency, suggesting good efficacy of ivermectin.

Preventive measures are the most important. Gnathostomiasis can be prevented by avoiding eating raw fish and meat and drinking infected water. Freezing the infected meat at -20℃ for 3-5 days will

also prevent gnathostomiasis.

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