

Case Report

Human gnathostomiasis infection in New Orleans as emerging foodborne zoonotic disease

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ABSTRACT

The third-stage larvae belong to the genus *Gnathostoma* are acquired by human through ingestion of raw or improperly cooked fish or other second intermediate hosts, or paratenic hosts. Among the many species of *Gnathostoma* that have been described, *Gnathostoma spinigerum* is of primary medical importance. Human gnathostomiasis is a foodborne zoonotic disease, which is particularly prevalent in Japan, Thailand, and Mexico where it is customary for people to eat raw freshwater fish and sporadic cases have occurred in Malaysia, Indonesia, China, Philippines, Ecuador, Israel, Tanzania, and other areas where raw freshwater fish are part of diet. Outside endemic areas, patients' travel history to endemic areas would suggest the possibility of human gnathostomiasis infection. An early manifestation consists of low-grade fever, pleuritis, creeping eruption, malaise, hypereosinophilia and pain on swellings. This form of Gnathostomiasis may be mild and unrecognized or may be severe and last for more than six weeks. The diagnosis of larval Gnathostomiasis is frequently difficult, and is presumptively suggested by the clinical characteristics of the disease. A definitive diagnosis can be made on isolation and identification of larvae. A serological test varies greatly in sensitivity and specificity, is not generally available worldwide, and merely supports the diagnosis in an appropriate clinical and epidemiological setting. In this case, a 37-year-old Thai woman who had immigrated to the U.S.A. infected Gnathostomiasis during a vacation in Bangkok, Thailand.

INTRODUCTION

Human gnathostomiasis is an extra-intestinal infection with larvae or immature nematode of the genus *Gnathostoma* and is characterized by space-occupying inflammatory lesions and/or hemorrhage as result of the migration of a single parasite^{1,2)}. Intermittent migratory cutaneous swelling over years is the most common manifestation and rare cerebral invasion can be fatal. *Gnathostoma spinigerum* had been considered as the causative species of human gnathostomiasis among 12

distinctive species until the recent discovery of human cases infected with *Gnathostoma hispidum*, *Gnathostoma doloresi*, and *Gnathostoma nipponicum* in Japan^{1~5)}. When the second intermediate hosts contaminated with the third-stage larvae are ingested, they cause human infection.

CASE REPORT

Patient : A 37-year-old woman who was born in Chonburi, Thailand before emigrating to New Orleans, Louisiana, U.S.A.

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Chief complaints: Acute onset of fever (40°C), diffuse arthralgias, diffuse myalgia, malaise, and headache.

Past history: Not remarkable

Present illness: The patient was seen at a private clinic in Bangkok, Thailand with erythema and swelling (5×5 cm) on the abdomen and the left hand after spending one month in August, 2000 visiting her family in the suburbs of Bangkok. This manifestation had persisted for two days. She was given an intramuscular injection of penicillin. Her condition, however, did not improve. She was referred to a larger hospital for examinations and then transferred to the Primary Care Center, the Department of Infectious Diseases, Tulane University Medical Center, New Orleans, Louisiana, U.S.A.

Findings on admission: The patient's general appearance was good except for swelling of the right hand (Fig. 1).

Laboratory evaluation: The blood cell count showed leukocytosis (13,500 white blood cells (WBC)/mm³ with 25% eosinophils) on the first day of admission, September 15, 2000. The examination of peripheral blood revealed a WBC count of 24,200/mm³ with 64% eosinophils, IgE 989.3 IU/ml, CRP (–). Subsequent medical examinations, blood chemistry, creatine phosphokinase, lumbar puncture, computed tomography of the head, chest radiography, analysis of stool for ova and parasites, examination of blood smears for microfilariae and *Plasmodia*, ultrasonography of the liver, urinalysis, blood cultures, purified protein derivative testing, and serological studies for human immunodeficiency virus (HIV), yielded normal results.

Onset & course: On the third inpatient day, temperature decreased to 37°C. Both of arthralgia and myalgia had also decreased; however, the patient had edematous

swelling over the left mandible and the left anterior area of the neck. In addition, edematous swelling localized to the right proximal arm had migrated to the elbow within two days. Intermittent cutaneous migratory swelling was painful. Subcutaneous swellings, eosinophilia, travel to Thailand, and eating raw freshwater fish raised the possibility of a parasitic infection. She was treated empirically with Albendazole at a dose of 400 mg once a day for three days. A skin biopsy from subcutaneous swellings did not reveal parasitic larva. She was discharged from hospital ten days post-admission with symptoms consisting only of localized pain on the right arm. On October 11, 2000, she complained of a two-day history of intense painful and pruritic edematous swellings over the left mandible and the right arm again. She had experienced similar episodes of swelling in the same areas one week previously and these episodes had lasted three days. A blood examination revealed a WBC count of 11,900/mm³ with 20% eosinophils and normal blood chemistry results. Three times' stool examinations for ova and parasites and a skin test for immediate hypersensitivity with *Gnathostoma* antigen were performed. Immunodiagnosis proved to be highly specific in ELISA using monoclonal antibodies and dots (multiple-dot ELISA test). They revealed larvae of *Gnathostoma spinigerum* (the third-stage larvae), which were identified by the Department of Tropical Medicine, Tulane University Medical Center and the surgical removal of larvae were strongly indicated. Chemotherapy for gnathostomiasis, Albendazole at a dose of 400 mg once a day for 14 days, was performed and a larva also was removed from edematous swelling of the right arm by surgical incision. The outcome was generally excellent since the larvae were not reported to migrate subcutaneously.

Parasitological morphology: The third-stage larva, 2.7×0.3 mm in size, bear four transverse rows of well-developed single-pointed hooklets on the head bulb

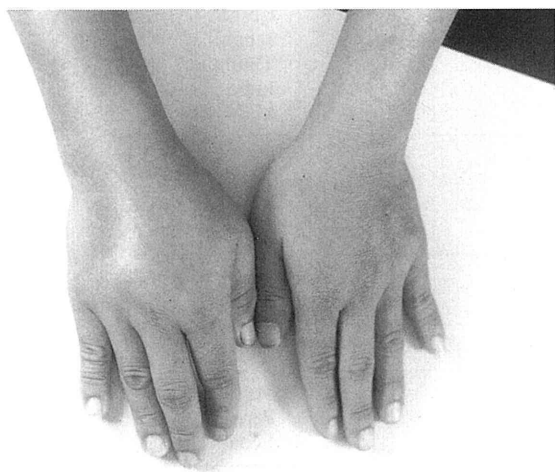


Fig. 1 Subcutaneous swelling of the right hand



Fig. 2 The third-stage larva of *Gnathostoma spinigerum*

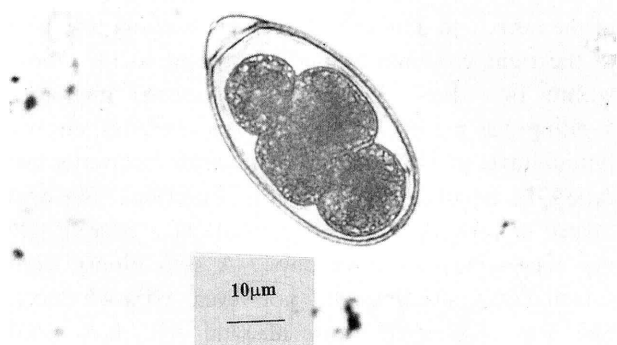


Fig. 3 The egg of *Gnathostoma spinigerum*

with numerous spines on the head and body (Fig. 2).

Stool examination findings : Fertilized egg was $67 \times 38 \mu\text{m}$ in size, oval shaped, and colorless. The eggshell was rough (Fig. 3).

DISCUSSION

Human gnathostomiasis is a foodborne zoonotic disease caused by the nematode *Gnathostoma spinigerum*^{1,2)}. Other species of *Gnathostoma* have occasionally been reported as human parasites^{6~10)} (Table 1). After ingestion of *Gnathostoma spinigerum* within 24–48 hours, the larvae penetrate through the intestinal wall and into the abdominal cavity and may produce epigastric pain, fever, vomiting, malaise, urticaria, and anorexia, which may persist for several weeks, and can migrate to tissue deeply. Any organ systems may become infected. Eosinophilia develops (with eosinophils not uncommonly making up more than 50% of the total WBC count) in association with larval penetration of the

gastric or intestinal wall. Cutaneous Gnathostomiasis is commonly manifested by intermittent episodes of localized migratory swelling lasting for one or two weeks.

The adult worms which live in tumors of the intestinal wall in fish-eating mammals, are stout, reddish, slightly transparent nematodes with a subglobose cephalic swelling separated from the remainder of the worm by a cervical constriction, males reaching 11 to 25 mm in length, females 25 to 54 mm. Eggs, measuring $69 \times 37 \mu\text{m}$, have a sculptured shell with a transparent knob at one end. Humans are unnatural hosts in whom the worms do not reach maturity but migrate throughout the body. The life cycle involves two intermediate hosts ; the first intermediate host is *Cyclops*, the second intermediate hosts are any of a number of fish, reptiles, or amphibians. Eggs, which erupt into the mammals' intestinal tract and are passed in the feces, in water produce motile larvae, which are ingested by *Cyclops*²⁾. In order to be infective to the definitive hosts, the larvae require further development in the second intermediate hosts such as freshwater fish, frogs, or snakes⁵⁾. The third-stage larvae in these second hosts, however, may be transferred to other hosts, namely paratenic hosts. Domestic fowls or pigs, paratenic hosts, are fed with infected fish wastes, the larvae simply re-migrate and form cysts in their skeletal muscles. When the suitable definitive hosts such as domestic cats or dogs ingest infected paratenic hosts, the larvae are digested free of their cyst wall and undergo a long migration through the abdominal cavity and muscles. The infections develop to maturity in the stomach wall in about six months to 12 months, completing the cycle.

Table 1 Human gnathostomiasis in the world

Species	1st IMH	2nd IMH & PH	DH	Locality
<i>G. spinigerum</i>	cyclops	snake-headed fish eel loach frog fowl	cat dog tiger	China Japan Thailand India Malaysia
<i>G. hispidum</i>	cyclops	loach	pig	China Japan Korea Taiwan
<i>G. doloresi</i>	cyclops	freshwater fish viper, snake	wild boar pig	Japan
<i>G. nipponicum</i>	cyclops	loach	weasel	Japan
<i>G. binucleatum</i>	cyclops	freshwater fish pelican	wild cat	Mexico Peru Ecuador

IMH : Intermediate Host
PH : Paratenic Host
DH : Definitive Host

Diagnosis of human gnathostomiasis infection is made on the basis of clinical symptoms and the patient's history in relation to food habits and residence. Definitive diagnosis is very difficult unless the third-stage larvae can be found and be characterized. A skin biopsy from a subcutaneous swelling is usually disappointing because larvae are tiny and moving into the skin tissues. Laboratory evaluation reveals only an inflammatory reaction with eosinophils. A skin test for immediate hypersensitivity with *Gnathostoma* antigens and other parasites have been described as being useful; however, they are not available in general. Immunodiagnosis has also been described as useful and highly specific in ELISA using monoclonal antibodies or immunoblotting^{3),4)}.

Treatment consists of surgically removal from subcutaneous and other accessible loci. Albendazole, 400 mg once a day for about 21 days, is highly effective, achieving over 90% cure rate¹¹⁾. Prognosis is usually good except in cases involving the central nervous system. Proper cooking of fish, pork, and chicken and drinking of potable water are strongly recommended in endemic area by way of prevention of human gnathostomiasis infection.

In conclusion, we report a case of cutaneous human Gnathostomiasis infection and confirmed by removal larva and ovum. The history of ingestion of raw or improperly cooked fish or other second intermediate hosts, or paratenic hosts from patient is very important for diagnosis of this infection.

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米国ニューオーリンズで確認された人畜共通感染症および 食品媒介寄生虫症としての顎口虫症例

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我が国で分布が確認されている顎口虫の種類は有棘顎口虫 (*Gnathostoma spinigerum*), ドロレス顎口虫 (*G. doloresi*), 日本顎口虫 (*G. nipponicum*) である。終宿主は有棘顎口虫はイヌ, ネコ, トラなどで胃壁に寄生, ドロレス顎口虫はブタ, イノシシで胃壁に寄生, 日本顎口虫はイタチで食道壁に寄生する。他に輸入種として剛棘顎口虫 (*G. hispidum*) の幼虫が輸入ドジョウから確認されている。これら4種の顎口虫の中で, 医学的に最も重要な種類, 即ち, 顎口虫症の原因となるのは主として有棘顎口虫である。顎口虫症は我が国を始め, タイ, マレーシア, 中国などのアジア諸国とメキシコやエクアドルの中南米で淡水魚などを生食する習慣のある地域で多くの発症が報告されている。これらの地域において第III期後期の顎口虫幼虫を経口摂取し, それが非好適宿主の人体内で成虫になれずに, 腸壁を穿通し肝内を移行した後, 全身を移動する幼虫移行症のひとつで人畜共通感染症として重要である。皮膚症状は幼虫摂取後数週間から数か月で発症し, 移動性線状疹または移動性限局性腫張で, 発赤, 掻痒, 疼痛を伴う。本症の治療については外科的に虫体摘出するのが最良であるほか, アルベンダゾール 400 mg, 分1, 21日間連続投与が有効とされる。私達はタイで淡水魚の生食で感染し, 米国ニューオーリンズにて有棘顎口虫症と確認された症例を経験したのでここに報告する。症例は37歳タイ女性で結婚後, 米国に移住。平成12年8月よりタイに帰省中の約1か月後, 腹部および左手の発赤腫張を訴え, タイ・バンコク市内の一般医を受診した。ペニシリン筋肉注射を受けたが症状の回復が見られなかったため, 同年9月15日より米国チューレーン大学医療センター感染症科に検査入院した。主要検査所見は末梢血白血球数 13,500/mm³, 好酸球 25%, IgE 989.3 IU/ml, CRP (-), 肝機能正常, その他腰椎穿刺, 頭部CT, 胸部X線, 糞便検査, マラリア・フィラリア血液塗抹検査, 腹部エコー, 血液培養, 蛋白分画検査, HIV検査を行うが正常所見を呈した。同年10月11日に再入院, 臨床症状 (移動性限局性腫張), タイでの淡水魚生食歴, 末梢血液検査所見 (白血球増加と著名な好酸球増加), 顎口虫即時型皮内反応陽性, 免疫血清学的検査 (ELISA) から有棘顎口虫症と診断された。虫体摘出とアルベンダゾール 400 mg, 分1, 14日間の内服治療を行い, その後, 皮下組織に幼虫移行が見られなかったため, 予後良好と判断された。

<Key words> 顎口虫症, 移動性限局性腫張, 淡水魚生食, 好酸球増加
