THREE CASES OF HUMAN GNATHOSTOMIASIS CAUSED BY *GNATHOSTOMA HISPIDUM*, WITH PARTICULAR REFERENCE TO THE IDENTIFICATION OF PARASITIC TARVAE

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Abstract. Human gnathostomiasis is well known to be caused by *Gnathostoma spinigerum*, *G. hispidum*, *G. doloresi* and *G. nipponicum* in Japan. In the present reported cases, skin biopsies were performed on three Japanese patients. As a result, cross sections of the larvae were clearly observed in the biopsied specimens. All cross sectioned larvae had an intestinal canal, which consisted from 25-35 cells. A large nucleus was observed at the center of each intestinal cell. The morphological features completely correlated with the characteristics of larval *G. hispidum*. Based on these findings, all three human cases were thus determined to be confirmed cases of gnathostomiasis caused by *G. hispidum*.

INTRODUCTION

Gnathostoma spinigerum is generally considered to be the only known species that is an agent of human gnathostomiasis. However, not all previously reported cases of gnathostomiasis are considered to be caused by a larval *G. spinigerum* infection. Up until the 1980s, morphological identification of the advanced third-stage larvae in biopsied tissues could not be established, as a result, all agents of human gnathostomiasis lumped together under the term larval *G. spinigerum*. However, Akahane *et al* (1986) reported that the intestinal cells of advanced third-stage larvae had a different number of nuclei among *G. spinigerum*, *G. hispidum* and *G. doloresi*. Moreover, Ando *et al* (1991) also mentioned that the morphology of the intestine of larval *G. nipponicum* also differed somewhat from that of *G. spinigerum*, *G. hispidum* and *G. doloresi*. Therefore, it is now possible to identify and distinguish the larvae in biopsied specimens from the patients. Shortly thereafter, the first human cases of *G. hispidum*, *G. nipponicum* and *G. doloresi* were reported in Japan (Ogata *et al*, 1998; Ando *et al*, 1998; Nawa *et al*, 1989: Kagei, 1991).

Live loaches have also recently been imported from China to Japan by airplane. Some Japanese people like to swallow live loaches while drinking either whiskey or Japanese rice wine. The loaches imported from China however, are sometimes infected with early third-stage larvae of *G. hispidum* in their viscera (Akahane and Mako, 1984). Therefore, many cases of human gnathostomiasis in Japan are now caused by the consumption of imported live loaches. However, there have so far only been a few reports of confirmed cases caused by *G. hispidum*.

We were recently able to identify larval *Gnathostoma* in biopsied specimens as originating from *G. hispidum* and herein report the identification of these agents.

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Case 1

This was the case presented at the Department of Dermatology, Hamamatsu University School of Medicine. The patient, a 55- year-old Japanese man, was a staff member of the District Forestry Office in a mountainous area of Shizuoka Prefecture, Japan. He had never been to any foreign countries, but he liked to consume various types of raw fresh meat including fish, snakes, frog, deer, pig and chicken. Twelve hours after consuming the raw meat of a snake, *Agkistrodon halys*, intense stomach convulsions with a fever of 41°C suddenly occurred. Then creeping eruptions appeared on his abdomen 1 week after first consuming the snake,

Fig 1–Creeping eruptions of Case 1.

Fig 2–Cross section of the larva in a biopsied tissue of Case 1 (scale: 100 mμ).

Fig 3–Cross section of the larva in a biopsied tissue ofCase 2 (scale: 100 mμ).

and the patient was hospitalized 6 days after appearance of these eruptions (Fig 1). At admission, a skin biopsy was performed and a parasitic larva was obtained from the biopsied tissue obtained from his lower abdomen. The result of the Ouchterolony test was positive for the adult antigen of *G. spinigerum*.

The parasite from the patient was the advanced third-stage larva of the genus *Gnathostoma,* which had a large intestinal canal. The intestinal canal consisted of about 35 intestinal cells, and a large nucleus was also observed at the center of each cell (Fig 2). The findings closely correlated with the characteristic findings of an advanced third stage larva of *G. hispidum* which was previously reported by the same authors (Akahane *et al*, 1986).

Case 2

This case presented at Kanto Chuo Hospital, Tokyo Japan. The patient was a 25-year-old man who developed symptoms of dry cough and a fever reaching up to 39° C about 2 weeks after swallowing 2 live loaches, *Misgurnus anguillicaudatus*. About five weeks after consuming the loaches, pulmonary infiltration was observed on an X-ray. The blood findings showed WBC 26,900/mm^3, 70% eosinophiles. Thereafter migrating creeping eruptions occurred 12 weeks after ingestion. An interdermal test and complement fixation test were positive against *G. spinigerum* adult antigen. A skin biopsy was performed three months after the ingestion and a cross section of the larva including 2 intestinal canals was observed in a biopsied specimen taken from his left chest. One of the intestinal canals had about 27 cells, and a large nucleus was also observed at the center of each intestinal cell of the larva as shown in Fig 3. The larva was identified as due to an advanced third-stage larva of *G. hispidum* based on the morphological findings of the intestine.

Case 3

The patient was a 44-year-old male chauffeur who presented at the Department of Dermatology of Hamamatsu University, School of Medicine. Linear erythema suddenly occurred in the patient's left trunk area, 2 months after the ingestion of live loaches. The erythema swelled and gradually moved

to other portions of his trunk. A fluorescence antibody analysis showed a positive identification for *G. hispidum* adult antigen. A skin biopsy was carried out after the appearance of symptoms and a parasitic larva including its intestine was confirmed in a biopsied specimen from the left area of his trunk. As shown in Fig 4, the intestinal canal consisted of about 30 cells, and each intestinal cell had a large nucleus at the center. This larva was identified to be an advanced third-stage larva of *G. hispidum* based on these findings.

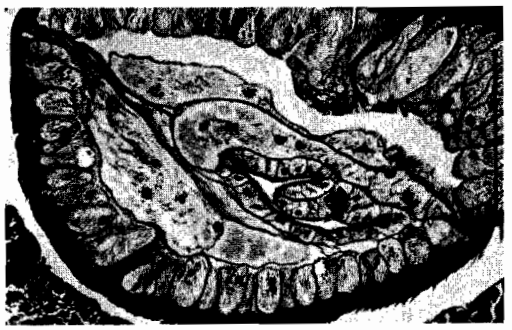

Fig 4–Cross section of the larva in a biopsied tissue of Case 3 (scale: 100 mμ).

DISCUSSION

According to Miyazaki (1991), there are 10 distinct species in the genus *Gnathostoma* in the world. In those species, *G. spinigerum*, *G. doloresi* and *G. nipponicum* are known to be distributed in Japan. In addition to these species previously identified in Japan, *G. hispidum* have been brought to Japan with live loaches from China. Therefore, there are now 4 species of the genus *Gnathostoma* in Japan and it has been reported that human gnathostomiasis were caused by these 4 species, *G. spinigerum, G. hispidum, G. doloresi and G. nipponicum.*

Gnathostomiasis caused by *G. spinigerum* sometimes occurred around the end of the World War II and continued until the 1980s in Japan. The first human cases of *G. nipponicum* and *G. doloresi* were reported by Ando *et al*(1988) and Ogata *et al*(1988), respectively. On the other hand, many human cases of *G. hispidum* have occurred in Japan since the 1980s due to the fact that many patients at that time began to ingest imported live loaches from China. As a result, the majority of recent gnathostomiasis are considered to be caused by *G. hispidum*. However, there have so far been a few reports on human cases caused by *G. hispidum*.

In the present cases, all larvae cross sections except case 2, had an intestinal canal, which consisted of 25-35 intestinal cells. A large nucleus was also observed at the center of each intestinal cell of the larvae. From these results, the nuclei number in each intestinal cell were similar to those of larval *G. hispidum* and larval *G. nipponicum*. However, the cell number of the intestinal canal observed in the cross sections were fewer than those seen in larval *G. nipponicum*. These features closely correlated with the characteristic findings of the advanced third-stage larvae of *G. hispidum*. Therefore, the parasites in the biopsied specimens from the present patients were taxonomically identified to be advanced third-stage larvae of *G. hispidum*.

The first two csaes of human gnathostomiasis due to *G. hispidum* were reported by Morishita (1924) and Chen (1949). However, Miyazaki (1960) reported that the identifications of Morishita and Chen were not reliable since, at the time those reports were made, the technology of taxonomy was still quite primitive. As a result, the specific identification of the advanced third stage larvae of the genus *Gnathostoma* was not considered to be possible.

Recently Kagei (1991) and Taniguchi *et al* (1992) reported confirmed human cases of *G. hispidum*. They identified the advanced third-stage larvae in biopsied specimens as *G. hispidum* based on the criteria of larval intestinal cells.

Human gnathostomiasis has two conspicuous clinical symptoms, namely migrating intermittent edema and creeping eruptions. These symptoms are observed when the larva migrates to the cutaneous and subcutaneous tissues and muscles. Many Japanese parasitologists believe that a great number of cases of gnathostomiasis caused by *G. spinigerum* show a remarkable degree of intermittent edema, while many cases of *G. hispidum*, *G. doloresi* and *G. nipponicum* also show conspicuous creeping eruptions. The three patients in the present cases, also showed creeping eruptions.

The patients in the present cases all showed a dramatic recovery after the removal of the larvae.

However, it is also considered that the above described patients would have recovered even if the parasitic larvae had not been removed because it is known that the symptoms of gnathostomiasis caused by *G. hispidum* do not continue for a long time, in comparison to the symptoms of *G. spinigerum* infection.

Based on the above findings, the occurrence of gnathostomiasis of *G. hispidum* will most likely continue to occur in Japan due to the popular importation of live loaches from China.

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