AN ENDEMIC HUMAN INFECTION WITH
HETEROPHYES NOCENS ONJI ET NISHIO 1916
AT MIKKABI-CHO, SHIZUOKA, JAPAN

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Abstract

Human Heterophyes nocens infection was confirmed in 2 areas of Mikkabi-cho, Shizuoka Prefecture where
high prevalence of Metagonimus yokogawai infection had been reported. The total prevalence showed 9.6% by
stool examination. Among the patients, the older age’s males predominated, and the infection within the same family
was often observed. Adult worms were collected from stool samples of the patients after treatment with
praziquantel. The worms were identified as H. nocens with morphological characteristics. The average size of eggs
(27.8 x 16.1 μm) appeared in stools of the patients was slightly larger than that reported earlier, and rather equivalent
to eggs of M. yokogawai. Questionnaire study revealed a correlation of a habit of eating raw fish, mullet in particular,
and the trematode infection in Hamana Lake.

INTRODUCTION

Heterophyid trematodes have occurred in various areas in the world. Among them Metagonimus yokogawai and
Heterophyes nocens are known to be distributed mainly in Korea and Japan (Ito, 1964; Saito, 1999; Chai and Lee,
1990; Chai et al., 1994; 1997; 1998). While human cases with M. yokogawai are common, those with H. nocens are
rather fewer and most cases in Japan have been reported from western areas except Chiba Prefecture (Yokogawa et
al., 1965). This distribution pattern may be related to the habit of eating raw fish that is the second intermediate host
of H. nocens (Ito, 1964).

In Shizuoka Prefecture, M. yokogawai is widely distributed and the metacercariae are found in the sweetfish,
Plecoglossus altivelis (Ito et al., 1967a, b; Mochizuki and Ito, 1975). Areas surrounding Hamana Lake in western part
of the prefecture were also reported to be endemic for M. yokogawai (Ito et al., 1991). In 1997, a stool examination
at a junior high school in Mikkabi-cho revealed 10 egg positive children with a rate of 1.5% for the heterophyid fluke. These children lived various places in the area, and it was suggested that the infection has been endemic through-out the area. In Mikkabi-cho, however, there are no rivers where the sweetfish can grow and the endemicity of
Metagonimus infection could not be explained. This suggests that the infection was caused by other fish species in
Hamana Lake.

The present study aimed to clarify prevalence of the infection in Mikkabi-cho and to determine the causative parasite species to the infection among the residents in the area.

MATERIALS AND METHODS

1) Study site

Mikkabi-cho is located in the north end of Hamana Lake in Shizuoka Prefecture and its population was 16,300
in 1997. Two districts were selected for the survey: Nueshiro and Daifukuji, located at lake side and at moun-tain side, respectively, with the population of 600 each.
2) Stool examination

Containers for stool collection were distributed to all residents in both districts and collected after a few days.
Stool samples were examined for trematode eggs with the Kato’s cellophane thick smear technique. Each sample was
examined 3 times under a microscope.

3) Treatment

Subjected people with egg positive were informed the result and asked to admit local clinics and to have praziquantel (Biltricide®) at a dose of 20mg/kg.

4) Adult recovery

Whole stool at the first defecation after treatment was collected. The stool samples were dissolved with tap water and washed several times to remove soluble contents and fine particles. Then sediments were sieved with a wire mesh to remove large particles, and remaining sediment was examined for adult worms under a dissecting microscope. When the worm was found, it was fixed with 70% alcohol and stained with borax carmine.

5) Measurement of eggs

Eggs were collected from positive stool samples with the centrifugation technique and the size was determined under a light microscope.

6) Questionnaire

A questionnaire was sent to 140 families, who cooperated to the stool examination, to ask on eating habit of fishes, fish species, way of cooking and frequency of eating fishes in Hamana Lake. Results were analyzed using χ² test with the contingency table.

RESULTS

A total of 457 stool samples was collected from the two districts, Nueshiro and Daifukuji. Results of stool examination are shown in Table 1. Eggs detected were small and ovoid in shape, and the operculum was seen at one end, showing characteristics of heterophyid trematode eggs (Fig. 1). Prevalence rates of the fluke infection were 7.5% (10/134) in Nueshiro and 10.5% (34/323) in Daifukuji, respectively, and with a total prevalence of 9.6% (44/457). The rates seemed higher in male than in female in both areas, but the differences were not significant. Among 44 positive persons, 15 persons belonged to 7 families and the number of positive family was 36 out of 140 families subjected (25.7%). Persons at age of 30’s or older composed of 90.9% (40/44) of the patients (Fig. 2). Out of 4 remaining

Table 1

<table>
<thead>
<tr>
<th>District</th>
<th>M</th>
<th>F</th>
<th>Total</th>
<th>M</th>
<th>F</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Daifukuji</td>
<td>153</td>
<td>170</td>
<td>323</td>
<td>20 (13.1)</td>
<td>14 (8.2)</td>
<td>34 (10.5)</td>
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<tr>
<td>Nueshiro</td>
<td>61</td>
<td>73</td>
<td>134</td>
<td>6 (9.8)</td>
<td>4 (5.5)</td>
<td>10 (7.5)</td>
</tr>
<tr>
<td>Total</td>
<td>214</td>
<td>243</td>
<td>457</td>
<td>26 (12.1)</td>
<td>18 (7.4)</td>
<td>44 (9.6)</td>
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M: male, F: female

Figure 1 An egg found in stool of a patient in Mikkabi-cho.

Figure 2 Age distribution of egg positive persons in Mikkabi-cho.

Figure 3 a, Adult worm of *Heterophyes nocens* found from human stool after treatment with praziquantel. b, Enlarged view of ventral sucker (upper) and gonotyl (lower). Chitinous rodlets are seen on the gonotyl.
younger positive persons, 2 had another positive person in the same family.

A total of 30 stool samples was collected from the patients after treatment, and adult worms were found from one patient in each area; 2 worms in Nueshiro and 8 worms in Daifukuji (Fig. 3). Although the worms were loosened and elongated, all worms had ventral sucker (acetabulum) and gonotyl indicating that they belong to genus Heterophyes (Fig. 3b). The worms were identified as H. nocens Onji et Nishio, 1916 from this finding and results of measurement shown in Table 2.

The size of 98 eggs from 6 patients is shown in Fig. 4. The size of eggs varied from 22.5 to 32.8 μm in length and 13.3 to 19.3 μm in width with an average of 27.8 x 16.1 μm.

Questionnaire for fish eating habit of residents was returned from 72 families (51.4%). The positive families were more (61.1%) than that of negative families (48.1%). Approximately 70% of the families had a habit of eating fishes caught in Hamana Lake. Among the fishes, sweetfish, mullet (Mugil cephalus) and gobby (Acanthogobius flavimanus) were preferably eaten by a half of the families. Mullet was eaten raw by 49% of the family, similarly, 23% for gobby and 26% for Shirauo (Salangichthys microdon). Seventy three percent of positive families particularly had the habit of eating raw mullet and it was significantly higher than that of negative families (P<0.05). This tendency was higher in Daifukuji, but not significant in Nueshiro. There was no significant relation between infection and eating raw fish for gobby and Shirauo with the fluke infection.

**DISCUSSION**

A relatively high level of human infection with heterophyid trematode has been known in areas around Hamana Lake and the infection was thought as that with M. yokogawai (Ito et al., 1991). However, the present result showed that the infection in Mikkabi-cho was caused by H. nocens. M. yokogawai is mainly found in the sweetfish in Miyakoda River flowing into Hamana Lake at northeast end of the lake, but there are no rivers where the sweetfish grows in Mikkabi-cho. These evidences suggest that the human infection with H. nocens is caused by catch and eating the fishes in the lake.

The adult worms collected from the patients were all relaxed and partly degenerated probably due to the treatment with praziquantel, therefore they may have caused a difference in the sizes. Even so, the measurements were among the ranges reported earlier for H. nocens (Suzuki et al., 1982; Chai et al., 1984; 1985; 1994; Sohn et al., 1989). The number of chitinous rodlets on the gonotyl can be a key to distinguish species of genus Heterophyes. Imported human cases with H. heterophyes have been reported in Korea (Chai et al., 1986; Chai and Lee, 1990) and it seems important to distinguish the present worms from H. heterophyes. The adult worms in the present study harboured the rodlets in a range from 49 to 58 as shown in Table 2. This range is apparently fewer than that of 68 to 85 for H. heterophyes (Chai et al., 1986).

The size of eggs was slightly larger than that of earlier reports for H. nocens in Korea (Lee et al., 1984; Chai and Lee, 1990), and rather equivalent to that of M. yokogawai appeared in those reports. The difference could be attributed to that the eggs measured in the present study were collected from human stool and the others were in adult uteri of H. nocens. The average size in individual patients varied in a wide rage. This suggests that the egg size may not be consistent among different geographical locations.

Questionnaire study well revealed the relationship between the infection and habit of eating raw fish caught in Hamana Lake. And it was strongly indicated that the significant correlation of prevalence with H. nocens was due to

<table>
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<th>Table 2</th>
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<tr>
<td>Measurement of adult worms shown in range among 5 worms (μm).</td>
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<tr>
<td>---</td>
</tr>
<tr>
<td><strong>Body length</strong></td>
</tr>
<tr>
<td><strong>Body width</strong></td>
</tr>
<tr>
<td><strong>Oral sucker</strong></td>
</tr>
<tr>
<td><strong>Pharynx</strong></td>
</tr>
<tr>
<td><strong>Esophagus</strong></td>
</tr>
<tr>
<td><strong>Acetabulum</strong></td>
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<tr>
<td><strong>Gonotyl</strong></td>
</tr>
<tr>
<td><strong>Ovary</strong></td>
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<tr>
<td><strong>Testis</strong></td>
</tr>
<tr>
<td><strong>No. of chitinous rodlets</strong></td>
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*Figure 4 Size distribution of eggs from 6 patients. Each symbol represents each patient.*
eating raw mullet, the second intermediate host of *H. nocens*. Predominance of males and older persons among the patients suggests a possible association with a general habit of alcohol intake among such persons. Although gobby is also known to harbour *H. nocens* and eaten raw by residents in the study area, no significant correlation was detected. Examination for metacercariae from the fishes including gobby will further clarify the role of these fishes in the life cycle of *H. nocens* in the area.

Recently, metagonimiasis has been increasingly found on stool examination at human dry dock in Japan (Ishizu et al., 1997). These infections may have been overlooked because of having no particular symptoms. This suggests that the infection has not necessarily increased and only opportunity to be detected has increased. In such cases the infection is usually diagnosed as metagonimiasis. However, it may also include infection with *H. nocens* or other heterophyid trematodes. In fact, the relatively high prevalence rates of heterophyid infections in the areas around Hamana Lake were once thought as metagonimiasis (Ito et al., 1991). This could be the case also in other areas in Japan where people have the habit of eating raw mullet or gobby. In Korea, for example, endemic foci of *H. nocens* infection have been reported in southern coastal areas where *M. yokogawai* is common among residents (Chai et al., 1994; 1997; 1998). Confirmation of species with adult worms should be required.

**REFERENCES**


