

An incidental case of human *Heterophyes nocens* infection diagnosed by sectional morphology in a biopsy specimen of the small intestine

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Abstract: A case of human infection with *Heterophyes nocens* (Heterophyidae) was incidentally found in a biopsy specimen of the Meckel's diverticulum at the upper part of the small intestine. The patient was a 58-year-old man living in a rural area of Talsong-gun, Kyongsangbuk-do. He had gastrointestinal symptoms such as epigastric pain, indigestion, and abdominal discomfort for 3 months, and severe diarrhea, abdominal pain, and vomiting for about 1 month before hospitalization. Endoscopy of the upper part of the small intestine revealed a Meckel's diverticulum, and it was excised and histopathologically examined. Three adult flukes were incidentally found sectioned in the mucosa, and they were identified as *H. nocens*. The patient had a history of eating raw mullets at a fish market in Pusan 6 months ago, and the mullets were presumed to be the source of infection. This case brings a considerable interest in that specific diagnosis of heterophyid infections could be done by sectional morphology of the worms.

Key words: *Heterophyes nocens*, heterophyid, case report, human, small intestine, Meckel's diverticulum

INTRODUCTION

Almost 20 species of minute intestinal flukes have been reported from human infections in Korea (Chai and Lee, 1990). Among them, it is agreed that heterophyids (Heterophyidae) are the most important species from epidemiological points of view. Especially, *Heterophyes nocens* (Chai et al., 1994, 1997, 1998) and

three species of *Metagonimus*, *M. yokogawai* (Chai and Lee, 1990), *M. takahashii* (Ahn and Ryang, 1988), and *M. miyatai* (Chai et al., 1993), are the major species showing considerable degrees of endemicity in various localities.

Heterophyes nocens was first described by Onji and Nishio (1916) and now is known to be distributed in southeast Asian countries, including Korea and Japan. In Korea, Seo et al. (1980) first identified the presence of *H. nocens* metacercariae in *Mugil cephalus*. The first human case was subsequently reported from a 52-year-old man living in Okku-gun, Chollabuk-do (Seo et al., 1981a). Since then,

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13 cases were sporadically reported (Chai et al., 1984, 1985; Sohn et al., 1989), and finally, several endemic foci were discovered in Shinan-gun, Muan-gun, Puan-gun, Chollanam-do, and Sachon-gun, Kyongsangnam-do (Chai et al., 1994, 1997, 1998).

The diagnosis of *H. nocens* infection in Korea has usually been based upon discovery of eggs in fecal samples followed by recovery of adult flukes after anthelmintic treatment and purgation (Chai et al., 1998). The worm recovery is needed because of great similarities in the morphology of eggs among different species of heterophyids in fecal smears. Alternatively, intestinal excision and histopathological observation could be helpful for a specific diagnosis (Africa et al., 1940; Seo, 1979). However, cases of *H. nocens* infection diagnosed in biopsy specimens have seldom been reported in the literature.

We histopathologically examined intestinal tissues of a 58-year-old man admitted to Yeungnam University Hospital with clinical complaints of severe diarrhea, abdominal pain, and vomiting, and diagnosed as the Meckel's diverticulum by endoscopy. Sections of *H. nocens* worms were incidentally found in the mucosa of the small intestine of the patient for which the present paper mainly focuses on.

CASE RECORD

The patient was a 58-year-old male farmer, living in a rural area of Talsong-gun, Kyongsangnam-do. He visited Yeungnam University Hospital with severe abdominal pain, diarrhea, and vomiting on September, 1998. He had a history of eating raw mullets several times in a fish market located in Pusan 6 months ago, and raw fresh-water fish caught from a small stream in Talsong-gun. He often drank alcohol, but didn't have any history of special diseases nor treatments. He experienced mild gastrointestinal symptoms such as indigestion for about 3 months and abruptly developed severe symptoms such as abdominal pain, diarrhea, and vomiting about 1 month before visiting the hospital.

Laboratory examinations revealed that the total number of white blood cells (WBCs), hematocrit, erythrocyte sedimentation rate,

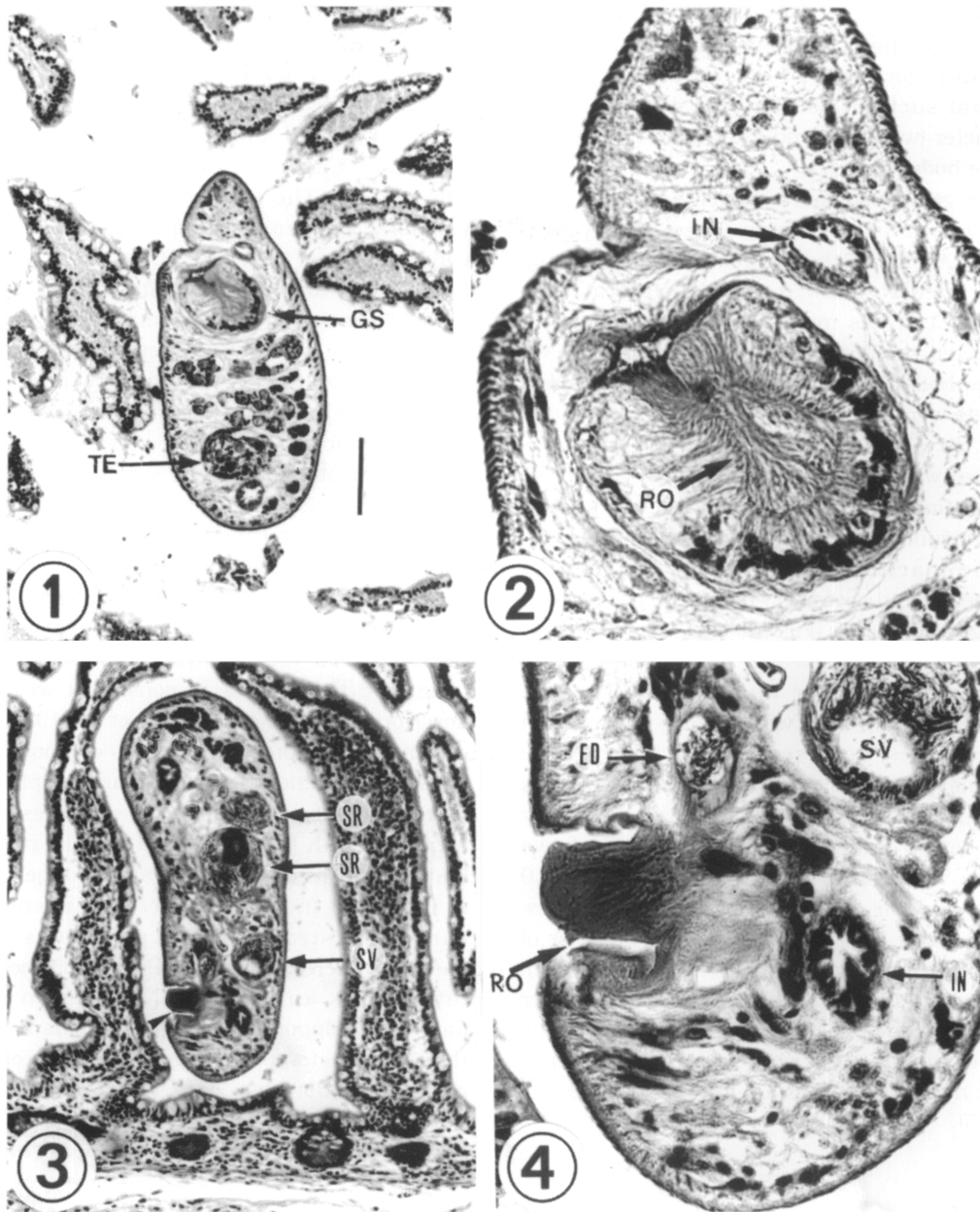
and leucocyte differential counts were within normal limits, but the levels of hemoglobin (12.8 g/dL) and platelets (141,000/mm²) were lower than normal values. In liver function tests, the total protein, albumin, aspartate aminotransferase, and alanine aminotransferase were within normal values, but the level of gamma glutamyl transferase (205 unit/L) was higher than normal. The blood glucose level was increased to 191 mg/dl, and the urine glucose level was triple positive (+++). Hepatitis B antigens and antibodies were all negative, except for HBc IgG antibody. The fecal occult blood was also positive.

In fecal examinations, heterophyid and *Trichuris trichiura* eggs were found by formalin-ether sedimentation technique. By Stoll's egg counting technique, the EPG (eggs per gram of feces) of heterophyid eggs was 400, and that of *T. trichiura* was below 100. The size of heterophyid eggs was 28.2 x 15.4 μ m. The skin tests for *Clonorchis sinensis* and *Paragonimus westermani* showed negative reactions.

PARASITOLOGICAL DESCRIPTION

The specimen was excised from the Meckel's diverticulum at the upper part of the small intestine. It was fixed in 10% formalin and a paraffin block was made. The block was sectioned serially at 6 μ m thickness and stained with hematoxylin and eosin. Three adult flukes (worms A, B and C) were sectioned which were identified as *H. nocens* Onji and Nishio, 1916 (Heterophyidae).

The worms A and B were sliced vertically with a little inclination from the central line (worm A; Figs. 1-2) or from the oral sucker to the posterior part of the genital sucker (worm C). The worm C was sectioned horizontally so that the protruded genital sucker was easily recognized (Figs. 3-4). The maximum length and width of the worm A were 512.0 μ m and 210.8 μ m, respectively, and the maximum length of the worm C was 358.4 μ m. The maximum thickness of the worm C, on the other hand, was 180.7 μ m (Fig. 3). The shape of the worm A looked like a long gourd dipper, and the narrow anterior part became wider and extended down to the posterior part (Fig. 1).



Figs. 1-2. Micrographs showing a longitudinally sectioned worm (worm A) in the small intestine of the patient. **Fig. 1.** A round genital sucker is located at the anterior 1/3 of the body. H & E stain. $\times 100$. **Fig. 2.** Along the inner side of the genital sucker, there were 62 chitinous rodlets on the gonotyl arranged ovally. H & E stain. $\times 450$.

Figs. 3-4. Micrographs showing a horizontally sectioned worm (worm C) in the small intestine of the patient. **Fig. 3.** The gonotyl (arrowhead) is protruded ventrally. The seminal receptacle and seminal vesicle are sectioned well. H & E stain. $\times 100$. **Fig. 4.** A rodlet is seen on the gonotyl. H & E stain. $\times 450$. ED; ejaculatory duct, GS; genital sucker, IN; intestine, RO; rodlet, SR; seminal receptacle, SV; seminal vesicle. TE; testis.

Small tegumental spines were distributed densely over the anterior 1/3 of the body at

the interval of about $1.2 \mu\text{m}$ (worm B). The average length of each spine was $5.4 \mu\text{m}$ with

the maximum thickness of 1.6 μm . The oral sucker was round, 87.0 μm in diameter (worm B), and consisted of strong muscles. The ventral sucker was also round, 89.6 μm in diameter (worm C), and located on the midline of the body.

The genital sucker was well sectioned, and its characteristic structures were clearly seen (worm A). In another section, it was ventrally protruded to show its typical lateral view (worm C). It was round in shape, 133.1 μm in diameter, and located at the anterior 1/3 level of the body (Fig. 1). Sixty-two small chitinous rodlets were arranged circularly on the gonotyl (Fig. 2). The gonotyl was typically hammer-shaped when it is protruded (worm C). One of the chitinous rodlets, 4.6 μm long, was seen to be protruded outwards (Figs. 3-4).

The ejaculatory duct was 18.0 μm in diameter, and cross-sectioned just posterior to the genital sucker (Fig. 4). The seminal vesicle with sperms was located postero-dorsally to the genital sucker and was 56.3 μm in diameter (Fig. 4). Two sections of seminal receptacles were seen posteriorly to the seminal vesicle at 84.5 x 6.8 μm and 64.0 x 43.5 μm in size, respectively (Fig. 3). The ovary was round and was located in front of two testes. Two testes were measured 140.8 x 87.0 μm in size (Fig. 1) and were located a bit askew at the lower part of the body. The diameter of the intestinal cecum was 38.4 μm (worm C). Round vitelline follicles were scattered over posterior sides of the worm (worm B). In the uterus, many eggs were seen, and the eggs were measured 28.1 x 15.4 μm in average size (n=15).

DISCUSSION

Although taxonomic problems were raised after *H. nocens* Onji and Nishio was first described in 1916 (Cort and Yokogawa, 1921; Faust and Nishigori, 1926; Witenberg, 1929), Asada (1934) compromised the situation by designating *H. nocens* as a sub-species of *H. heterophyes*. However, Chai and Lee (1990) acknowledged *H. nocens* as a distinct species because of a consistent feature in the number of chitinous rodlets on the gonotyl; *H. heterophyes* having 70-85 rodlets (Chai et al.,

1986) and *H. nocens* 52-64 rodlets (Chai et al., 1984).

In this study, however, it was fortunate that the genital sucker of the worm A was sectioned in a very good plane to show complete orientation and arrangement of the rodlets on the gonotyl. The number of rodlets in the worm A was counted as 62 which was consistent with *H. nocens* (Chai et al., 1984). In worms B and C, the genital suckers were not well sectioned, and the number of rodlets was difficult to count, but they were diagnosed also as *H. nocens* based on the presence of the genital suckers and other morphological characteristics.

Several mature eggs were seen in the uterus of 3 worms. They were operculated, ellipsoid to oval in shape, and measured 28.1 x 15.4 μm in average size. All of them agreed well with *H. nocens* (Chai et al., 1984). The arrangement of other genital organs such as the ejaculatory duct, seminal vesicle, ovary, seminal receptacle, and testes were all consistent with the descriptions of *H. nocens* (Chai et al., 1984).

Although the present case was diagnosed as *H. nocens* infection, the symptoms complained by the patient may have not been necessarily correlated with the fluke infection. The patient had a Meckel's diverticulum at the upper part of the small intestine, hence, occurrence of various gastrointestinal symptoms was possible. Therefore, it is likely that *H. nocens* infection is an incidental finding in this patient. A supporting evidence for this is that the EPG of heterophyid eggs in the feces of the patient was not high, only 400, which means that this patient is not heavily infected with *H. nocens* to cause significant clinical manifestations.

In clinicopathological aspects, the pathogenicity as well as symptoms caused by *H. nocens* infection in humans are yet unclear and have to be further documented. For example, two cases reported by Chai et al. (1984) suffered from epigastric discomfort and indigestion, but they were co-infected with *C. sinensis* and other intestinal parasites. Eight cases infected with *H. nocens* (Chai et al., 1985) complained of gastrointestinal troubles, but they were also co-infected with other kinds of intestinal parasites. Erratic parasitism in

the heart, brain, and spinal cord by eggs and/or adults of heterophyid flukes were reported (Africa et al., 1940). In *H. nocens* infection, however, such possibility has not yet been elucidated.

According to the past history of the present case, the source of infection is presumed to be raw mullets. In Korea, mullets, *Mugil cephalus*, and gobies, *Acanthogobius flavimanus*, caught from various localities were reported to have metacercariae of *H. nocens* (Seo et al., 1980, 1981b).

There are, however, difficulties when diagnosing human *H. nocens* infection; the low count of daily eggs produced by the worms (Chai and Lee, 1990), relatively low worm burdens in most infected cases (Chai et al., 1994, 1997, 1998), and morphological similarities of eggs to other heterophyids or *C. sinensis* (Chai and Lee, 1990). The present case brings a considerable interest in that a specific diagnosis was made based on sectional morphology of the worms in a mucosal biopsy specimen.

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