

Studies on Intestinal Trematodes in Korea

XI. Two Cases of Human Infection by *Heterophyes heterophyes nocens*

Jong-Yil Chai, Byong-Seol Seo and Soon-Hyung Lee

*Department of Parasitology and Institute of Endemic Diseases,
 College of Medicine, Seoul National University*

INTRODUCTION

The heterophyid flukes are minute intestinal trematodes of mammals and man. The major genera infecting man are *Metagonimus*, *Heterophyes*, *Centrocestus*, *Pygidiopsis*, *Stellantchasmus*, *Haplorchis* and *Procerovum* (Seo, 1979). Among them *Haplorchis*, *Stellantchasmus* and *Procerovum* were reported to be able to cause fatal erratic parasitism in heart, brain and spinal cord with their eggs (Africa *et al.*, 1940), and the eggs of *Heterophyes* were the causative agent of a granuloma at intestinal wall (Nakano *et Inoue*, 1955).

In Korea, *Metagonimus yokogawai* is known to be the most common heterophyid throughout the country (Seo, 1979). As for genus *Heterophyes*, the eggs were found from human stool (Stryker, 1914; Imanishi, 1914), the metacercariae from the mullets (Asada, 1934), and the worms from intestine of animals (Kobayashi, 1925; Furuyama, 1930). However, it was not until the experimental study by Seo *et al.* (1980) when the morphology of adult worm was described in detail and the species of the worms found in Korea determined as *H. heterophyes nocens*. There seems to have been considerably many human cases of this fluke infection where the brackish water fish such as mullets, the second intermediate host of *H. heterophyes nocens*, are preferably eaten raw. However, only one case so far was proven by collection of 3 worms concomitantly with *M.*

yokogawai and *Pygidiopsis summa* (Seo *et al.*, 1981a). In the present paper, the authors report two more cases of natural human *H. heterophyes nocens* infection in Korea.

CASES DESCRIPTION

Case 1: Lee, O.O., 37-year old male residing in Kohŭng-gun, Chollanam-do for 12 years. He said he used to eat several kinds of raw brackish water fish such as mullets (*Mugil cephalus*), perches (*Lateolabrax japonicus*) and gobies (*Acanthogobius flavimanus*) as well as cyprinoid fresh water ones. For one or two years he had the episodes of epigastric pain and discomfort, diarrhea and indigestion but otherwise was quite healthy. The heterophyid eggs, 26-32×14-17μm in size, were found in feces concomitantly with *Clonorchis sinensis* eggs in April 1983. The egg counts of the former were 4,000 in EPG and the latter 16,200. He was treated with 30mg/kg bithionol and purgated with magnesium sulfate. Two to three hours later 35 minute heterophyid flukes, *H. heterophyes nocens*, were collected from the diarrheal stools. The follow-up examination one month later revealed negative for the heterophyid eggs but positive for *C. sinensis* eggs and he was treated again with praziquantel.

Case 2: Han, O.O., 24-year old male residing in Seoul and whose native village is a coastal area in Kohŭng-gun, Chollanam-do. He visited Out-patient Department of Internal Medicine, Seoul National University Hospital in August

1983 with the complaints of easy fatiguability, palpitation, weakness, indigestion, diarrhea and abdominal pain. According to auscultation there were cardiac arrhythmia and grade II-III systolic murmur at apex and left sternal border. The EKG (electrocardiographic) diagnosis was ventricular premature beat. He had the history of eating raw brackish water fish as in Case 1 during the frequent visits to his home village. Routine stool examination revealed positive for the eggs of *Diphyllbothrium latum* but no heterophyid eggs were found. The case was referred to our Department for treatment of tapeworm infection and given 15mg/kg praziquantel (Distocide) followed by 30 g magnesium sulfate for purgation. One complete strobila of *D. latum* was recovered (Lee *et al.*, 1983). But concomitantly with the tapeworm, 4 kinds of heterophyid flukes were collected through stereomicroscopy of the diarrheal stools. The flukes collected were 67 *H. heterophyes nocens*, 188 *Stellantchasmus falcatus*, 2 *Heterophyopsis continua* and 2 *Stictodora* sp. The follow-up study was not performed in this case. And this paper only concerns with *H. heterophyes nocens* infection.

PARASITOLOGICAL DESCRIPTION

Heterophyes heterophyes nocens (Onji *et Nishio*, 1916)

A total of 20 worms, 10 worms from each case, were observed. Body dorsoventrally flat, ovoid in shape, and covered with fine scale-like spines from anterior to posterior one third body (Fig. 1 & 2). Body size 0.73-1.23mm in length and 0.39-0.60mm in width (Table 1). Oral sucker subterminal and 0.061-0.093mm in diameter. Prepharynx present, pharynx well developed and 0.029-0.063mm in diameter. Esophagus slender and muscular, and 0.067-0.122mm long. Intestinal bifurcation in front of ventral sucker and ceca terminating at mid- or post-testicular level. Two ceca frequently terminate unequally. Ventral sucker well developed and muscular on median line of body,

Table 1. Measurements of adult **Heterophyes nocens* in 2 cases (unit:mm)

Item	Case 1	Case 2	Average
Length	0.73-1.14	0.88-1.23	1.11
Width	0.39-0.54	0.44-0.60	0.49
Oral sucker (diam.)	0.061-0.093	0.070-0.087	0.079
Pharynx (diam.)	0.043-0.060	0.029-0.063	0.050
Esophagus	0.067-0.113	0.070-0.122	0.094
Ventral sucker			
length	0.180-0.213	0.197-0.255	0.212
width	0.166-0.200	0.162-0.220	0.188
Genital sucker			
length	0.106-0.133	0.110-0.179	0.132
width	0.080-0.113	0.070-0.127	0.099
No. rodlets	58-64	52-54	56.6
Ovary			
length	0.067-0.100	0.070-0.104	0.087
width	0.053-0.080	0.070-0.104	0.078
Right testis			
length	0.086-0.120	0.098-0.185	0.121
width	0.080-0.113	0.075-0.144	0.096
Left testis			
length	0.100-0.133	0.087-0.162	0.120
width	0.067-0.100	0.058-0.116	0.086
Intrauterine eggs			
length	0.024-0.028	0.025-0.028	0.026
width	0.012-0.017	0.013-0.015	0.014

* The worms from each case were measured after acetocarmine stain

measuring 0.180-0.255mm by 0.162-0.220mm in size. Genital sucker prominent, anteroventrally protrude toward ventral sucker, and 0.106-0.179mm by 0.070-0.127mm in size (Fig. 3 & 4). Chitinous rodlets on gonotyl 52-64 in number, arranged in a row but interrupted near ventral sucker, and each consisted of about 5 small hook-like spines. Two testes side by side but not exactly parallel, ovoid or globular in shape, and 0.086-0.185mm by 0.075-0.144mm for right one and 0.087-0.162mm by 0.058-0.116mm for left one in size. Seminal vesicle well developed and C-shape between ventral sucker and ovary. Cirrus pouch absent. Ovary round or globular, located on median line of body in front of testes, and 0.067-0.104mm by 0.053-0.104mm in size. Seminal receptacle behind ovary but not well seen. Vitellaria

consisted of 4-6 dense follicles on both sides between testes and seminal vesicle. Uterus long between ventral sucker and testes with numerous eggs. The eggs in stool of Case 1 oval in shape (Fig. 5) and 0.026-0.032mm by 0.014-0.017mm in size. Intrauterine eggs yellowish in color, oval in shape with a little attenuated anterior end, and 0.024-0.028mm by 0.012-0.017mm in size (Fig. 6). The egg surface lacks the muskmelon pattern which is characteristically seen in *C. sinensis* eggs (Fig. 7).

DISCUSSION

The species *Heterophyes nocens* was firstly described by Onji *et* Nishio (1916). And Cort *et* Yokogawa (1921) stressed the validity enlisting the differential points from Egyptian *H. heterophyes*. Witenberg (1929) also retained the validity appreciating the different number of chitinous rodlets on genital sucker, 50-60 in *H. nocens* and 75-87 in *H. heterophyes*, to be a distinct character. However, Lane (1922) and Faust *et* Nishigori (1926) denied *H. nocens*. Such situation was compromised by Asada (1934) putting it as a subspecies; *H. heterophyes nocens*.

The heterophyid flukes collected from the present cases were identified *H. heterophyes nocens*. Among the three species of *Heterophyes* from man, the measurements of the present specimens agree well both to *H. heterophyes* and *H. heterophyes nocens* but the number of

rodlets is only compatible with the latter (Table 2). The present worms also agree to *H. katuradai* (Ozaki *et* Asada, 1926) so far as the rodlet number is concerned. However, this species is regarded synonym of *H. heterophyes nocens* because its morphological characters were not distinct (Witenberg, 1929) and no further convincing reports have been made so far.

The heterophyid flukes are known to be able to cause erratic parasitism in man. According to Africa *et al.* (1940) and Nakano *et* Inoue (1955), the eggs were detected from the inflammatory heart valves of fatal patients in the Philippines and from a tumor mass near appendix of a girl in Japan. In this regard, Yokogawa (1940) described that such visceral complication may be resulted from malnutrition and decreased resistance to parasites to invade into intestinal mucosa and to flow their eggs into blood stream. The Case 2 of the present paper had the complaint of palpitation and EKG finding of ventricular premature beat. However, whether or not such heart problem was related with the present heterophyid infections; *Heterophyes*, *Stellantchasmus*, *Heterophyopsis* and *Stictodora*, is not certain because further investigation to detect eggs in heart is not possible.

As for the second intermediate host of *H. heterophyes nocens* in Korea, the mullets and gobies caught at southern coastal areas are known to harbour the metacercariae (Seo *et al.*, 1980 & 1981b). Therefore, it is certain that the source of infection is brackish water fish

Table 2. Comparison of the measurements of three species of the genus *Heterophyes* occurring in man (size unit:mm)

Item	<i>H. heterophyes</i> (Asada, 1934)	<i>H. katuradai</i> (Ozaki <i>et</i> Asada, 1926)	<i>H. nocens</i> * (Asada, 1934)
Body size	0.975-1.175 × 0.50-0.65	0.61-0.89 × 0.40-0.47	0.90-1.30 × 0.40-0.65
Oral sucker	0.080-0.100 × 0.095-0.110	0.061-0.063	0.065-0.085
Ventral sucker	0.200-0.225 × 0.225-0.250	0.195-0.220	0.190-0.220 × 0.200-0.230
Ovary	0.065-0.085	0.055-0.092	0.105-0.140
Intrauterine eggs	0.025-0.028 × 0.015-0.017	0.025-0.026 × 0.014-0.015	0.025-0.028 × 0.015-0.017
Genital sucker	0.125-0.190 × 0.125-0.175	0.11-0.14 × 0.07-0.085	0.115-0.170 × 0.095-0.120
No. of rodlets on genital sucker	68-75	52-57	52-63

* This species is called *H. heterophyes nocens* after Asada (1934)

which they said to have eaten.

Although the raw flesh of such fish is favoured by many Koreans, there have been detected only three human cases of *H. heterophyes nocens* so far. It seems largely due to some difficulties in diagnosis, such as much similarity in shape among the heterophyid and even *C. sinensis* eggs, and small number of eggs produced by them, for example, only 35-45 eggs daily per worm of *M. yokogawai* (Ahn *et al.*, 1981). Many heterophyid infections other than *M. yokogawai* might have been misinterpreted as *M. yokogawai* or *C. sinensis*, or missed during mass fecal examinations. Africa *et al.* (1940) described that they could not detect any eggs from stool of the postmortem cases of intestinal and visceral heterophyidiasis, even though 500 adult worms were recovered from mucosal scrapping of a heaviest case. Therefore, the failure in detection of heterophyid eggs from Case 2 seems to have been due to small number of eggs in stool.

SUMMARY

Two human cases of *Heterophyes heterophyes nocens* infection were proved by identifying adult worms after treatment with bithionol or praziquantel in 1983 in Korea. They are 37 (Case 1) and 24-year old (Case 2) males whose residence or native village is a southern coastal area in Kohŭng-gun, Chollanam-do. The Case 1 had the gastrointestinal symptoms such as epigastric pain and indigestion, and the Case 2 heart problems such as arrhythmia and ventricular premature beat in EKG and digestive symptoms such as diarrhea and abdominal pain. After the treatments, 35 and 67 specimens of *H. heterophyes nocens* respectively were collected from the diarrheal stools through stereomicroscopy. The Case 1 was concomitantly infected with *Clonorchis sinensis* and the Case 2 with 3 other kinds of heterophyid flukes and with *Diphyllobothrium latum*. The cases said to have eaten raw brackish water fish such as mullets (*Mugil cephalus*), perches (*Lateolabrax japonicus*) and

gobies (*Acanthogobius flavimanus*) which are the intermediate hosts of *H. heterophyes nocens* in Korea.

REFERENCES

- Africa, C.M., de Leon, W. and Garcia, E.Y. (1940) Visceral complications in intestinal heterophyidiasis of man. *Acta Medica Philippina*, Monographic Series, No. 1.
- Ahn, Y.K., Soh, C.T. and Lee, S.K. (1981) Egg laying capacity of *Metagonimus yokogawai*. *Yonsei Rep. Trop. Med.*, 12(1):11-16.
- Asada, J. (1934). On the *Metagonimus* and its related species. *Clinical Med.*, 22(2):43-56 (in Japanese).
- Cort, W.W. and Yokogawa, S. (1921) A new human trematode from Japan. *J. Parasit.*, 8:66-69.
- Furuyama, T. (1930) On the fluke family Heterophyidae in Korea. *J. Chosen Med. Ass.*, 20:251-252 (in Japanese).
- Faust, E.C. and Nishigori, M. (1926) The life cycles of two new species of Heterophyidae, parasitic in mammals and birds. *J. Parasit.*, 13(2):91-130.
- Imanishi, Y. (1914) On the examination of intestinal parasites. *J. Chosen Med. Ass.*, No. 13:45 (in Japanese).
- Kobayashi, H. (1925) On the animal parasites in Korea. *Japan Med. World*, 5(1):9-16.
- Lane, C. (1922) A note on *Heterophyes nocens* as a distinct species of trematode parasite. *Lancet*, II: 505.
- Lee, S.H., Seo, B.S., Chai, J.Y., Hong, S.T., Hong, S.J. and Cho, S.Y. (1983) Five cases of *Diphyllobothrium latum* infection. *Korean J. Parasit.*, 21(2):150-156 (in Korean).
- Nakano, T. and Inoue, M. (1955) One human case of intestinal tumor caused by the eggs of *Heterophyes heterophyes nocens*. *Geka No Ryoiki*, 3(4): 272-274 (in Japanese).
- Onji, Y. and Nishio, T. (1916) On the trematodes whose intermediate host is brackish water fish. *Chiba Igaku Semmon Gakko Zasshi*, 81, 82:229-249 (in Japanese).
- Ozaki, Y. and Asada, J. (1926) A new human trematode, *Heterophyes katsuradai* n.sp. *J. Parasit.*, 12:215-218.
- Seo, B.S. (1979) Biology and clinical aspects of Heterophyidae. *Human Science*, 3(10):784-791 (in Korean).

- Seo, B.S., Cho, S.Y. and Chai, J.Y. (1980) Studies on intestinal trematodes in Korea II. Identification of the metacercariae of *Heterophyes heterophyes nocens* in mullets of three southern coastal areas. *Seoul J. Med.*, 21(1):30-38.
- Seo, B.S., Hong, S.T. and Chai, J.Y. (1981a) Studies on intestinal trematodes in Korea III. Natural human infections of *Pygidiopsis summa* and *Heterophyes heterophyes nocens*. *Seoul J. Med.*, 22(2): 228-235.
- Seo, B.S., Hong, S.T., Chai, J.Y. and Cho, S.Y. (1981b) Studies on intestinal trematodes in Korea IV. Geographical distribution of *Pygidiopsis* and *Heterophyes metacercariae*. *Seoul J. Med.*, 22(2): 236-242.
- Stryker, E. de M. (1914) Extracts from report for 1913, Suan Mine Hospital, Korea. *China Med. J.*, 28:277-280.
- Witenberg, G. (1929) Studies on the trematode-Family Heterophyidae. *Ann. Trop. Med. Parasit.*, 23:131-268.
- Yokogawa, S. (1940) On the visceral heterophyidiasis, especially on the etiology of heart, brain and spinal cord heterophyidiasis. *Taiwan Igakkai Zasshi*, 39(10):1, 729-1, 730 (in Japanese).

＝國文抄錄＝

韓國의 腸吸蟲에 관한 研究

XI. *Heterophyes heterophyes nocens*의 人體感染 2례

서울대학교 醫科大學 寄生蟲學教室 및 風土病研究所

蔡 鍾 一 · 徐 丙 高 · 李 純 炯

異形吸蟲類의 하나인 *Heterophyes heterophyes nocens*에 의한 人體感染 2례가 治療후 蟲體를 얻음으로써 확인되었다. 患者는 37세(第1例) 및 24세(第2例) 남자로 전남 고흥군 해안마을이 고향이거나 현재 거주지이며 第1例는 上腹部 痛症 및 消化不良 등의 症狀을, 第2例는 EKG검사상 不整脈 및 ventricular premature beat 등 心臟機能異常과 泄瀉, 腹痛 등 消化器 症狀을 호소하였다. 1983年 4月 및 8月에 bithionol 30mg/kg 또는 praziquantel 15mg/kg을 투여하고 泄瀉便을 입체해부현미경하에서 검사한 바 각각 35 및 67마리의 *H. heterophyes nocens*가 수집되었다. 大便檢査 또는 蟲體檢査上 第1例는 肝吸蟲이, 第2例는 3種의 다른 異形吸蟲類와 廣節裂頭條蟲이 동시 감염되어 있었다. 患者들은 *H. heterophyes nocens*의 중간숙주인 숭어(*Mugil cephalus*), 농어(*Lateolabrax japonicus*) 및 문질망둑(*Acanthogobius flavimanus*) 등 반염수산 魚類를 膾로 먹은 경력이 있었다.

EXPLANATION FOR FIGURES

- Fig. 1.** Adult of *H. heterophyes nocens* from Case 2. Note the relationship between ventral sucker and genital sucker (arrows). Unstained specimen (Scale: 0.1mm).
- Fig. 2.** *Ibid* from Case 1. Acetocarmine stained (Scale: 0.1mm).
- Fig. 3.** Ventral view of genital sucker. Formalin-fixed specimen (Scale: 20 μ m). The number of chitinous rodlets on gonotyl is about 58.
- Fig. 4.** Scanning electron microscopic view of genital sucker of a worm from Case 1 treated with bithionol. Note the protruded appearance of genital sucker with rodlets (arrows) on it (Scale: 10 μ m).
- Fig. 5.** An egg of *H. heterophyes nocens* in stool of Case 1 (Scale: 10 μ m). There is nearly no muskmelon pattern or wrinkling at its shell surface.
- Fig. 6.** Scanning electron microscopic view of an intrauterine egg of *H. heterophyes nocens* (Scale: 5 μ m). Note operculum at the upper end and relatively smooth shell surface.
- Fig. 7.** *Ibid* of *C. sinensis* (from a worm obtained by experimental infection with the metacercariae) (Scale: 5 μ m). Note the markedly rough shell surface in muskmelon pattern and compare with that of *H. heterophyes nocens* in Fig. 6.

