

Anisakiasis: Report of 15 Gastric Cases Caused by *Anisakis* Type I Larvae and a Brief Review of Korean Anisakiasis Cases

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Abstract: The present study was performed to report 15 anisakiasis cases in Korea and to review the Korean cases reported in the literature. Total 32 *Anisakis* type I larvae were detected in the stomach of 15 patients by the endoscopy. Single worm was detected from 12 cases, and even 9 larvae were found from 2 cases. Epigastric pain was most commonly manifested in almost all cases, and hemoptysis and hematemesis were seen in 1 case each. Symptom manifestations began at 10-12 hr after eating fish in 73.3% cases. Endoscopy was performed 1-2 days after the symptom onset in most cases. The common conger, *Conger myriaster*, was the probable infection source in 7 cases. In the review of Korean anisakiasis cases, thus far, total 645 cases have been reported in 64 articles. *Anisakis* type I larva was the most frequently detected (81.3%). The favorable infection site of larvae was the stomach (82.4%). The common conger was the most probable source of human infections (38.6%). Among the total 404 cases which revealed the age and sex of patients, 185 (45.8%) were males, and the remaining 219 (54.2%) were female patients. The age prevalence was the highest in forties (34.7%). The seasonal prevalence was highest in winter (38.8%). By the present study, 15 cases of gastric anisakiasis are added as Korean cases, and some epidemiological characteristics of Korean anisakiasis were clarified.

Key words: Anisakiasis, *Anisakis* type I larva, review, Korean anisakiasis

INTRODUCTION

Anisakiasis is one of the fishborne zoonotic diseases, especially in localities, where people have a custom of eating raw marine fish and squids like in Japan and Korea [1,2]. The concept of this disease was first raised by van Thiel et al. [3] in the Netherlands. After then, human infection cases were consequently reported in England, Japan, and the Republic of Korea (Korea) [4-7]. Nowadays, this zoonotic nematode disease is a clinical concern worldwide, including Japan, Korea, the Netherlands, Spain, France, Italy, Germany, and the United States. Especially in Japan, it has been known that more than 2,000 cases occurred annually [1,2].

Since the first human case was reported by Kim et al. [7] in 1971, until now numerous patients have increasingly occurred

in Korea. Especially the increasing tendency of cases was accelerated by the common use of endoscopy in the diagnosis and treatment of gastric anisakiasis [8]. Chung et al. [9] and Seol et al. [10] reported 27 and 20 cases that occurred in Busan Metropolitan City. Im et al. [11,12] analyzed 39 and 107 cases of gastric anisakiasis occurred in Jeju-do. Song et al. [13] reported total 39 cases residing in Incheon Metropolitan City. Recently, Lee et al. [14] analyzed total 141 cases diagnosed by the endoscopy in a local clinic in Jinju-si, Gyeongsangnam-do. Most recently, Lim et al. [15] clarified the etiologic agents of 16 human anisakiasis in Korea, 15 of which were confirmed as *Anisakis pegreffii* larvae and only 1 was *Anisakis simplex* larva using a molecular analysis. In this study, we report an additional 15 gastric anisakiasis cases that occurred in Gyeongsangnam-do, and then analyzed the epidemiologic and clinical characteristics of Korean anisakiasis cases through a literature review.

CASE RECORD

Total 15 anisakiasis cases were diagnosed with the gastric endoscopy in the Gyeongsang National University Hospital

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Table 1. Summary of the 15 cases of gastric anisakiasis caused by *Anisakis* type I larvae

Case no.	Age	Sex	Date of occurrence	Fish eaten	Chief complaints	Time from eating fish to symptom onset	Time from symptom onset to endoscopy	Detection site of worm in stomach
1.	33	M	Oct., '99	Common conger	Severe epigastric pain	12 hr	2 days	Middle body G.C ^a
2.	47	M	Feb., '00	Several kinds of marine fishes	Epigastric pain, nausea & vomiting	12 hr	3 days	Upper body Anterior wall
3.	37	M	Jun., '00	Common conger	Hemoptysis	10 hr	1 day	Lower body G.C ^a
4.	27	M	Jun., '00	Several kinds of marine fishes	Epigastric pain	12 hr	36 hr	Upper body G.C ^a
5.	41	M	Aug., '00	Several kinds of marine fishes	Epigastric pain & nausea	24 hr	3 days	Upper body G.C ^a
6.	28	M	Oct., '00	Common conger	Epigastric pain	6 hr	12 hr	Middle body G.C ^a
7.	55	M	Jun., '01	Several kinds of marine fishes	Severe epigastric pain	12 hr	2 days	Lower body G.C ^a
8.	59	M	Jan., '02	Common conger	Epigastric pain	12 hr	12 hr	Middle body G.C ^a
9.	45	F	Sep., '02	Common conger & Pacific cutlass fish	Epigastric pain & hematemesis	6 hr	3 days	Uncertain ^b
10.	36	F	Oct., '02	Several kinds of marine fishes	Severe epigastric pain	12 hr	2 days	Lower body G.C ^a
11.	42	M	Apr., '03	Anchovy	Epigastric pain, nausea & vomiting	10 hr	1 day	Upper body Anterior wall
12.	51	M	May., '04	Common conger	Severe epigastric pain	12 hr	1 day	Uncertain ^b
13.	61	M	Mar., '09	Anchovy	Epigastric pain, nausea & vomiting	10 hr	1 day	Upper body lesser curvature
14.	52	M	Dec., '09	Uncertain	Epigastric pain & nausea	7 hr	1 day	Lower body G.C ^a
15.	46	F	Jan., '10	Common conger	Severe epigastric pain	12 hr	2 days	Uncertain

^aGreater curvature.^bNine larvae were detected in each case.**Table 2.** Measurements^a and indices of *Anisakis* type I larvae from human cases

Items	3rd stage (n=7)	4th stage (n=7)	Chai et al. (1986) [7] ^b
Body length	16.55-29.0 (23.98)	17.10-22.75 (20.68)	13.4-25.0 (20.7)
Body width	0.35-0.58 (0.48)	0.45-0.58 (0.50)	0.23-0.54 (0.41)
Esophagus (total)	2.0-3.0 (2.46)	2.35-3.38 (2.88)	1.86-2.70 (2.36)
Muscular part	1.55-2.08 (1.85)	1.75-2.50 (2.18)	1.27-1.89 (1.65)
Ventricular part	0.45-0.92 (0.62)	0.55-0.88 (0.71)	0.57-0.83 (0.71)
Tail	0.08-0.12 (0.10)	0.10-0.15 (0.13)	0.07-0.12 (0.10)
Mucron	20-25 (21) μ m	-	-
Indices ^c			
α	37.59-58.0 (49.96)	34.20-50.0 (41.36)	43.7-66.3 (50.6)
β_1	7.20-10.04 (9.75)	6.63-8.24 (7.18)	7.02-9.92 (8.73)
β_2	10.08-13.94 (12.96)	8.95-10.56 (9.49)	10.01-14.70 (12.5)
β_3	24.34-40.34 (38.68)	23.58-37.50 (29.13)	25.5-39.4 (29.2)
γ	157.9-290.0 (239.8)	145.57-186.5 (159.08)	167.6-271.3 (213.4)

^aUnit is mm.^bfrom the yellow corvine, *Pseudosciaena polyactis*.^cLegend: α =Body length/Body width; β_1 =Body length/Esophagus; β_2 =Body length/Muscular part of esophagus; β_3 =Body length/Ventriculus; γ =Body length/Tail.

and a local clinic located in Jinhae-gu, Changwon-si, Gyeong-sangnam-do from October 1999 to January 2010. Most of the cases (80%) were men, and only 3 were women. Total 32 *Anisakis* type I larvae were detected in the stomach of 15 patients. A single worm was detected from 12 cases, 2 worms from 1

case, and even 9 larvae were found from 2 cases. Epigastric pain was the most common symptom in almost all cases, and nausea and vomiting were accompanied in some cases. Hemoptysis and hematemesis occurred in 1 case each. Symptom manifestations began at 10-12 hr after eating fish in most cases

Table 3. Number of anisakiasis cases and number of papers reported among the Korean literature

Duration of report	No. of cases (%) reported	No. of papers (%) published
1971	1 (0.2)	1 (1.6)
1980-1989	77 (11.9)	18 (28.1)
1990-1999	249 (38.6)	25 (39.1)
2000-2009	163 (25.3)	10 (15.6)
2010 and later	155 (24.0)	10 (15.6)
Total	645 (100)	64 (100)

Table 4. Anisakiasis cases by the occurrence localities

Locality	No. of cases (%)
Jeju-do	217 (34.4)
Gyeongsangnam-do (Jinju-si)	144 (22.8)
Seoul	126 (20.0)
Busan	64 (10.1)
Incheon	41 (6.5)
Gyeongsangbuk-do (Pohang-si)	20 (3.2)
Daegu	5 (0.8)
Gwangju	4 (0.6)
Daejeon	2 (0.3)
Jeollabuk-do	2 (0.3)
Gangwon-do	2 (0.3)
Others ^a	4 (0.6)
Total	631 (100)

^aGyeonggi-do (Uijeongbu-si); Chungcheongbuk-do (Chungju-si), Chungcheongnam-do (Cheonan-si) and Jeollanam-do (Suncheon-si) each 1 case.

(73.3%). Endoscopy was performed in 1-2 days after symptom onset in most cases (66.7%). As the probable source of infection, 7 (46.7%) and 2 (13.3%) cases recalled that they had eaten raw common conger, *Conger myriaster*, and anchovy, respectively. However, 6 cases could not remember the exact species of fish; several kinds of fish mixed or uncertain. The case information is summarized in Table 1. Among the total 32 *Anisakis* type I larvae (either the 3rd or 4th-stage), 7 were morphologically observed and measured with a micrometer (Table 2).

Review of Korean anisakiasis cases

The articles of Korean anisakiasis cases were basically searched through PubMed site using the internet. The references in all articles were strictly seen to prevent missing cases. Until now, a total of 645 cases have been reported in 64 articles since the first case recorded by Kim et al. [8] in 1971. During 1990-1999, a total of 249 cases (38.6%) were reported in

Table 5. Age and sex distribution of patients

Age (years)	No. of cases (%)		
	Male	Female	Total
Below 19	1	6	7 (1.7)
20-29	19	20	39 (9.7)
30-39	62	71	133 (32.9)
40-49	68	72	140 (34.7)
50-59	22	38	60 (14.9)
Over 60	13	12	25 (6.2)
Total	185 (45.8)	219 (54.2)	404 (100)

Table 6. Fishes or cephalopods, the probable source of infection, consumed by anisakiasis cases

Fishes (scientific name)	No. of cases (%)
Common conger (<i>Conger myriaster</i>)	120 (38.6)
Croaker (<i>Pseudosciaena</i> spp.)	36 (11.6)
Squid	32 (10.3)
Yellowtail (<i>Seriola</i> spp.)	30 (9.7)
Flatfish	17 (5.5)
Pacific cod (<i>Gadus macrocephalus</i>)	6 (1.9)
Anchovy (<i>Engraulis japonica</i>)	4 (1.3)
Rockfish (<i>Sebastes</i> spp.)	4 (1.3)
Sea breams	3 (1.0)
Pacific cutlass fish (<i>Trichiurus lepturus</i>)	3 (1.0)
Gizzard shad (<i>Konosirus punctatus</i>)	2 (0.6)
Skates	2 (0.6)
Others ^a	5 (1.6)
Several species of fish mixed	47 (15.1)
Total	311 (100)

^a*Halichoeres tenuispinis* (motleystripe rainbowfish), *Miichthys miiuy* (brown croaker), mullet, tuna and *Octopus vulgaris* (common octopus) each 1 case.

25 papers (39.1%). The number of anisakiasis cases reported in the Korean literature is shown in Table 3. The incidence rate was the highest in Jeju-do (34.4%), followed by in Gyeongsangnam-do (22.8%), Seoul (20.0%), Busan (10.1%), Incheon (6.5%), Gyeongsangbuk-do (3.2%), and other 9 administrative regions (0.16-0.79%) (Table 4). Among a total of 404 cases which revealed the age and sex of patients, 185 (45.8%) were men and the remaining 219 (54.2%) were women. The age prevalence was the highest in forties (34.7%), followed by thirties (32.9%), fifties (14.9%), twenties (9.7%), over sixty (6.2%), and teens (1.7%) (Table 5). As the probable source of human infections, the common conger was most frequently mentioned by patients (38.6%), followed by croaker (11.6%), squid (10.3%), yellowtail (9.7%), flatfish (flounder: 5.5%), and the other 12 species of marine fish (Table 6). The etiologic larval type was designated in 203 cases in the lit-

Table 7. Morphologic identification of anisakid larvae among the literature

Type of larvae	No. (%) of larvae identified
<i>Anisakis</i> type I	165 (81.3) ^a
<i>Anisakis</i> type II	8 (3.9)
<i>Terranova</i> type A	24 (11.8)
<i>Anisakis</i> sp.	3 (1.5)
<i>Contracaecum</i> sp.	3 (1.5)
Total	203 (100)

^a15 cases of *A. pegreffii* were included.

Table 8. Location of worms detected

Location	No. (%) of cases
Stomach	333 (82.4)
Small intestine ^a	46 (11.4)
Gastro-esophageal junction	14 (3.5)
Large intestine ^b	6 (1.5)
Esophagus	2 (0.5)
Others ^c	3 (0.7)
Total	404 (100)

^aIleum (12 cases); jejunum and duodenum (2 cases each).

^bColon (5 cases); cecum (1 case).

^cPalatine tonsil, ileo-cecal region and mesocolic lymph node (1 case each).

eratures. Among them, 165 cases (81.3%) were due to *Anisakis* type I larvae, 24 (11.8%) were by *Terranova* type A, and 8 cases (3.9%) were by *Anisakis* type II. Each of the 3 cases were due to *Contracaecum* sp. and *Anisakis* sp. larvae (Table 7). The predilection site was the stomach (82.4%), followed by small intestines (11.4%), gastro-esophageal junction (3.5%), large intestines (1.5%), esophagus (0.5%), and others including the palatine tonsil, ileo-cecal region, and mesocolic lymph node (Table 8). In most cases (65.7%), symptoms were manifested before 12 hr from eating raw flesh of fish (Table 9). The seasonal prevalence was the highest in winter (38.8%), followed by spring (23.1%), autumn (19.9%), and summer (18.2%) (Table 10).

DISCUSSION

By the present study, 15 cases of gastric anisakiasis have been added among the Korean anisakiasis cases. Only 1 anisakid larva was detected in most of the cases. However, interestingly, even 9 worms were recovered from each of 2 cases. Like in the previous studies, epigastric pain was the chief complaint and most commonly manifested in almost all cases.

Table 9. The time intervals from eating raw flesh of fish to onset of symptoms

Time (hr)	No. (%) of cases
≤6	109 (32.4)
7-12	112 (33.3)
13-24	51 (15.2)
25-72	36 (10.7)
≥73 (chronic)	28 (8.3)
Total	336 (100)

Table 10. The frequency of patients by season

Season	No. (%) of cases
Spring	71 (23.1)
Summer	56 (18.2)
Autumn	61 (19.9)
Winter	119 (38.8)
Total	307 (100)

However, hemoptysis and hematemesis were revealed in 1 case each. It has been known that severe bleeding can occur due to anisakid larva infection in patients with gastric ulcer [15,17-19]. Therefore, these 2 cases may have had some ulcer lesions in their stomach. Time intervals from fish eating to symptom onset and from symptom onset to endoscopy were 10-12 hr and 1-2 days in most cases. These findings were in accordance with previous studies [11,15]. The common conger, *C. myriaster*, is suspected as the most probable source of infection in 7 patients (46.7%). Until now, in Korea, a total of 645 cases have been reported in 64 papers since the first case reported by Kim et al. [8]. Accordingly, as 15 cases have been added by this study, the total number of anisakiasis cases in Korea became 660 cases in the Korean literature.

Among 32 *Anisakis* type I larvae detected, 7 were in the fourth-stage (L_4), which had molted in the stomach of the patients. They were similar in size with the third stage larvae (L_3), but they can be morphologically differentiated from L_3 by the following characteristic features: (1) absence of the boring tooth at the anterior end and the mucron at the posterior end; (2) the presence of the 3 well-defined lips; (3) the appearance of transverse striations on the cuticular body surface; (4) the appearance of altered ventriculus and intestine (Table 2) [20,21].

The number of human anisakiasis cases (38.6%) and papers (39.1%) published in Korea were the highest during 1990-1999, while 163 cases (25.3%) were reported in 10 articles (15.6%) during 2000-2009, and only 77 (11.9%) were record-

ed in 18 papers (28.1%) during 1980-1989. During 1980-1989, each anisakiasis case was meaningful and could be easily published in journals. However, recently, anisakiasis case reports were done after gathering large numbers of cases to demonstrate something different and unique findings [15,22-24]. So, the number of articles published was not so many during the recent years.

The higher incidence rate was found in coastal areas, such as Jeju-do, Jinju, (Gyeongsangnam-do), Busan, Incheon, and Pohang (Gyeongsangbuk-do), where people favorably consume raw flesh of marine fish. Moreover, the presence of medical authorities, who are able to produce manuscripts describing case reports, is also an important factor [10-15,25,26].

Among total 404 cases that revealed the age and sex of patients, the number of women was slightly more than that of men, with the ratio of women to men of 1.18:1. This finding was largely influenced by the report of Lee et al. [15], who analyzed 141 gastrointestinal anisakiasis cases in a local clinic in Jinju-si, Gyeongsangnam-do. In their study, the number of women (91 cases) was much more than that of men (50) [15]. Meanwhile, Im et al. [13] reported total 107 cases in Jeju-do, the number of women (47 cases) was lesser than that of men (60), with the ratio of women to men of 0.78:1 [13]. Regarding the age prevalence, most of the cases (67.6%) were patients in their thirties and forties.

Various species of marine fish and cephalopods have been known as the sources of human infections. In European countries, especially in The Netherlands and Spain, raw or pickled fish, such as herring, hake, anchovy, and cod, are known to be important infection sources [3,27]. In Japan, some species of flounders, Japanese common squid, the Pacific cod, and the bluefin tuna are the main sources in Hokkaido, and the spotted sardine, the chub mackerel, the horse mackerel, the oceanic bonito, and the chum salmon are important infection sources in Kyushu [28,29]. However in Korea, the common conger was the most frequently mentioned by the patients as the probable source of infections, followed by the croaker, squid, yellowtail, flatfish, and the other 12 species of marine fish.

It has been known that the majority of human infections were caused by the larvae of *A. simplex* (*Anisakis* type I), and rarely or occasionally by those of *Anisakis physeteris* (*Anisakis* type II), and *Pseudoterranova decipiens* (*Terranova* type A) [13,14,30-33]. In the present review, 81.3% cases were due to *Anisakis* type I larvae, and 11.8% and 3.9% were by *Terranova*

type A and *Anisakis* type II larvae, respectively. Recently, the etiologic agents of human anisakiasis in Korea, which were morphologically *Anisakis* type I larvae, were molecularly confirmed to be *A. pegreffii* larvae [16]. Moreover, most of the *Anisakis* type I larvae detected in 7 fish species from the Yellow Sea and the South Sea in Korea were also identified as *A. pegreffii* [34]. Although only 15 human cases were enrolled by Lim et al. [16], it seems that most of the Korean anisakiasis cases may be caused by *A. pegreffii* based on the above 2 molecular studies. Molecular methods should be more frequently adopted to identify the causative agent of human anisakiasis in the future.

The stomach was the main site of infection in most cases (82.4%). However, anisakid larvae were found rarely in other digestive organs, i.e., esophagus, small intestines, large intestines, and mesocolic lymph node. In most cases, symptoms were manifested before 12 hr from eating of the raw fish flesh. The seasonal prevalence was the highest in winter, followed by in spring, autumn, and summer. This seasonality seemed directly related to the frequency of eating raw fish flesh in each season. The consumption of raw fish meat is more popular in winter season rather than in summer season in Korea because of the anxiety for food poisoning.

CONFLICT OF INTEREST

We have no conflict of interest related to this work.

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