

Clinicopathological Studies on Larval Anisakiasis, with Special Reference to the Report of Extra-gastrointestinal Anisakiasis

HIROYUKI YOSHIMURA, NOBUAKI AKAO,
KAORU KONDO AND YOSHIHIRO OHNISHI

*Department of Parasitology, School of Medicine, Kanazawa
University, Kanazawa City, Japan*

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Since larval *Anisakis* infections in man were reported from Holland (van Thiel *et al.*, 1960), the disease has been regarded as a public health problem also in Japan.

During the past fifteen years, more than 500 cases of the gastrointestinal anisakiasis have been studied by the Japanese workers (Asami *et al.*, 1965; Yoshimura, 1966 a, b; Yokogawa and Yoshimura, 1967; Iwano *et al.*, 1974; Ishikura, 1969; Otsuru, 1975). On the other hand, following the first report of human infections due to a *Terranova* larva penetrating the stomach wall (Suzuki *et al.*, 1972), more than fifteen of similar cases have been recognized in Japan (Nagano *et al.*, 1973, 1975; Koyama *et al.*, 1976).

With regard to the extra-gastrointestinal involvement due to *Anisakis* infection, van Thiel and van Houten (1967) were the first to find a living larva in the abdominal cavity of the patient treated by the surgical operation because of the acute abdominal conditions. Since then, such cases involving extra-gastrointestinal tissues have been reported in the Japanese papers (Furukawa *et al.*, 1974; Nishimura *et al.*, 1974; Sasaki *et al.*, 1977; Kagei and Sakaguchi, 1978).

The present study dealt with the clinicopathological analysis of 200 cases clinically

diagnosed as anisakiasis, collected in our Department from September 1976 to March 1979, with special reference to the two cases of extra-gastrointestinal infections.

Clinical Diagnoses and the Proven Cases of *Anisakis* or *Ter- ranova* Infections

Except for a few cases out of the 200 patients, their residential areas were Kanazawa city and its vicinity. The majority of patients complained of the gastric pain or colic, vomiting, fullness and sometimes diarrhea, within twenty hours after eating raw sea fishes ("sashimi" or "sushi") such as the mackerel (*Pneumatophorus japonicus*), cod (*Gadus macrocephalus*), pacific halibut (*Hippoglossus stenolepis*), squid (*Todarodes pacificus*), scad (*Trachurus japonicus*) and others which are usually eaten raw by the Japanese people (Oshima, 1972).

Gastric anisakiasis was the diagnosis in 78 (39.0%) out of 200 cases, intestinal anisakiasis in 75 (37.5%), acute appendicitis in 7 (3.5%), acute abdomen in 24 (12.0%), gastric ulcer and cancer in 5 respectively, intestinal tumor in 2, terminal ileitis in one and others in three (Table 1). Of 200 patients 159 (79.5%) were male and 41 (20.5%) female. More than two thirds of them were 30 to 50 years of age. The parasites were detected from the 49 patients: 26 by means of gastroscopic

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Table 1 Clinical diagnoses of 200 patients of anisakiasis examined from September, 1976 to February, 1979

Clinical diagnoses	Number of cases		
	Male	Female	Total
Gastric anisakiasis	54	24	78
Intestinal anisakiasis	63	12	75
Acute abdominal condition	22	2	24
Acute appendicitis	7	0	7
Gastric ulcer	5	0	5
Gastric cancer	4	1	5
Intestinal tumor	2	0	2
Terminal ileitis	1	0	1
Others	1	2	3
Total	159	41	200

examination, 8 when vomiting, 5 by surgical operation, 8 by histopathologic observation and two by X-ray of the stomach. Of the 26 patients examined by the gastroscopy two cases were harboring three *Anisakis* (type 1) larvae each and other two patients had *Terranova* infections. The larvae vomited from 3 of 8 patients were identified as *Terranova* (type A) larva (Koyama *et al.*, 1969) (Table 2). At the histopathological observations, *Anisakis* larvae were seen in the stomach wall of two cases, in the intestinal submucosal layer of three and in the extra-gastrointes-

Table 2 Techniques of detection and localization of the parasites from the 49 proven cases of anisakiasis

Technique or localization of parasite	Cases
Gastroscopic	26
Vomiting	8
Intestinal lumen (at surgical operation)	5
X-ray (Stomach)	2
Histopathological	
Intestinal wall	3
Gastric wall	2
Large omentum	2
Subcutaneous tissue	1*

* A case reported by Kagei and Sakaguchi (1977).

tinal tissues of another three of which the details of one case was previously reported by Kagei and Sakaguchi (1977).

Case Report of Extra-gastrointestinal *Anisakis* Infestations

Case 1 (No. 8 in Table 3). A 22 year-old man living in Kanazawa city complained of the abdominal pain, vomiting and tarry or bloody stool of 8 day duration. The day before the onset of the disease, he took raw mackerel and bluefin tuna (*Thunnus thynnus*) and the symptoms began to appear at mid-

Table 3 Case reports of extra-gastrointestinal anisakiasis

Case Number	Year and Sex	Residence	Location of <i>Anisakis</i> larva	Reporters (Year)
1	13 female	Holland	abdominal cavity	Van Thiel & Van Houten(1967)
2	28 male	Japan(Tokyo)	abdominal cavity	Furukawa <i>et al.</i> (1974)
3	43 male	Japan(Osaka)	mesentery	Nishimura <i>et al.</i> (1974)
4	67 male	Japan (Kashiwara)	mucous membrane of oral cavity	Nishimura <i>et al.</i> (1974)
5	58 female	Japan(Toyonaka)	mucous membrane of pharynx	Nishimura <i>et al.</i> (1974)
6	32 female	Japan (Wakayama)	large omentum	Sasaki <i>et al.</i> (1977)
7	30 male	Japan (Kanazawa)	abdominal wall	Kagei & Sakaguchi (1977)
8	22 male	Japan (Kanazawa)	large omentum	Yoshimura <i>et al.</i> (1978)
9	78 female	Japan(Maizuru)	large omentum	Yoshimura <i>et al.</i> (1978)

night. Leucocyte count was 9,000 and the eosinophil was 2%. The occult blood in the stool was strongly positive. The surgical operation was performed on the ninth day of the illness. At laparotomy, a tumor sized $2.2 \times 1.3 \times 1.6$ cm was found on the large omentum near the large curvature of the stomach, suggesting the metastatic focus of the malignant neoplasm (Figs. 1, 2). On section, a disintegrated thread-like nematode was found in the tumor tissues. Histopathologically no malignant cell or tissue was recognized and a nematode larva was observed in the eosinophilic granulations. The marked edema and proliferation of the fibroblasts were seen in the focus.

Parasite (Fig. 3): The transverse sections of a nematode, approximately 0.46×0.25 mm in diameter were found in the serial sections of the affected tissues. The inner structure of the parasite was not always clearly seen because of a little degeneration. However, the polymyarian-type muscle cell layer under the smooth cuticle, muscular esophagus, reticulate cell and particularly Y-shaped lateral chords were considerably well preserved; therefore the parasite was identified as *Anisakis* larva.

Case 2 (No. 9 in Table 3). A 78 year-old woman living in Maizuru city, Kyoto, complained of the epigastric colic and vomiting of one week duration. The leucocyte count was 13,400 and eosinophil was 6%. The occult blood in the stool was positive. On X-ray examinations the shadow defect suggesting gastric cancer was located at the antrum of the large curvature of the stomach. Because of the clinical symptoms started to appear 8 hours after eating raw fish "sashimi" of the spanish mackerel (*Scomberomorus niphonius*), the surgical operation was performed on the eighth day of the disease. At laparotomy, a localized tumor measuring 8×4 cm in diameter was seen at the antrum of the large curvature of the stomach. On the macroscopic observation, the erosive and ulcerated tissues approximately 8×4 cm in diameter was located near the pylorus of the stomach. At the central site of the ulcerated

and hemorrhagic focus was noticed a small punched out hole penetrating through the stomach wall. On the other hand, two enlarged and hard nodules suggesting the cancerous metastatic lumps or granulomas as big as a bean were located on the large omentum of the stomach (Fig. 4). Histopathological diagnosis was given as the subacute gastric ulcer and perforation possibly due to penetration by a parasite. No malignant proliferation was seen microscopically, but abundant eosinophils were seen in the stomach wall. The histopathologic features characterized by the edematous tissues with the massive eosinophils were observed in the sectioned tissues of the nodules surgically resected. The transverse sections of the nematode larva revealed the characteristic feature of *Anisakis* larva measuring 0.39×0.22 mm in diameter (Fig. 5).

Discussion

So far as the gastric anisakiasis is concerned, the gastroscopic examination is regarded as indispensable technique for the correct diagnosis at present time (Namiki *et al.*, 1970; Oshima, 1975). In the present paper, 26 (one third) of 78 cases with clinical diagnosis of gastric anisakiasis were proved to harbor live *Anisakis* or *Terranova* larvae. The gastroscopic findings of the foci around the parasite revealed marked edema often with small multiple hemorrhage, erosion and sometimes ulceration. Two such cases were found to be infected with three live *Anisakis* larvae each, penetrating into the stomach wall.

In all cases excepting three of intestinal anisakiasis diagnosed by the histopathologic observation, it was so difficult to distinguish the proven cases from the patients with other intestinal diseases such as acute appendicitis, tumor and gynecologic conditions.

The surveys of parasitic Anisakidae in the sea fish mainly from the Japan Sea have shown that *Terranova* larvae are frequently found in the cod, pacific halibut and atca mackerel (*Pleurogrammus azonus*), which are

usually eaten raw by Japanese people. Therefore, *Terranova* as well as *Anisakis* larva is incriminated as the pathogenic parasite causing anisakiasis-like symptoms in man (Otsuru *et al.*, 1968; Koyama *et al.*, 1969; Nagano *et al.*, 1973, 1975; Konishi *et al.*, 1976). The two cases of the *Terranova* infection described in the present paper had similar episode of eating raw cod prior to the onset of the disease.

Seven cases of extra-gastrointestinal anisakiasis in Japan have been known by the previous reports (Table 3). Two additional new cases described in the present paper harbored an *Anisakis* larva each in the tumors of large omentum of the abdominal cavity. In one case, a hole or canal suggesting the penetration due to *Anisakis* larva was found in the center of the ulceration of the stomach. The extra-gastrointestinal anisakiasis could be easily made in the experimentally infected animals with larvae (Yoshimura, 1966 a; Asami and Inoshita, 1967; Oyanagi, 1967; Inamoto, 1972; Nishimura, 1969).

The diagnosis of the extra-gastrointestinal involvement seems to be so difficult because of the complicated clinical features. More reliable immunodiagnoses of anisakiasis are needed, and so many trials have been carried out by the previous investigators (Suzuki, 1968, 1970; Kobayashi, 1968 a, b; Ruitenber, 1970). Recently Yoshimura *et al.* (1978) found that the latex agglutination test was highly promising for diagnosis of *Anisakis* infection both in animals and man, as compared with complement fixation test, double diffusion and immunoelectrophoresis. The antibody titers of the proven cases particularly with the extra-gastrointestinal involvements were significantly much higher than those of non-parasitic controls.

Further clinicopathologic and immunodiagnostic studies of *Anisakis* infection including the extra-gastrointestinal anisakiasis should be carried out not only for the clinical medicine, but also for the understanding of the entity of *Anisakis* infestation.

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アニサキス症の臨床病理学的研究・特に幼虫の消化管外寄生例について

吉村裕之 赤尾信明 近藤力王至 大西義博

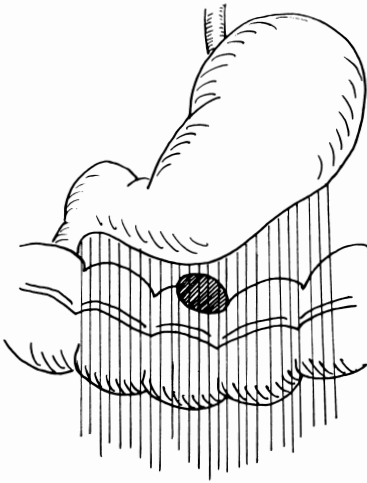
(金沢大学医学部寄生虫学教室)

著者らは1976年9月より1979年3月までの期間に、臨床的にアニサキス症を疑わせた患者200症例について病理学的解析をなした。初診時の臨床診断の内訳はTable 1に示したように、胃アニサキス症78例(39.0%)、腸アニサキス症75例(37.5%)、急性腹症24例(12.0%)、その他虫垂炎7例、胃癌または胃潰瘍各々5例等であった。性別では男159例(79.5%)、女41例(20.5%)で、全例のほぼ2/3は30~50歳代であった。これら200例中幼虫を検出した症例は内49例で、その内訳はTable 2に示したごとく胃内視鏡によるもの26例、吐出8例、腸切除術による腹腔内よりの摘出例5例、病理組織切片標本で虫体断端像をみとめたもの8例、胃X線透視による幼虫透亮像2例であった。胃内視鏡摘出例のうち2例はそれぞれ3虫のアニサキス(I型)幼虫寄生例であった。この他の3例はテラノーバ(A型)幼虫と同定されたものであった。その他虫体吐出の8例中3例もテラノーバ幼虫と同定された。今回の集計の中に消化管外の異所寄生例が2例含まれていたため、これについてのべた。

第1例：22歳男。金沢市在住。サバとマグロの刺身を食べた夜半より腹痛、嘔吐を訴えタール様便を認め、症状が8日間続いた。便の潜血反応は強陽性であったので10病日に開腹手術した。胃大彎部大網組織内に2.2×

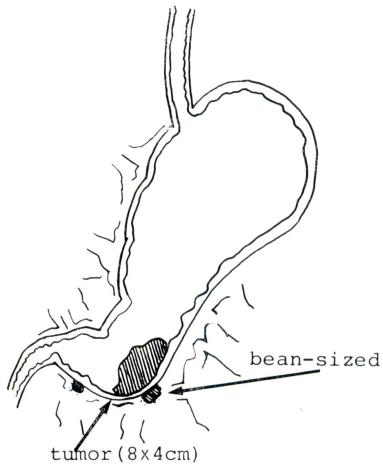
1.3×1.6 cm 腫瘤(Figs. 1, 2)を認めたので、悪性腫瘍の転移を疑い切除した。腫瘤の断面に変性した線虫らしいものを認めたのでそのまま組織標本を作製して観察したところ、変性過程の幼線虫の断面が好酸球肉芽組織内に存在していた。虫体の大きさ経0.46×0.25 mm、筋性食道、renette cell および対称性に不完全ながら双葉状に分岐した側索をみとめ、角皮下筋細胞はpolymyarian型(Fig. 3)であることから、本虫をアニサキス幼虫と同定した。

第2例：78歳女。舞鶴市在住。患者は刺身を嗜好し、今回はサワラの刺身を食べてから約8時間後に急性腹症を訴え入院した。X線所見で胃大彎前庭部に大きい陰影欠損を認め、胃癌を疑い胃切除術を施行した。上記胃病巣部は広範な出血性糜爛性潰瘍で、ほぼ中心部に小穿孔を確認した。病理組織学的には癌組織は全くなく、好酸球の多数浸潤する広範潰瘍であった。上記病巣部に近接する大網に2個の小豆大結節を認め(Fig. 4)、その組織学的所見は何れも好酸球肉芽腫で、その1個中に定型的なアニサキス幼虫の構造を保持する断面像を認めた(Fig. 5)。これまで内外で報告されたアニサキス幼虫の異所寄生例をまとめ(Table 3)、これら異所寄生例や腸アニサキス症の診断法として著者らの試みているラテックス凝集反応にふれて討議した。

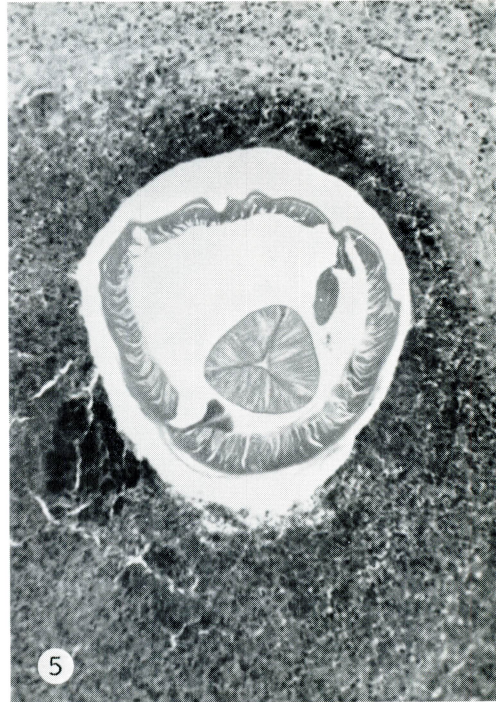


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Explanation of Figures

- Fig. 1 The cutting surface of the tumor resected in Case 1. (Arrow indicates a disintegrated nematode larva)
- Fig. 2 The localization of the tumor on the large omentum harboring *Anisakis* larva (Case 1 in present paper).
- Fig. 3 The microscopic finding containing the larva sectioned at the level of esophagus. Renette cell and Y-shaped lateral chords in the body cavity of the nematode were well seen.
- Fig. 4 The enlarged nodule (Arrow) located on the large omentum of Case 2.
- Fig. 5 The transverse section of the parasite showing morphological characteristics of *Anisakis* larva. The larva is surrounded by the eosinophilic granulation.