

Case Report: Anisakiasis Causing Acute Dysentery in Malaysia

Amirah Amir,¹ Romano Ngui,¹ Wan Hafiz Wan Ismail,¹ Kum T. Wong,² Jaxinthe S. K. Ong,³
Yvonne A. L. Lim,¹ Yee-Ling Lau,¹ and Rohela Mahmud^{1*}

¹Department of Parasitology, Faculty of Medicine, University of Malaya, Kuala Lumpur, Malaysia; ²Department of Pathology, Faculty of Medicine, University of Malaya, Kuala Lumpur, Malaysia; ³Sunway Medical Centre, Petaling Jaya, Selangor, Malaysia

Abstract. Human anisakiasis is a zoonosis acquired by eating raw or undercooked infected seafood. Herein, we report a case of acute dysentery caused by anisakiasis in a 64-year-old man in Malaysia. A colonoscopy was performed and a nematode larva was found penetrating the mucosa of the ascending colon. Bleeding was observed at the site of penetration. Y-shaped lateral epidermal cords were seen from the cross section of the worm, which is a prominent feature of *Anisakis* larva. Molecular analysis using polymerase chain reaction of cytochrome oxidase 2 (*cox2*) gene confirmed the specimen to be larva of *Anisakis simplex*.

INTRODUCTION

Anisakiasis is a zoonosis caused by the nematode belonging to the *Anisakis* genus.¹ Two most common species to cause infection in humans are *Anisakis simplex* and *Anisakis pegreffii*.² This parasite undergoes a complex life cycle that requires multiple hosts. In brief, the adult nematode that resides in the stomach of marine mammals lays unembryonated eggs which are shed through the host's feces. In water, the eggs become embryonated and the larvae mature into the second stage (L2). The free-swimming L2 larvae hatch and are consumed by crustaceans, where they develop into L3 larvae. When fish, squid, clams, or eels ingest the infected crustaceans, the larvae migrate to the new host's muscle tissues. Humans acquire the infection by eating raw or undercooked infected marine fish, squid, clams, or eels.^{3–5}

After ingestion of the L3 larvae, humans can exhibit gastric, intestinal, extraintestinal, or allergic symptoms.^{3,4,6–8} Patients may present with epigastric pain, nausea, vomiting, symptoms of bowel obstruction, acute abdomen, or symptoms of allergic reaction such as urticaria, and angioedema.^{3,4,9} These manifestations are predominantly caused by the attachment, embedment, or penetration of the L3 larvae into the gastric and intestinal mucosa.¹⁰ The time to the onset of symptoms after ingestion of raw or undercooked infected marine animals vary from a few hours to several weeks.^{3,10}

The larva cannot survive in humans and dies within a few weeks. Humans are an accidental host and larva cannot develop into adult in human tissue. Salting of marine fish does not kill the parasites. The parasites are killed if the fish is frozen at -20°C for a few days or cooking at 60°C .

Although anisakiasis cases were reported mainly in Japan in the past, this condition has now been diagnosed in many countries where eating of raw or undercooked seafood such as sushi and sashimi has become a trend. In Malaysia, with the burgeoning of Japanese restaurants, anisakiasis should be suspected in patients who give a history of ingesting raw or undercooked seafood and presenting with acute gastrointestinal symptoms.

CASE REPORT

A 64-year-old man presented to a private hospital complaining of abdominal discomfort and passing stool with fresh blood in it. The day before presentation, the patient had brought an empurau fish (*Tor tambroides*) from Sarawak, Malaysian Borneo, to be cooked for dinner at a restaurant in Kuala Lumpur. In less than 30 minutes after ingesting the fish, he developed abdominal discomfort and passed out stool mixed with fresh blood twice. He also admitted to have eaten sushi 2 days before. The patient had a history of ischemic heart disease diagnosed a few years ago, and was started on clopidogrel, an antiplatelet drug.

On examination, the patient was afebrile, had a blood pressure of 124/88 mmHg and a pulse rate of 82 beats per minute. Abdominal examination was unremarkable with no tenderness or guarding upon palpation. Blood test showed hemoglobin of 10.1 g/dL, total white cell count of 4.3 k/ μL (neutrophils 47%, lymphocytes 40%, monocytes 9%, eosinophils 3%, and basophils 1%), platelet count of 162 k/ μL , and erythrocyte sedimentation rate of 7 mm/hour. A colonoscopy was performed on the patient on the same day. A worm was observed burrowing into the mucosa of the ascending colon (Figure 1). There was blood oozing from the penetration site with blood clots forming around the worm. The whole worm was pulled out and sent to Parasite Southeast Asia Diagnostic (Para:SEAD) Laboratory, Department of Parasitology, Faculty of Medicine, University of Malaya, for identification. The specimen was examined under a stereomicroscope, and it showed a nematode larva measuring approximately 25 mm long, off-white in color, and moving actively (Figure 2). Histological examination of the cross sections of the worm showed the characteristic Y-shaped lateral epidermal cords which is diagnostic of *Anisakis* (Figure 3).

For species-specific identification, the worm was therefore subjected to polymerase chain reaction targeting the mitochondrial cytochrome oxidase 2 (*cox2*) gene as described previously with minor modification.¹¹ In brief, the larva was ground with a sterile pestle using mechanical vortex and the homogenate was then incubated overnight with proteinase K followed by genomic DNA extraction using a commercial kit. DNA amplification was performed and the positive amplicon was subjected to DNA sequencing. Homology search using the National Center for Biotechnology Information (NCBI) reference sequences with the Basic Local Alignment Search Tool confirmed the worm species as *A. simplex*. The sequence

*Address correspondence to Rohela Mahmud, Department of Parasitology, Faculty of Medicine, University of Malaya, Kuala Lumpur 50603, Malaysia. E-mail: rohela@ummc.edu.my



FIGURE 1. Colonoscopy image of ascending colon. A worm (arrow) was observed burrowing into the mucosa with blood oozing from the penetration site.

generated was then deposited in NCBI GenBank (accession no. KU257692).

During follow-up at 1 week, the patient was well and did not complain of any more rectal bleeding.

DISCUSSION

After the first human infection reported in 1960 in the Netherlands, cases of anisakiasis have been described in other countries including Korea, Japan, the United Kingdom, Spain, Italy, France, Germany, the United States of America, and Egypt.¹² Herein, we report, for the first time, a case of anisakiasis in Malaysia.

Misdiagnosis is common when dealing with anisakiasis due to the nonspecific symptoms of the disease. Diagnosis such as appendicitis, gastric ulcer, gastric tumor, cholecystitis, peritonitis, and Crohn's disease were frequently made before anisakiasis was confirmed.^{7,10} Furthermore, infection with this nematode can lead to a multitude of complications such as

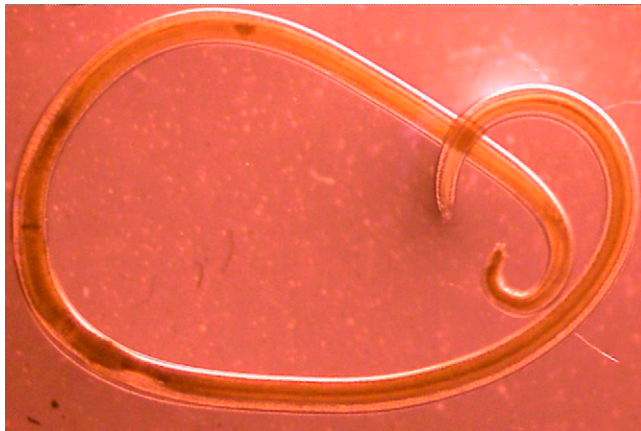


FIGURE 2. Stereomicroscope examination of *Anisakis* sp. larva. It has the common features of a nematode with vermiform, non-segmented body. The mouth is located anteriorly with projections used in feeding.



FIGURE 3. Hematoxylin-eosin stained cross section of *Anisakis* sp. larva. C = external cuticle; M = overlying muscle layer; LEC = Y-shaped lateral epidermal cords ($\times 10$ magnification).

intestinal obstruction, eosinophilic enteritis, eosinophilic granuloma, and spontaneous rupture of the spleen which may further mask the underlying diagnosis.^{7,13,14}

In the present case, the clue to the diagnosis was acquired when the patient gave a history of consuming sushi 2 days before clinical presentation at one of the Japanese restaurants in Kuala Lumpur. The empurau fish from Sarawak that he consumed 1 day before presentation is a freshwater fish and anisakiasis is associated with only marine fish. Since the patient was on clopidogrel, the attending physician was aware that the acute dysentery could also be due to the drug that the patient was taking. Gastrointestinal bleeding is an adverse effect of clopidogrel. On the basis of acute bleeding and the blood test on admission which revealed mild anemia, a colonoscopy was performed which showed bleeding at the site of worm penetration at the ascending colon.

Eosinophilia has been observed in less than half of the patients diagnosed with anisakiasis. In early diagnosis of gastrointestinal anisakiasis, eosinophil count is not useful.¹⁵ Eosinophil count was not raised in this patient. This may be explained by the fact that the larva had just started to burrow its way through the ascending colon and diagnosis was made early. Therefore, it may have been too early for the eosinophilic response.

Investigations that can aid clinicians in diagnosing anisakiasis include endoscopic examination that may provide visual evidence and removal of the worm for identification as has been performed in this patient. Imaging modalities such as barium studies or computed tomography scan may reveal narrowing of intestinal lumen. Serological studies have been used to detect *Anisakis*-induced IgE.^{4,6,16,17} This antibody, however, lacks specificity as a result of cross-reactivity with other nematode antigens. The serological test is not generally available and it is of limited benefit in early diagnosis. Nevertheless, there have been many instances where the diagnosis was only made after viewing histological sections from resected bowel after laparotomy.^{3,15,18} The most prominent

morphological feature from a cross section of the nematode are the Y-shaped lateral epidermal cords.^{3,15} However, morphological identification is dependent on how well the worm has been conserved. Therefore, the molecular method has recently been used for the identification of *Anisakis* larvae.^{19,20} A very simple yet often overlooked aspect of diagnosis is acquiring history of ingestion of raw fish or seafood. This history is the only definite clue to the diagnosis.²¹

Unlike other helminths that infect humans, the *Anisakis* larvae do not respond to anthelmintics such as mebendazole, albendazole, or thiabendazole.²² The preferred treatment is the extraction of the worm via endoscopy.³ However, in cases of surgical complications, laparotomy or bowel resection may have to be performed.^{3,7,18} Corticosteroids are helpful to reduce the inflammatory response to the worm or when dealing with allergic reactions.^{10,23} Recently, conservative therapy has been found to be successful in treating intestinal anisakiasis.²⁴ The conservative therapy that Shrestha and others suggest, requires the correct diagnosis of intestinal anisakiasis followed by close monitoring, the patient kept nil by mouth, insertion of a nasogastric tube, and analgesics for pain management.²⁴ Patients are only allowed oral diet once the abdominal symptoms have subsided.

Culinary vacation and the introduction of food and cooking methods from foreign countries are becoming a trend worldwide. This trend may include eating raw or lightly cooked seafood. Anisakiasis, a seafood-borne disease that has never been seen in Malaysia is now reported for the first time. Therefore, clinicians in this part of the world should be aware of this diagnosis. Detailed history including dietary history has to be taken from patients with gastrointestinal symptoms. Thorough physical examination and investigation cannot be overemphasized.

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Authors' addresses: Amirah Amir, Romano Ngui, Wan Hafiz Wan Ismail, Yvonne A. L. Lim, Yee-Ling Lau, and Rohela Mahmud, Department of Parasitology, Faculty of Medicine, University of Malaya, Kuala Lumpur, Malaysia, E-mails: amirahamir@hotmail.my, skyromano@gmail.com, wanhafiz@ummc.edu.my, yvonne@ummc.edu.my, lauyeeling@um.edu.my, and rohela@ummc.edu.my. Kum T. Wong, Department of Pathology, Faculty of Medicine, University of Malaya, Kuala Lumpur, Malaysia, E-mail: wongkt@ummc.edu.my. Jaxinthe S. K. Ong, Sunway Medical Centre, Selangor, Malaysia, E-mail: jaxint@gmail.com.

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