



Commentary

Anisakiasis—a neglected diagnosis in the West

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Anisakiasis is a gastrointestinal infection caused by ingestion of uncooked saltwater fish, contaminated by nematode larvae belonging to the family Anisakidae, including *Anisakis simplex* and *Pseudoterranova decipiens*. Humans are not the primary host for these parasitic roundworms, and they are infested by accidental ingestion of the larvae.

The parasite which infects humans was first identified by Van Thiel in 1960 as the stage III larva of *Anisakis* [1], acquired by eating raw or undercooked fish. The disorder is common in areas where raw fish is consumed such as Japan, Pacific coast of South America and the Netherlands. In Japan, 2000 cases per year are reported, accounting for over 90% of incidences [2], primarily from the consumption of sushi and sashimi.

The lifecycle of *Anisakis* involves marine animals and the seawater. The adults live in the stomach of marine animals, and adult female worms produce unembryonated eggs, which after faecal excretion, become embryonated in the seawater to form first stage larvae. After molting to form stage II larvae, they hatch to become free swimming, and following ingestion by crustaceans, develop into stage III larvae that are parasitic. When the host animal dies, the larvae migrate to muscle, and via predation are transferred from fish to fish. Fish and squid maintain the third stage larvae, which molt twice in the marine animals to form adult worms. Humans are infected by eating raw or undercooked marine fish carrying the parasites (Fig. 1).

Anisakis causes damage due to allergic reactions ranging from urticaria to anaphylaxis mediated by IgE [3], and by direct tissue damage. Ingestion of dead parasites in fish might also be potentially dangerous due to allergic reactions [4]. Tissue damage results from the invasion of the gut wall,

formation of eosinophilic granulomata, or perforation. The parasite adheres to the GI mucosa with the aid of proteases, and this evokes a Th2 anti-parasite response via stimulation of dendritic cells [5], with the increased expression of IL-4 and IL-5, inducing an inflammatory response along with raised total and specific IgE levels [6]. In addition, *A. simplex* L3, dead or alive, can induce cholinergic hyperactivity and adrenergic blockade in the whole small intestine resulting in gastrointestinal symptoms [7]. Patients with anaphylaxis to *Anisakis* will require avoiding exposure to raw or undercooked fish.

There are two major forms of anisakiasis: gastric and intestinal. In Japan, gastric anisakiasis predominates; whereas intestinal anisakiasis is more common in Europe [4]. Human infection is as a result of ingestion of the 1.5–2.5 cm larvae, which may then cause irritation of the throat inducing coughing and expectoration. It is estimated that one-third of *Anisakis* larvae ingested are evacuated in faeces, one-third die in the walls of the GI tract, and one-third die following invasion of the intestinal wall or granuloma formation.

Acute gastric anisakiasis presents with self-limiting abdominal pain, nausea and vomiting 2–5 h following ingestion of raw seafood [8] or even angina-like chest pain. *Anisakis* larvae can be seen and curatively removed endoscopically. Chronic gastric anisakiasis may simulate peptic ulcers and chronic gastritis. Giant gastric folds may be a result of gastric infestation [9] and diagnosis by ultrasonography, endoscopy or endoscopic ultrasound is possible, though a specific diagnosis will depend on history, serodiagnosis or identification of *Anisakis* at endoscopy.

Intestinal anisakiasis usually presents with lower abdominal pain, which settles conservatively. Development of an acute abdomen, as described in the paper by Pellegrini et al. [10] in this issue, is usually due to inflammatory intestinal

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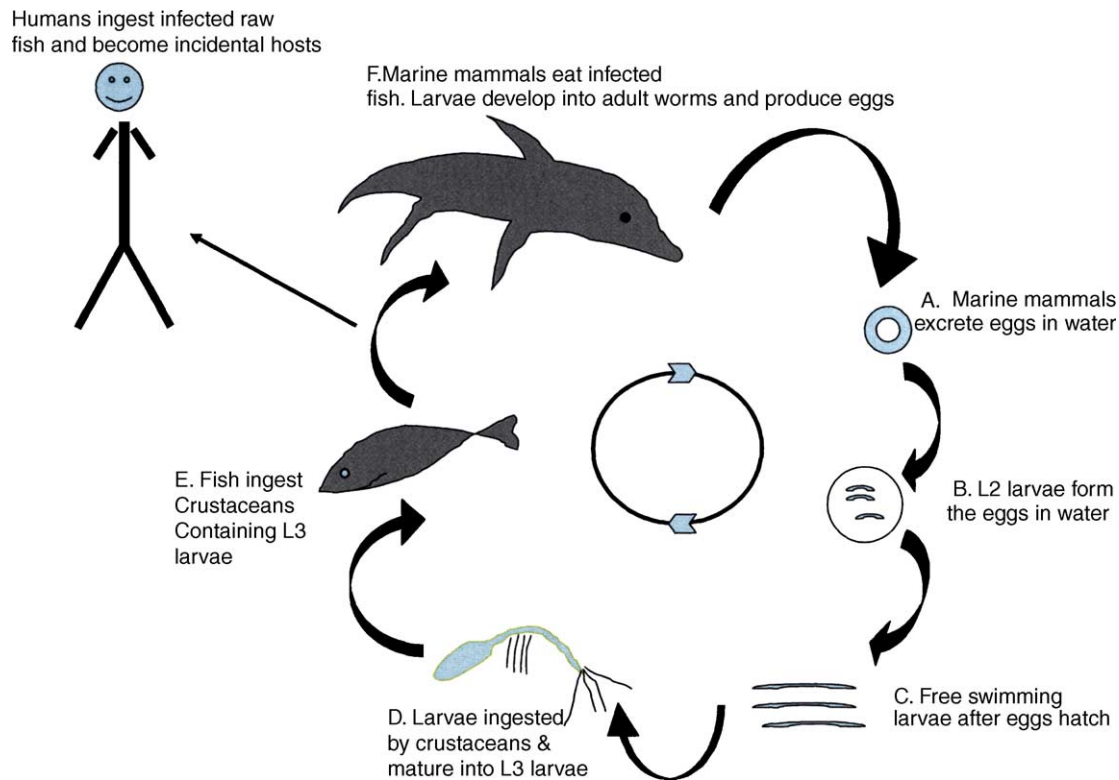


Fig. 1.

sub-acute obstruction and results in laparotomy and discovery of signs of the primary infection. Preoperative diagnosis is rare due to symptoms that mimic appendicitis, cancer, Crohn's disease or TB peritonitis. A non-specific peripheral eosinophilia may occur. Haemorrhagic ascites is not uncommon due to peritoneal irritation. Many cases are diagnosed as eosinophilic gastroenteritis, as described in the paper by Montalto et al. [11] in this issue. Colonic involvement may present as right iliac fossa mass or ileocaecal valve involvement. A history of preceding raw fish consumption is the most important diagnostic clue.

The majority of intestinal anisakiasis is localised to the terminal ileum, with colonic involvement in just 2%. Migration to other sites such as the omentum, mesentery, pancreas, liver, spleen and lung has been reported [12]. Histologically, the lesions range from diffuse oedema to submural necrosis, often containing sections of the parasite, and a marked eosinophilic granulomatous inflammatory reaction. The development of Crohn's disease type "skip-lesions" may occur. To further confuse the differential diagnosis with Crohn's disease, gingivostomatitis after ingestion of *Anisakis*-infested fish has been reported [13].

Definitive diagnosis by identification of the parasite microscopically may not be possible, in which case, serological tests such as enzyme-linked immunosorbent assay (ELISA) and specific IgE may be helpful. Detection of circulating antigens in experimental anisakiasis in rats by two-site ELISA suggest potential application of such tests in making a diagno-

sis of human infestation [14]. In a Spanish study of dyspeptic patients undergoing upper endoscopy, specific IgE against Ani s 1 protein, a major parasite allergen of *A. simplex*, was present in 13.8% of patients. Seropositivity was correlated with consumption of raw fish, fish in vinegar and smoked fish [15]. Serum levels of eosinophilic cationic protein may be raised, and anisakiasis should be considered in the differential diagnosis of eosinophilic gastroenteritis. Imaging can be useful; small bowel barium studies may allow visualisation of the larvae as tiny 10–20 mm linear filling defects, or stenosis and thumb-printing due to oedema. Ultrasound provides a non-invasive and highly sensitive test of intestinal involvement, including rare intussusception by pseudo-kidney sign, but not a specific diagnosis.

In a series of 23 Spanish patients, gastroduodenal involvement had less severe symptoms and diagnosis was made on clinical suspicion and subsequent endoscopy, whereas more than half of patients with intestinal involvement required histological examination of a surgical specimen for correct diagnosis [16].

The increased popularity of raw fish and the proliferation of Japanese fast food outlets in the West make the Western population susceptible to *Anisakis* infestation. In addition, widespread travel may also result in presentation in the West. In Japan, sushi chefs are experts in identifying *Anisakis* infestation, and such expertise may be lacking in the West. Endoscopic identification of *Anisakis* also requires experience and familiarity with the appearance. Most Western

Table 1
Conditions mimicked by anisakiasis

Peptic ulcer
Gastritis
Vanishing gastric tumour
Giant gastric folds
Subacute intestinal obstruction
Acute abdomen
Appendicitis
Crohn's disease
Carcinoma
Tuberculous peritonitis
Haemorrhagic ascites
Eosinophilic gastroenteritis

gastroenterologists do not consider *Anisakis* in their differential diagnosis of a wide range of gastrointestinal symptoms (Table 1).

It is thought that there is no drug-treatment for anisakiasis, and anti-helminthics are ineffective against nematodes, though response to albendazole has been reported from London [17]. Symptoms usually resolve in 1–2 weeks when the larvae die. Surgery is required in cases of complication. Endoscopic or surgical removal of the worms shortens the recovery period. Prophylaxis and prevention is most important with avoidance of consumption of raw fish, and ensuring adequate processing and refrigeration of fish products; cooking to temperatures $>60^{\circ}\text{C}$ or refrigerating fish for raw consumption at -20°C for at least 24 h should kill the larvae.

In summary, anisakiasis clinically may simulate peptic ulceration, appendicitis, Crohn's disease and eosinophilic gastroenteritis, or induce allergic manifestations such as urticaria or anaphylaxis. The diagnosis needs to be considered especially in patients presenting with abdominal pain who had consumed raw or undercooked fish in the past 72 h. Eosinophilia may be present. Diagnosis is by endoscopic or microscopic identification of the parasite, the use of X-ray, ultrasound and immunoserology, along with a clinical history of ingestion of raw or undercooked fish. Prevention is by adequate food preparation and storage techniques, and treatment is conservative unless surgery is required for complications, with removal of worms endoscopically or surgically hastening recovery. It is important to be aware of anisakiasis as a problem in Europe and the worm has been demonstrated in a wide range of species of fish in European waters [18].

Conflict of interest statement

None declared.

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