Acute Small-Bowel Obstruction From Intestinal Anisakiasis After the Ingestion of Raw Clams; Documenting a New Method of Marine-to-Human Parasitic Transmission

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Enteric anisakiasis is a known parasitic infection. To date, human infection has been reported as resulting from the inadvertent ingestion of the anisakis larvae when eating raw/undercooked fish, squid, or eel. We present a first reported case of intestinal obstruction caused by anisakiasis, after the ingestion of raw clams.

Keywords. anisakiasis; small-bowel obstruction; clams.

Anisakiasis is a known parasitic infection caused by the inadvertent ingestion of the anisakiasis larvae when consuming raw/undercooked fish, squid, or eel. Anisakiasis is most frequently reported in Asian countries where eating raw seafood is common [1–23].

Marine mammals such as dolphins, sea lions, and whales are the natural hosts of Anisakis species. The nematodes reside within the stomach of their hosts, laying eggs that exit through the feces of the mammal. Subsequently, second-stage larvae hatch and are eaten by small crustaceans. These infected first intermediate hosts are consumed by marine fish, squid, and eel. Third-stage larvae then develop within these marine animals. The Anisakis life cycle is completed when the infected fish, squid, or eel are consumed by marine mammals, enabling the larvae to grow into their adult nematode form [1, 2, 7, 9, 11, 13, 21–23].

Humans can become infected upon the inadvertent ingestion of raw/undercooked seafood inculturated with third-stage Anisakis larvae. Humans are not suitable hosts, however, and the larvae die before replication or growth into nematode adulthood. Yet infection with Anisakis larvae can cause significant symptoms relating to gastric, intestinal, extraintestinal, or allergic manifestations [1–23]. Reported incidences from the largest historical study to date note gastric cases as >95%; intestinal >4%; and extraintestinal >1% [20]. A more contemporary study, however, indicates a higher incidence of the intestinal type of disease [19]. The incidence of allergic responses remains poorly defined [1, 6, 19].

In all reported cases, human infection by anisakiasis has resulted from the ingestion of raw/undercooked fish, squid, or eel. We present the first case of intestinal anisakiasis resulting from the ingestion of raw clams.

CASE REPORT

A 64-year-old man presented to the Thomas Jefferson University Hospital Emergency Department with 1–2 days of progressive abdominal pain associated with nausea and watery diarrhea. The patient reported his pain as initially focused in the epigastric region then progressing to diffuse abdominal pain. His past medical history was significant only for an open appendectomy (years previously), done via a right lower quadrant incision. The patient’s origin is from Spain, but he denied recent significant travel beyond his home area (Philadelphia, Pennsylvania, and adjacent New Jersey).

On physical exam, the patient appeared uncomfortable. His pain was significant only for an open abdomen. His vital signs were within normal limits. A brief period of observation then began, including intravenous fluids, nasogastric tube decompression, and nothing by mouth. His pain however, progressed, and computed tomography (CT) of the abdomen and pelvis was done 3 hours after the initial evaluation (Figure 1). This indicated ascites and a mid-distal small-bowel obstruction at a site of thickened small-bowel loops, as well as concern for focal small-bowel ischemia. Due to the patient’s progressive symptoms,
Upon opening the peritoneum, a large volume of clear ascites was encountered. An adhesive band was found at the distal ileum causing a near-complete obstruction at that portion of the bowel. The band was lysed. The bowel at that site was erythematous, indurated, and markedly stenotic. Enlarged lymph nodes in the adjacent mesentery were indurated and hemorrhagic appearing. The stenotic portion of the bowel was resected. The specimen was opened intraoperatively showing no gross mass, but the bowel lumen was nearly obliterated. The small-bowel specimen was sent for pathology. A small-bowel anastomosis was performed and the laparotomy closed. The patient was discharged on postoperative day 5, tolerating a regular diet and symptom free.

The pathology specimen showed an ileal segment measuring 7 cm in length and 4.5 cm in circumference. Upon opening the bowel, a 1.0-cm exposed worm was identified invading the mucosa, with associated surrounding mucosal erythema (Figure 3). Histologic sections through this area revealed cross-sections of a parasite invading the bowel, extending into the submucosa. An eosinophilic microabscess surrounded the parasite, and dense eosinophilic inflammation expanded all layers of the bowel wall extending into the serosa. Sections of the parasite showed morphology diagnostic of *Anisakis* species third-stage larvae: an unpaired excretory gland (renette cell) with a single duct and an irregular-shaped nucleus, an intestine composed of a single layer of columnar epithelium, a thin external cuticle with no lateral alae, a muscle layer with minute dorsal and ventral epidermal cords, and prominent Y-shaped lateral epidermal cords (Figure 4). A reproductive system was absent. Using an Aperio slide scanning device (Leica Biosystems), the diameter of the parasite measured 462 ± 48 µm (range, 414–510 µm) and the cuticle thickness measured 5–7 µm. Based on the gross and microscopic characteristics as well as the clinical presentation of acute abdominal pain, a diagnosis of intestinal anisakiasis was made by the pathologist (JPB).
Figure 4. Hematoxylin and eosin staining, ×200. A cross-section of the nematode shows a thin external cuticle (C) overlying a muscle layer (M), Y-shaped lateral epidermal cords (LEC), an excretory gland (EG) (renette cell) with a single duct and irregular-shaped nucleus, and intestine (I) composed of a single layer of columnar epithelium forming a central tripartite lumen. Surrounding the parasite is an inflammatory infiltrate rich in eosinophils and neutrophils.

Upon questioning the patient, after the above pathology reviewed, he reported consuming raw clams with his son 2 days prior to his initial symptoms. The clams were of the hardneck (eg, quahog) "littleneck" variety, harvested from the New Jersey shore. The patient denied eating any other raw or undercooked seafood at that time or in prior weeks, specifically stating "I do not eat sushi." His son was not ill in subsequent days.

DISCUSSION

Anisakiasis reflects human infection from nematodes of the Anisakidae family. The disease was first reported by Van Thiel in 1960 [23]. Since then, >20,000 cases have been reported worldwide, the vast majority in Japan [1–22]. Reported cases in the United States number <100, but this likely reflects underreporting [1].

Four major clinical types of human infection result from anisakiasis: gastric, intestinal, ectopic (or extragastrointestinal), and allergic [1–23]. Gastric anisakiasis typically manifests within 12 hours of ingestion of raw fish. Symptoms include acute epigastric pain, nausea, and vomiting. A low-grade temperature is often associated. Acute symptoms typically resolve within a few days. However, presenting symptoms may persist subclinically on occasion for weeks and months. Chronic anisakiasis-related gastric ulcers have been reported. Endoscopic extraction, if undertaken in the first few days of disease, is the preferred treatment. The larvae typically degenerate, die, or are eliminated after several days otherwise [1–3, 7, 10, 11, 13].

Intestinal anisakiasis symptoms typically develop later (within 5–7 days) than the gastric form of the disease (<1 day). Yet reported intervals from ingestion to symptoms vary widely with intestinal anisakiasis (1–37 days) [1–18] (Table 1). Sites of involvement typically involve the terminal ileum, but other parts of the small bowel, colon, and appendix have been reported [1–18, 20]. Symptoms relate to the intense, mostly eosinophilic inflammatory response that occurs within the bowel wall at sites of larval invasion [2, 4, 7, 10–15]. Hence, obstructive symptoms predominate [1–19]. Radiographic findings on CT typically include short segment bowel thickening/inflammation, mucosal edema, luminal narrowing, and bowel obstruction at sites of involvement. Lymphadenopathy and ascites are associated radiographic findings [1, 3, 4, 5, 7–13]. Of note, bowel intussusception with its typical associated radiographic findings has been documented as well [1, 2, 5, 13]. Interestingly, most singular reported cases of intestinal anisakiasis resulted in need of laparotomy and bowel resection (Table 1) [1–18], yet a recent Japanese inpatient database review of intestinal anisakiasis (201 cases) found that laparotomy was needed in only 14 cases (7.0%) [19]. Thus, indications for surgical intervention appear appropriately individualized. Typical findings at laparotomy included a focal area of thickened, erythematous, edematous, and stenotic bowel with associated clear ascites and mesenteric lymphadenopathy. Histopathology of resected specimens shows inflammatory infiltrates, mostly eosinophils within the bowel wall, as well as characteristic histomorphologic features of an Anisakis larval nematode [1, 2, 4–7, 17]. Published reports of surgically resected intestinal cases of Anisakis are rare, with only 13 nonintussusception cases reported since 1990 in the English-language literature [2–4, 7–15]. (The 2010 Yasunaga study of 201 intestinal anisakiasis cases did not categorize the type of surgical intervention effected for the 14 surgical patients it described [19].) Only 11 intussusception cases have been reported overall (English-language and Japanese literature) [5, 19].

Extraintestinal, intraperitoneal, or extraintestinal anisakiasis have been reported, including larval migration to sites within the pleural cavity, mesentery, liver, pancreas, ovary, and subcutaneous tissue [1, 9, 14–17, 21]. As one example of such extraintestinal disease, histopathologic confirmation of the Anisakis larvae was documented within a peritoneal band excised at laparotomy (surgery undertaken regarding acute small-bowel obstruction) [16]. Our report also likely reflects one such case of extraintestinal/adhesive band–involved anisakiasis; however, we did not send portions of our lysed peritoneal band for histopathology review as we did not anticipate that diagnosis prospectively. Chronic inflammatory responses to extraintestinal disease have also led to mesenteric masses [14, 21].

Last, strong systemic allergic responses have been associated with anisakiasis. Symptom onset typically occurs within several hours of the ingestion of infected fish, of which anchovies have been particularly implicated. Allergic reaction symptoms include urticaria, gingivostomatitis, angioedema, and even anaphylaxis.
Table 1. Current Case and Literature Review of Acute Intestinal Anisakiasis Causing a Small-Bowel Obstruction

| Author          | Age/ Sex | Presentation                  | Food Ingestion | Time From Ingestion to Onset of Symptoms | Imaging | Time From Ingestion to Operative Intervention | Operation | Site of Obstruction | Imaging | Operative Findings: Ascites/Bowel Edema | Eosinophilia of Bowel Wall |
|-----------------|----------|--------------------------------|----------------|------------------------------------------|---------|----------------------------------------------|------------|-------------------|---------|----------------------------------------|--------------------------|
| Shweiki (2014)  | 64/M     | Abdominal pain, nausea, diarrhea | Raw clams      | 2–3 days                                 | CT      | 4 days                                       | Ex lap, SBR | Distal ileum       | Yes/Yes | Yes                                    | Yes                      |
| Takano (2013)   | 63/M     | Abdominal pain, vomiting        | Raw fish       | 2 days                                   | AXR, CT | NA                                           | Nonoperative therapy with ileus tube | Small bowel | NA | NA                          |                          |
| Kojima (2013)   | 61/M     | Abdominal pain                  | NA             | NA                                       | AXR, CT | NA                                           | Ex lap, SBR | Jejunoileal junction | Yes/Yes | Yes                                    |                          |
| Juric (2013)    | 14/M     | Abdominal pain, nausea, vomiting| Raw fish       | 2 days                                   | AXR     | 3 days                                       | Ex lap, appendectomy | Terminal ileum | NA/Yes | Yes                                    |                          |
| Kang (2010)     | 60/F     | Abdominal pain, nausea, vomiting| Raw fish       | 1 day                                    | AXR, CT | 1 day                                       | Ex lap, SBR | Jejunum           | NA/Yes | Yes                                    |                          |
| Masui (2006)    | 51/F     | Abdominal pain, nausea, fever   | Raw fish, raw scallops | 14 days                                 | AXR, CT | 14 days                                     | Ex lap, lysis of adhesion | Ileum       | Yes/Yes | NA                          |                          |
| Yoon (2004)     | 54/M     | Abdominal pain                  | Raw eel        | 2 days                                   | AXR, CT | 3 days                                       | Ex lap, SBR | Jejunum           | Yes/Yes | Yes                                    |                          |
| Couture (2003)  | 50/M     | Abdominal pain, nausea, constipation | Raw fish     | 1 day                                    | AXR, CT | 3 days                                       | Ex lap, SBR | Jejunum           | Yes/Yes | Yes                                    |                          |
| Caramello (2003)| 31/F     | Abdominal pain, vomiting, diarrhea | Raw fish      | 7 days                                   | AXR, US, CT | 7 days                        | Ex lap, SBR | Terminal ileum | Yes/Yes | Yes                                    |                          |
| Sasaki (2003)   | 59/M     | Abdominal pain                  | Raw fish       | <1 day                                    | AXR, CT | <1 day                                       | Ex lap, SBR | Small bowel       | Yes/Yes | Yes                                    |                          |
| Maggi (2000)    | 43/F     | Abdominal pain                  | Raw fish, raw crustaceans | 4 days                                 | US      | 4 days                                       | Ex lap, appendectomy, | Jejunum    | Yes/No | Yes                                    |                          |
| Takabe (1998)   | 60/F     | Abdominal pain, vomiting        | Raw fish       | <2 days                                  | AXR     | <2 days                                       | Ex lap, SBR | Terminal ileum | Yes/No | Yes                                    |                          |
| Appleby (1982)  | 30/F     | Abdominal pain                  | Raw fish       | 42 days                                  | AXR, UGI Study | 42 days                        | Ex lap, lysis of adhesion | Jejunum    | Yes/No | NA                          |                          |

Abbreviations: AXR, abdominal radiograph; CT, computed tomography; Ex lap, exploratory laparotomy; F, female; M, male; NA, not available; SBR, small-bowel resection; UGI, upper gastrointestinal; US, ultrasound.
Serum antibody titers are reported to follow a typical initial IgM, then converting to longer term IgE, IgG, and IgA iso-type pattern. But results from these assays are difficult to assess clinically, as cross-reactivity with other parasites, insects, or crustaceans is known [3]. Also, asymptomatic persons with a history of frequent consumption of raw fish have been found to have elevated Anisakis antibodies without manifestation of disease otherwise [1]. Laboratory tests with better specificity are thus needed to diagnose anisakiasis in this manner [3].

Although thousands of cases of anisakiasis have been reported since the initial publication in 1960, all appear to be related to the ingestion of raw/undercooked fish, squid, or eel [1–23]. We now report a case resulting from the ingestion of raw clams. Importantly, specifically noted in this case was the lack of consumption of any other type of raw/undercooked seafood at that time, or in prior weeks. The initial presenting symptoms and time course of this case, as well as the radiographic, intraoperative and histopathologic findings, all corroborate the diagnosis of anisakiasis. Based on the known life cycle of Anisakis species, we posit that second-stage larvae, found within marine water after their excretion in the feces of marine mammals, find their way to the ocean bottom. There they are taken in by clams in process of siphon/filter feeding (clams claim as food those particles that are suspended in the water from which they filter feed). Thus, acquiring an intestinal form of anisakiasis from the ingestion of raw clams is plausible.

Of note, Sulcascaris species are a different type of helminth that have intermediate hosts in scallops and other mollusks/bivalves (ie, clams), with definitive hosts in marine turtles. Although 50 types of helminth species have been reported to cause parasitic infections in humans worldwide (through the ingestion of fishes, crabs, crayfishes, snails, and bivalves), a review of the literature lacks evidence defining Sulcascaris species as one of such parasite species [24, 25].

In conclusion, Anisakis is a known nematode-type parasitic infection in humans, acquired after the ingestion of raw/undercooked fish, squid, and/or eel. Our case documents a new method of transmission related to the ingestion of raw clams.

Notes

Author contributions. All authors have seen and approved of the manuscript, and contributed significantly to the work.

Potential conflicts of interest. All authors: No reported conflicts.

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