Anisakidosis is a parasitic infection caused by anisakid nematodes in the genera Anisakis and Pseudoterranova. Infection is not uncommon in the United States due to increased raw seafood consumption. We report the first known case of parametrial anisakidosis in a 42-year-old woman and review existing literature.

CASE REPORT

The patient was a 42-year-old German American female who presented with a 1-year history of intermittent, clear, odorless vaginal discharge and intermittent abdominal bloating. She denied fever, abdominal pain, nausea, vomiting, diarrhea, or weight loss and had regular menstrual cycles. Her past medical history was significant for childhood bronchitis, but she was otherwise in good health with no chronic medical conditions. She had quit smoking tobacco recently, reported drinking wine socially, and denied illicit substance abuse. She also denied any allergic symptoms or rash.

Physical examination revealed an endocervical polyp which was removed and diagnosed as adenocarcinoma in situ by histopathologic examination. A LEEP (loop electrosurgical excision procedure) subsequently revealed invasive, moderately differentiated adenocarcinoma and squamous cell carcinoma of the cervix. She therefore underwent a robotic-assisted radical hysterectomy with bilateral pelvic and periaortic lymphadenectomy. Intraoperatively, a 1-centimeter friable area was observed on the anterior cervix, consistent with her previously diagnosed carcinoma. There were no ectocervical or vaginal lesions, and the bilateral ovaries, fallopian tubes, appendix, and peritoneal cavity appeared normal. However, a firm mass was noted on the external aspect of the posterior cervix in the parametrium when the recto-vaginal space was dissected. A hematoxylin-and-eosin-stained section of the mass demonstrated two cross-sections of a presumed single roundworm surrounded by granulomatous inflammation and numerous eosinophils (Fig. 1A). On higher magnification, narrow Y-shaped lateral cords arising from the internal aspect of the muscular coat were observed in the cross sections of the worm (Fig. 1B), most consistent Anisakis larvae, allowing a diagnosis of anisakidosis to be made. The patient was informed about this incidental finding. No serological or molecular tests were done, due to the unavailability of such testing in the United States.

During a subsequent interview, the patient stated that she enjoys eating raw seafood and eats sushi from Japanese restaurants and ceviche from Peruvian restaurants in Miami approximately once a month. She does not buy fish from local markets and denied making these dishes at home. She had lived in the United States for the past 24 years, with most of this time spent in Florida and a few years spent in Arizona and New York. She visited her family in Germany frequently and had also traveled to Thailand the year before, but did not recall eating raw seafood during these trips. She was educated about the risks of acquiring future anisakidosis and the methods of prevention.

Anisakidosis is acquired by the consumption of raw or undercooked marine fish or squid. Human infection occurs due to the accidental ingestion of the third-stage larvae of marine mammal nematodes belonging to the family Anisakidae. The two organisms that are commonly associated with human cases are Anisakis spp. and Pseudoterranova decipiens (1, 2).

Anisakidosis denotes disease caused by any member of the family Anisakidae, whereas anisakiasis is used for disease caused by members of the genus Anisakis and pseudoterranovosis for disease caused by members of genus Pseudoterranova (3). The first description of this infection was in 1845 by Dujardin, who described a worm in dolphins and called it Anisakis. The term Anisakis is derived from the Greek words “anisos,” meaning unequal, and “akis,” meaning point (4). However, it was not until 1960 that the first human infection was reported in a patient from the Netherlands who had been eating raw herring (5).

Anisakid-infected marine life exists in all the oceans and seas, and the disease is distributed worldwide (6). The prevalence of disease is related to the practice of raw seafood consumption in communities. Currently, around 20,000 new cases are reported worldwide annually; the majority of them (over 90%) are from Japan (7). Most of the other cases occur in parts of coastal Europe (Netherlands, Spain, Germany, and France) and South America where raw fish is consumed. In the United States, the frequency of anisakidosis is unknown, since it is not a reportable disease and may be underdiagnosed (8). The frequency was approximately 10 reported cases per year in the 1970s and may be higher now (8). The incidence is expected to rise in coming years due to increased awareness of infection, advances in endoscopic techniques, increasing popularity of raw seafood consumption, and increasing marine mammal (definitive host) populations since the enactment of the Marine Mammal protection act of 1972 (1, 9).
dishes that are commonly implicated in anisakidosis are Japanese sushi and sashimi, South American ceviche, Dutch salted or smoked herring, Filipino bagoong, and Spanish pickled anchovies (9, 10). The risk of infection is lower in Japanese restaurants and sushi bars that serve sushi and sashimi prepared by professional sushi chefs (2, 6). Cheap marine fish and shellfish, such as cod, herring, mackerel, and squid, which are mainly consumed at other ethnic restaurants or at home, tend to be heavily infected with anisakid larvae (Fig. 2) (2). In the United States, salmon and rockfish are commonly implicated in transmitting anisakidosis (11). Wild-caught salmon in the Pacific northwest are commonly infected with anisakid larvae (12) and may cause anisakidosis if consumed raw (11).

Adult worms live and reproduce in the stomach of marine mammals, such as dolphins, whales, seals, and sea lions, who serve as the definitive hosts for this parasite. The eggs are excreted with

FIG 1 Low-power magnification of the mass (left) from the external aspect of the posterior cervix, demonstrating two cross-sections of the anisakid roundworm (arrows) surrounded by fibrous tissue and inflammatory cells (hematoxylin-and-eosin [H&E] staining, ×20 magnification). On higher magnification, narrow Y-shaped lateral cords are seen within the worm cross sections (arrow), characteristic of *Anisakis* sp. Numerous eosinophils are seen in the granulomatous inflammation to the right of the worm (H&E staining, ×400 magnification).

FIG 2 Coiled anisakid larva in a frozen cod fillet from a local grocery store. The coiled worm measures approximately 5 mm in diameter. This is a common finding in cod fillets.
the feces into seawater, where they molt into free-living larvae. The second-stage larvae are ingested by small crustaceans (first intermediary hosts), which are then consumed by marine fish and squid (second intermediary hosts), where the larvae undergo further development. The third-stage larvae present in fish and squid can penetrate the gut wall and migrate to tissues in the peritoneal cavity and muscles. Ultimately, marine mammals ingest the larvae in infected marine fish or squid. Upon reaching the stomach of the definitive host, the third-stage larvae will transform into adult worms and complete their life cycle. The adult worms superficially invade the stomach lining of the marine mammals as part of their attachment process and are embedded in the gastric mucosa. This may explain their tendency to accidentally perforate the human stomach and intestine. Humans are considered accidental dead-end hosts since the larvae cannot reach maturity and usually die within a span of 3 weeks after infection (13).

There are four main clinical forms of human anisakidosis: gastric, intestinal, extragastrintestinal/ectopic, and allergic disease (9). Symptoms associated with gastric or intestinal forms in humans are usually the result of the third-stage anisakid larvae attempting to penetrate the gastric or intestinal mucosa. Gastric invasion is most commonly associated with Pseudoterranova species, while intestinal invasion is most commonly associated with Anisakis species (1).

Acute gastric anisakidosis manifests with sudden onset of epigastric pain accompanied by nausea or vomiting within a few minutes to hours of ingesting raw seafood. Live larvae are often expelled via the nose or mouth. Symptoms of acute disease may also mimic angina-like chest pain (14, 15). Chronic gastric anisakidosis, which usually occurs due to the host inflammatory response to dying larvae, may mimic symptoms of peptic ulcer disease and chronic gastritis (6). Occasionally, patients may present with gastric perforation and pneumoperitoneum (16).

Intestinal anisakidosis occurs more frequently in Europe and is less common in Japan, where more than 97% of cases involve the stomach (17, 18). The terminal ileum is involved in the majority of cases (19, 20), although the ileocecal valve may also be involved (21). Symptoms include intermittent or constant abdominal pain, fever, vomiting, or diarrhea, all of which usually start 5 to 7 days after ingestion of the seafood (6). Because of the nonspecific nature of these symptoms, intestinal anisakidosis has frequently been misdiagnosed as acute appendicitis, Crohn’s disease, or colonic cancer, occasionally resulting in unnecessary laparotomy and bowel resection. In chronic intestinal anisakiasis, the formation of eosinophilic granulomas around the larvae may present as intestinal obstruction or tumor (18, 22), with resultant segmental colitis, small bowel obstruction, intussusception, or intestinal perforation presenting as acute abdomen (23–27). Intestinal anisakidosis may also present as eosinophilic gastroenteritis (28).

Ectopic disease is much less common than the gastric and intestinal forms (2) and occurs when the anisakid larvae traverse the intestinal wall and reach the peritoneal cavity. Peritoneal involvement may result in hemorrhagic ascites (29). Rarely, the larvae have been detected in peritoneal dialysis effluent (30, 31). From the peritoneal cavity, the larvae may then enter surrounding organs and induce an eosinophilic granulomatous response. Presentations of ectopic disease include mesenteric mass (32), omental nodules (33, 34), and involvement of mesocolic lymph nodes (35) and spleen (36). Anisakid larvae may also enter the pleural cavity from the peritoneal cavity by penetrating the diaphragm and causing an eosinophilic pleural effusion (37, 38). Finally, cases of tonsillar and laryngeal anisakidosis have been described, where the larvae migrated back up the esophagus and into the tonsils or larynx (39, 40).

The fourth form of human disease is acute allergic anisakidosis. Manifestations may range from urticaria and angioedema to anaphylactic shock; concurrent gastrointestinal symptoms may also be present (gastroallergic anisakiasis) (41). Most cases of allergic anisakidosis have high levels of IgE specific to A. simplex, but sensitization to the actual fish products is uncommon (42). Therefore, it may be prudent to evaluate patients with presumed fish allergy for A. simplex sensitization. Rarely, allergic reactions can manifest as allergic gingivostomatitis, intractable chronic pruritus, nephrotic syndrome, autoimmune pancreatitis, or rheumatic manifestations (43–47). Anisakid sensitization in fish-processing workers has been associated with bronchial hyperreactivity and dermatitis (48).

Diagnosis of gastric, intestinal, and ectopic anisakidosis is most reliably achieved through direct visualization and examination of the larvae by endoscopy, resected surgical specimen, or gross morphological examination of expelled, intact worms. Gastric anisakidosis is often easily diagnosed by endoscopy, although the worm may be hidden among gastric folds or can be confused with gastric mucus (49). In chronic cases, diagnosis is often difficult due to the nonspecific nature of symptoms and infrequent visualization of larvae on endoscopy due to deep tissue penetration of larvae (10). Other adjuncts to diagnosis are history (onset of abdominal symptoms following raw seafood consumption), histopathology, imaging studies, and serology. Imaging studies may show mucosal edema, irregular bowel wall thickening, lymphadenopathy, focal mass, or ascites (6).

The criteria for diagnosing allergy to A. simplex are a compatible history and measurement of antibodies to anisakids using commercially available enzyme-linked immunosorbent assay (ELISA) (50) or Western blotting (51). Cross-reactivity with other nematodes, insects (cockroaches), or crustaceans (shrimp) (6) has been reported and may cause false-positive serology results. Molecular methods of identifying anisakids in fish (52) and in humans (53) have also been developed but are not widely available.

When the intact worm is submitted (from vomitus or stool or retrieved via endoscopy), the third-stage larvae may be identified by morphological features, including the striated outer cuticle, one dorsal and two ventral lips, a boring tooth and excretory pore at the anterior end, and a mucron at the posterior end (54). These features allow anisakid larvae to be differentiated from third- or fourth-stage Ascaris larvae, which may also be retrieved from the throat or vomitus. Anisakis larvae may be differentiated from Pseudoterranova larvae in that they are generally smaller and have a simple digestive tube, whereas Pseudoterranova larvae are larger and have an anteriorly directed cecum (54). In histologic sections, anisakid larvae can be distinguished from related nematodes, such as Ascaris, by the absence of lateral alae. Anisakis larvae have tall, prominent muscle cells and Y-shaped lateral chords (Fig. 1B), whereas Pseudoterranova larvae have the characteristic intestinal cecum and butterfly-shaped lateral chords (54). Determination of the genus of an anisakid nematode is often not performed due to limited availability of the expertise needed for pathological diagnosis and the lack of molecular tests. While the CDC currently does not offer serological or molecular testing, it may still be a good resource for the identification of these nematodes.
Removal of larvae by endoscopy is curative for acute gastric anisakidosis. Suspected intestinal anisakidosis, on the other hand, may be managed conservatively, given that the larvae die after a few days. Occasionally, surgery is required for management of intestinal or extraintestinal infections, especially if there are complications like appendicitis, intestinal obstruction, perforation, or peritonitis. Isolated cases of presumed intestinal anisakiasis have been treated with albendazole (55), although the benefits of albendazole are unknown.

Prevention of anisakidosis is best achieved by following the guidelines put forth by the Food and Drug Administration (FDA). The FDA recommends cooking seafood to temperatures of 63°C (145°F), while fish intended for raw consumption should be frozen at −4°F (−20°C) or below for 7 days or flash-frozen to −31°F (−35°C) or below for at least 15 h. In addition, consumers, patients, and individuals preparing fish for consumption should be educated about the risks of ingesting raw seafood. Fishermen should eviscerate fish immediately after catching them to prevent postmortem migration of larvae from intestines to fish musculature but are discouraged from throwing the eviscerated products back into the sea since this can increase the infection rate in local marine life (1).

We report the first case of parametrial anisakidosis. We believe that the larva gained access to the peritoneal cavity through the stomach or intestinal wall, entering the peritoneal cavity, and eventually reaching the retrouterine pouch (Pouch of Douglas) (Fig. 3) through the known pathways of peritoneal fluid circulation. Given that the retrouterine pouch is a watershed area in the peritoneal fluid circulation pathway, it is a common location for tumor (56) and endometriosis implants (57). The host response subsequently encased the larva within eosinophilic granulomas and fibrous tissue, thus causing it to adhere to the posterior aspect of the uterine cervix. The parametrial location in this patient with cervical cancer led to an initial impression of either malignant tumor spread or a benign cervical lesion. However, recognition of key anatomic anisakid structures allowed for definitive identification, while an understanding of the parasite life cycle and circulation route of the peritoneal fluid allowed for reconstruction of the presumed pathway of infection.

REFERENCES


