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CASE REPORT



## IgE-mediated gastroallergic anisakiasis with eosinophilic oesophagitis: a case report

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### ABSTRACT

#### Background

Anisakiasis is an emerging zoonosis caused by the fish parasitic nematode *Anisakis* infecting the gastrointestinal tract.

#### Case presentation

We describe a case of a 58-year-old woman diagnosed with gastro-allergic anisakiasis, in which the patient developed an acute food-induced IgE-mediated hypersensitivity reaction as well as concurrent gastro-intestinal manifestations after consumption of raw fish. The patient presented with epigastric pain, anaphylaxis and acute dysphagia caused by eosinophilic oesophagitis.

#### Discussion

Anisakis allergy should be considered as causative agent in patients presenting with acute urticarial rash, anaphylaxis and/or abdominal manifestations, especially when symptoms occur after consumption of seafood. Moreover, eosinophilic oesophagitis may be a rare but important complication of *Anisakis* infection. Endoscopic evaluation with esophageal biopsies should therefore be considered if suggestive symptoms are present. Patients with confirmed gastro-allergic anisakiasis are advised to properly freeze or cook fish prior to consumption, although caution is advised, since heat-stable allergen proteins have been described. An adrenaline auto-injector should be prescribed.

### KEYWORDS

Anisakis; anisakiasis; food allergy; gastro-allergic anisakiasis; eosinophilic oesophagitis; raw fish

## Introduction

Anisakiasis is an emerging zoonosis caused by the nematode *Anisakis* spp. infecting the gastrointestinal tract. The *Anisakis* spp. have complex lifecycles in which different larval stages pass through a number of marine hosts. Humans become infected by consuming raw or undercooked, infected fish or squid. Due to changes in culinary habits, increasing international travels, cultural and demographic changes, the incidence of foodborne zoonoses is increasing [1,2]. We present a case of gastroallergic anisakiasis with eosinophilic oesophagitis, a rare complication.

## Case

A 58-yo woman presented at the emergency department with acute retrosternal and epigastric pain, dysphagia, nausea, slight fever (38.1°C), itchiness and diffuse urticarial papules. She referred to have eaten raw cod with vegetables the night before. Apart from grass pollen allergy, the medical history was completely negative for allergy.

A blood examination showed elevated levels of white blood cell count ( $9.88 \times 10^3/\mu\text{L}$ ) with elevated neutrophils

(8880/ $\mu\text{L}$ ), low eosinophils (20/ $\mu\text{L}$ ), clearly increased D-dimer (14,780 ng/mL) and total IgE level (387.2 kU/L). Thoracoabdominal computer tomography revealed the presence of diffuse intra-abdominal free fluid and slight thickening of the gastric and duodenal intestinal wall (Figure 1). There were no signs of pulmonary embolism. Oesophagogastroduodenoscopy showed an erosive esophagitis grade A (Los Angeles classification) and mild esophageal edema. Ileocolonoscopy was normal. Biopsies of the oesophageal mucosa revealed intercellular edema and basal hyperplasia, with a high number of eosinophils (228 per high-power field; HPF). There was no visualization of intestinal metaplasia. Histologic evaluation of the gastric, duodenal and ileal mucosa showed no abnormalities.

One week later, follow-up laboratory data showed normalized levels of D-dimers and WBC, but clearly elevated eosinophils (780/ $\mu\text{L}$ ) and further increase of total IgE (887.4 kU/L). Skin prick tests were positive for histamine (7 mm) and apple (3 mm). Subsequently, blood examination with serum-specific IgE measured by Immuno-CAP was performed. Total IgE count was significantly elevated (2500 kU/L) with negative IgE to cod (<0.35 kU/L) and slightly, not significantly elevated

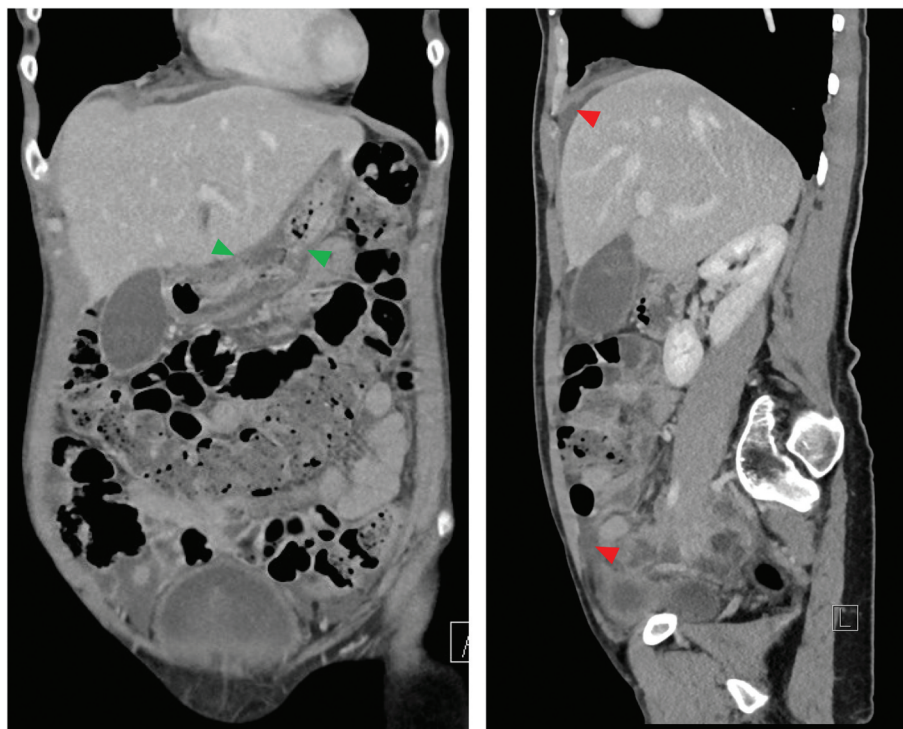


**Figure 1.** Thoracoabdominal computer tomography revealed the presence of diffuse intra-abdominal free fluid (red arrows) and thickening of the gastric wall (green arrows).

IgE to PRU p3 (0.31 kU/L), PRU p4 (0.18 kU/L), and fish rGad c1 (0.31 kU/L). Most striking, however, was the high level of specific IgE to *Anisakis* Larvae (>100 kU/L).

In the acute episode, proton-pump inhibitors and antihistaminic treatment were started, but were stopped within a week because of fast and complete disappearance of the symptoms. Follow-up abdominal ultrasonography a week later showed a complete resolution of the intra-abdominal free fluid. Because there were no persistent symptoms, no follow-up esophago-gastroduodenoscopy was performed. After restraining from eating raw seafood, no recurrence occurred in over 2 years.

## Discussion

Anisakiasis is a marine food-borne zoonosis resulting from the ingestion of nematodes larvae of the *Anisakis* genus. Acute gastric anisakiasis is the most prevalent clinical presentation of infection with symptoms of abdominal pain, nausea, diarrhea and vomiting, caused by mucosal adherence or penetration of the nematode. In our case, the patient showed symptoms of acute retrosternal and epigastric pain, nausea and mild fever with radiographically thickening of the gastric and duodenal intestinal wall, probably caused by mucosal adherence of the living larvae. The usual presentation of acute infection is self-limiting as the larvae cannot reproduce in the human body and die within approximately 14 days [3]. Because of the nonspecific and self-

limiting symptoms, anisakiasis is often mis- or under-diagnosed [1,3]. The only effective treatment is the endoscopic removal of the living larvae. In a case series of 226 patients, *Anisakis* larvae could be demonstrated in 56.3% of the cases during endoscopy [4]. In this case, no living nematode was visualized on endoscopy. The nematode might have been removed by vomiting or could have proceeded to the lower gastro-intestinal tract. Another clinical entity is a food-induced IgE-mediated allergy, which is caused by an allergic reaction to antigens of the *A. simplex* [5]. *Anisakis* is considered the most important hidden food allergen causing urticaria and angioedema in adults, and is thought to be responsible for 8% of acute urticarial rashes and 10% of anaphylaxis previously diagnosed as idiopathic [6,7]. The clinical symptoms range from rhinoconjunctivitis, dermatitis and asthma to acute urticaria, angioedema and anaphylaxis [6]. Our patient showed symptoms of itching and diffuse urticarial papules.

The diagnosis is based on a compatible history, a positive skin prick test and/or a positive serum-specific IgE level, a negative history of allergic symptoms, and negative in vivo and in vitro tests to fish and/or other possible cross-reactive allergens [1]. Subclinical sensitization, characterized by *Anisakis*-specific IgE detection in asymptomatic individuals, may also occur. *Anisakis* proteins demonstrate considerable immunological cross-reactivity to proteins of related helminthes (e.g. hookworm) or invertebrates such as dust mites, cockroaches and shrimps. The use

of specific IgE alone, without a suggestive history, is therefore insufficient in the diagnostics of Anisakis allergy. Currently, 12 allergens have been identified in *Anisakis*. The major allergens, found in over 50% of patients, are Ani s 1 and Ani s 7 [5]. Exposition may occur to somatic antigens from dead larvae in food, excretory-secretory antigens when there is expulsion of the intact larva, or both in cases where the larva penetrates the tissue and is killed and subsequently degenerated inside the host [5,8]. Allergic reactions to *Anisakis* proteins may also occur by inhalation or by direct contact in the domestic or occupational environment while preparing fish [5].

The occurrence of abdominal manifestations in combination with hypersensitivity symptoms has been termed gastroallergic anisakiasis, an overlap between food allergy and parasitic disease. The IgE response is caused by a type I hypersensitivity reaction in combination with the physiologic response against parasite invasion. Eosinophilia is also a typical feature of helminth infection. At the moment of presentation, however, the eosinophilic level may initially be low with a gradual increase over several days and a peak after 7 to 10 days [9,10]. These typical features have been observed in our case.

Interestingly, our patient presented with symptoms of dysphagia and transient food impaction. Oesophagogastroduodenoscopy showed an erosive esophagitis grade A with mild edema. Oesophageal biopsies revealed a high number of eosinophils (228/HPF), the clinicopathological features of an eosinophilic esophagitis, which is a rare complication of anisakis infection with only a few documented cases in literature [3]. Esophageal biopsies should be obtained from all patients with suggestive symptoms, regardless of endoscopic appearance, since sensitivity of endoscopic findings are low and predictive values are inadequate for diagnostic purposes [11]. It is important to note that esophageal eosinophilia in the absence of clinical features is not sufficient to make a diagnosis of eosinophilic esophagitis and that many other conditions may be associated with esophageal eosinophilia, such as gastroesophageal reflux disease. Large numbers of intraepithelial eosinophils on histologic examination (more than 20/HPF) are, however, suggestive for non-acid-related causes of esophagitis [12]. Elevated serum IgE levels and peripheral eosinophilia are, respectively, seen in approximately 50–60% and 40–50% of patients with eosinophilic esophagitis and may support the diagnosis. IgE antibodies and eosinophil activation seem to play a role in the pathogenesis, but neither seems to be absolute since not all patients have high levels of either total or specific IgEs [13,14].

An important difference between the clinical entities of anisakiasis is the time interval between fish

ingestion and onset of symptoms. In most cases of acute gastric anisakiasis, the abdominal symptoms develop within approximately 12 hours of ingestion. Hypersensitivity symptoms, however, may appear much later (in contrast to most other food allergies), in some cases even more than 24 hours after consumption. This is important to consider, since the diagnosis can be delayed or missed when food intake was not questioned thoroughly [10]. In our case, abdominal and hypersensitivity symptoms appeared within 6 hours after digestion and resolved spontaneously the next day with only symptomatic treatment.

Freezing at  $-20^{\circ}\text{C}$  for at least 24 h or thorough cooking above  $60^{\circ}\text{C}$  for at least 10 minutes are considered effective preventive measures to inactivate *Anisakis* spp. in infected fish. Many patients with *Anisakis* allergy are able to tolerate frozen or well-cooked fish. However, some of the allergen proteins are heat-stable; therefore, a small number of patients may react even to well-processed fish. In our patient, we advised strict avoidance of raw or undercooked fish and an adrenaline auto-injector was prescribed. Consumption of a small amount of well-processed fish can be tried.

## Conclusion

We report a case of gastroallergic anisakiasis, in which the patient developed an acute food-induced IgE-mediated hypersensitivity reaction as well as concurrent gastro-intestinal manifestations after consumption of raw fish. *Anisakis* allergy has to be considered as causative agent in patients presenting with acute urticarial rash and anaphylaxis, especially when symptoms occur after consumption of seafood. The diagnosis can be made based on a positive history in combination with a positive skin prick test and/or positive serum-specific IgE level. In this specific case, the patient was also diagnosed with a histologically confirmed eosinophilic oesophagitis, a rare but important complication of *Anisakis* infection. Endoscopic evaluation with esophageal biopsies should therefore be considered in patients with anisakiasis if suggestive symptoms are present. Patients with confirmed gastroallergic anisakiasis are advised to properly freeze or cook fish prior to consumption, although caution is advised, since heat-stable allergen proteins have been described. An adrenaline auto-injector should be prescribed.

## Key points

- Anisakiasis is a marine food-borne zoonosis resulting from the ingestion of parasite nematodes larvae of the *Anisakis* genus.

- Clinical manifestations include abdominal manifestations, as well as an IgE-mediated allergy. The concurrence of both has been termed gastroallergic anisakiasis, an overlap between food allergy and parasitic disease.
- Hypersensitivity symptoms may appear up to 24 hours after ingestion.
- The diagnosis is based on a positive history in combination with a positive skin prick test and/or positive serum-specific IgE level.
- Eosinophilic oesophagitis is a rare complication. Endoscopic evaluation with esophageal biopsies should be considered if suggestive symptoms are present.
- Endoscopic removal of the nematode is the only definitive treatment, although gastric anisakiasis is usually self-limiting with conservative management.
- Patients are advised to properly freeze or cook fish prior to consumption, although caution is advised, since heat-stable allergen proteins have been described.
- An adrenaline auto-injector should be prescribed in case of anisakis allergy

## Disclosure statement

The authors declare that they have no competing interests.

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## Authors' contributions

JD, HV and PD analyzed and interpreted the patient data regarding the gastro-intestinal disease. HL, BV and EH analyzed and interpreted the patient data regarding the dermatologic disease and were contributors in writing the manuscript. All authors read and approved the final manuscript.

## Consent for publication

Consent was obtained.

## Availability of data and materials

Data sharing is not applicable to this article as no datasets were generated or analyzed during the current study.

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