

GASTROALLERGIC ANISAKIASIS

Gastroallergic anisakiasis: Findings in 22 patients

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Abstract

Background and Aims: Ingestion of Anisakidae larvae in raw seafood may cause anisakiasis. However, despite the high level of consumption of seafood in Spain, only a few cases of anisakiasis have been reported until now. *Anisakis simplex* can cause allergic reactions in sensitized patients as a result of its parasitism in the gastrointestinal tract. The purpose of this study was to analyse the clinical findings in 22 patients with gastroallergic anisakiasis.

Methods: Patients with allergic and/or gastric symptoms after seafood ingestion were evaluated in the emergency room of the La Paz General University Hospital. Skin testing for *Anisakis simplex* and tests on the implicated seafood were performed and amounts of serum-specific immunoglobulin E were assessed. A gastroscopy was performed in those patients with severe allergic or/and persistent gastric symptoms after ingestion of raw or undercooked seafood.

Results: Twenty-two patients were diagnosed with gastroallergic anisakiasis in 1 year. Most patients presented to the emergency room of our hospital with allergic symptoms. Gastric symptoms were usually moderate. Gastroscopy revealed local mucosal oedema and gastric erosion at the point of fixation. Two or more worms were detected in three patients. The mean time of latency of allergic symptoms was 5 h, while the mean time for gastric symptoms was 3 h.

Conclusion: *Anisakis simplex* parasitism was the causative agent of allergic and gastric symptoms. Gastroallergic anisakiasis appears to be a relatively common disease, that may have been underdiagnosed.

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Key words: allergy, anisakiasis, *Anisakis simplex*, fibre-optic gastroscopy, gastroallergic anisakiasis.

INTRODUCTION

Anisakis simplex is a nematode of the Anisakidae family, Ascaridoidea superfamily, Ascaridida order; that in its adult stage parasitizes sea mammals. The common intermediary host species are codfish, hake, sardine, anchovy, salmon, red mullet, tuna fish, mackerel, horse mackerel and squid.¹ In the intermediary hosts the larvae enter the third larval stage. The ingestion of *Anisakis* spp. third-stage larvae in raw or undercooked seafood may cause the human disease known as anisakiasis.^{2–12} After ingestion, *A. simplex* larvae can attach themselves to the gastric mucosa (acute anisakiasis); or penetrate into the host stomach or intestinal wall (chronic anisakiasis). In this latter form, the invasion may lead to abscess formation or eosinophilic granulo-

mas, and can mimic appendicitis, gastroduodenal ulcer, eosinophilic colitis, inflammatory bowel disease and intestinal obstruction.^{2–8} Anisakiasis is common in Japan because of the consumption of raw seafood.^{2–8} In Europe, several cases have been reported over the years.⁸ However, in Spain most reported cases seemed to be anecdotal findings.^{9–12}

The larvae of *A. simplex* cannot survive at greater than 60°C for 10 min, or lower than –20°C for 48 h. However, the ingestion of safely cooked salt-water fish, without viable larvae, has been reported to cause allergic reactions.^{13,14}

Three years ago, allergists in Spain began to look for allergic diseases caused by *A. simplex*,^{12–14} and led us to learn more about *Anisakis* parasitism. As in other diseases caused by parasites, we believed it would be

possible to find live parasites in the patients with acute allergic symptoms.^{2-7,12} As we detected live larvae in some cases,¹² we designed a protocol to detect live larvae in patients with allergic reactions related to the ingestion of raw or undercooked seafood.

METHODS

The initial patient evaluation was made in the emergency room of 'La Paz' General University Hospital in the acute setting. We selected the patients who presented to the emergency room with digestive or allergic symptoms, such as urticaria, bronchospasm, angioedema and/or anaphylaxis that occurred approximately 24 h after the ingestion of raw or undercooked seafood. Gastric symptoms were also present but moderate.

A fibre-optic gastroscopy was performed if any digestive symptom persisted for more than 8 h, or if a marked allergic reaction (anaphylaxis) was present. Skin testing was performed on the volar side of the forearms of the patients by means of allergy pricker lancets (DHS, Madrid, Spain). Skin prick tests using a variety of commercial seafoods (Bencard, Worthing, UK); *A. simplex* extract at 1 mg/mL (I.P.I. Pharmaceutical, Madrid, Spain); and suspected raw seafood (hake, anchovies, cod, tuna and salmon) were performed. Histamine (10 mg/mL) and saline solutions were used as positive

and negative controls. The skin tests were read after 15 min. Those with wheal diameter 3 mm larger than the negative control were regarded as positive. Serum-specific immunoglobulin (Ig) E was determined against the implicated seafood and *A. simplex* by the CAP system fluoro-enzyme-immunoassay (Pharmacia Diagnostics, Upsala, Sweden) according to the manufacturer's instructions.

RESULTS

Twenty-two patients (nine males, 13 females) median age 48.5 years (range 17–73 years) were diagnosed with acute gastroallergic anisakiasis. They were detected during the 12-month study. Table 1 shows the characteristics of the patients.

All patients were admitted to the emergency room of our hospital because of their allergic reactions. Raw anchovy prepared in vinegar sauce was the implicated seafood in 16 cases, undercooked hake in four cases and raw sardines in two cases. Thirteen patients showed generalized urticaria, with or without angioedema, and systemic anaphylaxis was seen in nine. The latency of the allergic symptoms ranged from 15 min to 26 h, with a mean time of 5 h from ingestion. Details of the gastric symptoms were usually elicited by questioning. The patients considered them to be less important than their allergic symptoms. Gastric symptoms were evident

Table 1 Clinical and serological findings of the 22 patients

	Sex/Age	Allergy	Gastric symptoms	LA	LD	SPT	IgE-As	Gastroscopy
1	F/37	A	E + D	240	15	+	+	1
2	M/53	U/Ae	E + V	120	90	+	+	2
3	F/17	A	E	285	300	+	+	1
4	M/25	U/Ae	E	240	360	+	+	1
5	F/30	U/Ae	E + V	360	450	+	+	1
6	F/27	U/Ae	E + V	120	120	+	+	1
7	M/46	U/Ae	E	210	210	+	+	1
8	M/51	A	E + D	180	180	+	+	1
9	M/66	A	E	180	30	+	+	1
10	M/59	A	E + V	225	225	+	+	1
11	M/63	U/Ae	E + D	120	60	+	+	> 10
12	F/58	U/Ae	E + V	240	240	+	+	2
13	F/40	U/Ae	E + V + D	270	240	+	+	1
14	F/73	U/Ae	E + V	1560	480	+	+	1
15	F/46	U/Ae	E + V	1200	120	+	+	1
16	F/53	U/Ae	E	300	270	+	+	1
17	M/53	A	E	150	30	+	+	1
18	M/55	A	E + V	120	120	+	+	1
19	F/66	A	E	15	20	+	+	1
20	F/48	U/Ae	E + D	300	330	+	+	1
21	F/45	U/Ae	E	60	60	+	+	1
22	M/57	A	E + V + D	90	95	+	+	1

SPT, skin prick test for *Anisakis simplex* extract; IgE-As, immunoglobulin E for *Anisakis simplex*; A, anaphylaxis; U/Ae, urticaria and/or angioedema; E, epigastralgia; V, vomiting; D, diarrhoea; LA, latency of allergic symptoms (min); LD, latency of digestive symptoms (min). Specific IgE was considered positive when greater than 0.70 kU/L. +, positive. Gastroscopy, number of *A. simplex* larvae detected.

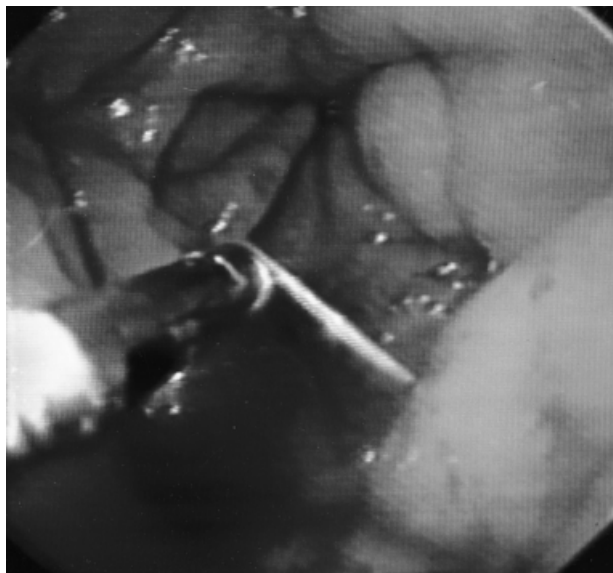


Figure 1 An *Anisakis simplex* larva fixed in the gastric mucosa and has produced an erosion and marked oedema.

15 min to 8 h (mean 3 h) after ingestion of the under-cooked seafood. Gastric fullness and mild epigastric pain were present in all cases. Ten patients experienced vomiting and six were affected by mild diarrhoea. All patients had a positive skin test to *A. simplex*, and negative results to seafood tests. All patients also had positive serum-specific IgE to *A. simplex* (>0.7 kU/L).

After fibre-optic gastroscopy, one worm was detected in 19 patients (Figs 1,2) and multiple worms were detected in three patients (Fig. 3). A small erosion at the point of fixation was seen in all patients, but in one of the patients with several worms, an ulcer was also detected. At gastroscopy, forceps were used to remove all the worms, which were later identified as *A. simplex* larvae by microscopy. The patients' allergic symptoms were treated in the emergency room and the gastric symptoms disappeared after removal of the larvae by gastroscopy. In two patients, however, mild epigastric pain persisted for 1 week.

DISCUSSION

Twenty-two cases of acute gastroallergic anisakiasis were detected during the prospective study. The protocol for patient selection was based mainly on allergic symptoms. More worms were detected during the 12-month study than have been reported in several years in Spain and nearly in all Western Europe. We propose that this form of acute anisakiasis, with its allergic and gastric symptoms was usually misdiagnosed. This view is supported by large Japanese studies that report a local allergic reaction in the gastric mucosa but few instances of systemic allergic symptoms. All the present patients suffered systemic allergic symptoms. They gave a marked importance to the local allergic reaction in gastric mucosa.⁶



Figure 2 An *Anisakis simplex* larva fixed in the gastric mucosa and has produced an erosion.

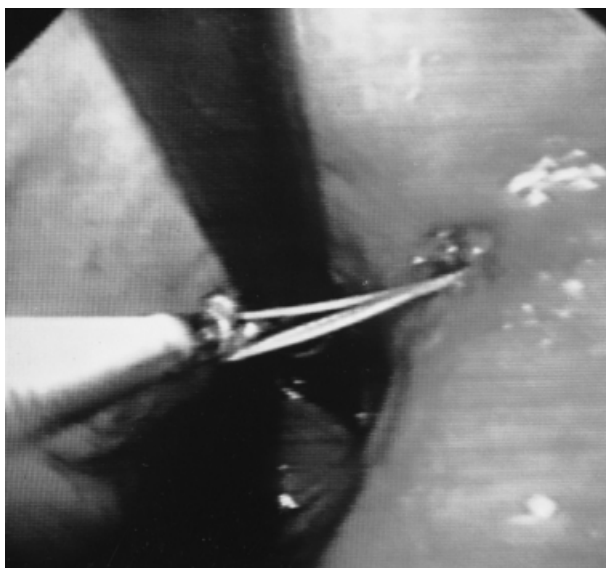


Figure 3 *Anisakis simplex* larvae fixed in the gastric mucosa with an ulcer.

In our experience, symptoms of seafood hypersensitivity, without evidence of seafood sensitization could be caused by an allergy to *A. simplex*. The thermostability of *A. simplex* allergens has previously been confirmed, and could explain the allergic manifestations after ingestion of cooked or frozen seafood.^{13,14} As we detected worms in some patients with allergic reactions

after seafood ingestion, a prospective study was undertaken.¹² Allergic symptoms after fixation of live worms are a manifestation of a different disease; an allergy to the live parasite. The latency of reactions in the present patients was longer than in other hypersensitivity food reactions, possibly due to the time taken for larval mucosal attachment. The delayed onset of allergic symptoms may result in misdiagnosis at presentation and it is important to seek a history of recent raw or undercooked seafood ingestion. Gastroscopy and clinical findings showed that these patients became sensitized to the *Anisakis* allergens in response to being parasitized.^{6,7,12,15} It is proposed that patients develop a systemic IgE-mediated reaction following fixation and penetration of the gastric mucosa by the larvae. The two events, allergy and infestation occurred together, and an allergic reaction with gastric symptoms can be the marker of acute disease.¹² The allergic reaction may be severe. Nine of the 22 patients developed anaphylaxis. Whether other syndromes develop as a result of invasive anisakiasis disease, however, remains to be seen. The finding of 22 cases of gastroallergic anisakiasis in the present 12-month study suggests that this disorder is more common than was previously realized. Our study indicates that there is a delayed onset of symptoms after raw seafood ingestion and only occasionally is the parasite attached to the gastric mucosa and detectable by gastroscopy. Many patients have transient digestive and/or allergic symptoms including vomiting that may quickly dislodge the nematode from the gastric mucosa. For these reasons the diagnosis may be missed unless a history of recent raw or undercooked seafood ingestion is sought. Fibre-optic gastroscopy should be used in patients with allergic reactions after raw or undercooked seafood ingestion, especially in those with persisting severe allergic symptoms and gastric symptoms, in order to prevent penetration of live larvae into the gastric mucosa or more intense allergic reactions. Allergic evaluation of patients with a suggestive history has been useful to diagnose and to initiate successful treatment.

The present management of anisakiasis recommends a non-seafood diet if patients have skin tests positive for *A. simplex*. However, patients develop allergic reactions only after being infected with live nematodes, and can tolerate well-heated or deep-frozen seafood, as food challenge with non-infecting *A. simplex* has demonstrated.¹⁵ Many patients have probably had previous contact with the parasite, and some of these are sensitized, as shown by a positive skin test or serum-specific IgE, but have had no acute symptoms, or symptoms of allergy to the parasite. Therefore, it is important to determine whether there is a history of eating seafood that was undercooked or raw; if gastroallergic anisakiasis is suspected, a challenge could be necessary.¹⁵ Further investigations are needed to assess the indications for gastroscopy at presentation. The best treatment for anisakiasis is prophylaxis. Larvae die at temperatures maintained at higher than 60°C for 10 min, or at lower than -20°C for at least 48 h. The only therapy for acute anisakiasis is removal of larvae

by gastroscopy (when the larvae continue to be fixed to the gastric mucosa, usually the nematode leaves the mucosa spontaneously).

This recently described entity, including *Anisakis simplex* allergy and the anisakiasis-invasive disease, draws attention to the need for recommendations to control the human consumption of seafood parasitized by nematodes.

REFERENCES

- 1 Cheng TC. *Parasitología General. Superfamilia Heterocheiloidea*. Madrid: Eds. AC 1978.
- 2 Ishikura H, Kikuchi K, Nagasawa K *et al.* Anisakidae and anisakidosis. *Progr. Clin. Parasitol.* 1994; **3**: 43–101.
- 3 Ishikura H, Kikuchi K, Nagasawa K *et al.* Anisakidae and anisakidosis. In: Sun T, ed. *Progress in Clinical Parasitology*, vol III. New York: Springer Verlag, 1993; 43–102.
- 4 Muraoka A, Suehiro I, Fujii M *et al.* Acute gastric anisakiasis: 28 cases during the last years. *Dig. Dis. Sci.* 1996; **41**: 2362–5.
- 5 Kakizoe S, Kakizoe H, Kakizoe K *et al.* Endoscopic findings and clinical manifestation of gastric Anisakiasis. *Am. J. Gastroenterol.* 1995; **90**: 761–3.
- 6 Asaishi K, Nishino C, Ebata T, Totsuka M, Hayasaka H, Suzuki T. Studies on the etiologic mechanism of anisakiasis. 1. Immunological reactions of the digestive tract induced by anisakis larvae. *Gastroenterol. Jpn.* 1980; **15**: 120–7.
- 7 Asaishi K, Nishino C, Totsuka M, Hayasaka H, Suzuki T. Studies on the etiologic mechanism of anisakiasis. 2. Epidemiologic study of inhabitants and questionnaire survey in Japan. *Gastroenterol. Jpn.* 1980; **15**: 128–34.
- 8 Bouree P, Paugam A, Petithory JC. Anisakidosis: report of 25 cases and review of the literature. *Comp. Immunol. Microbiol. Infect. Dis.* 1995; **18**: 75–84.
- 9 Mira Gutierrez J, García Martos P, Hilario Madrid LM, Rodríguez Iglesias MA. Anisakiasis, una patología emergente en nuestro medio. *Rev. Clin. Esp.* 1995; **195**: 51–4.
- 10 Acebes Rey JM, Fernandez Orcajo P, Díaz Gonzalez G *et al.* Dos casos de anisakiasis en el hospital Del Río Hortega. *Rev. Esp. Enferm. Dig.* 1996; **88**: 59–60.
- 11 Canut Blasco A, Labora Loriz A, de Torre Ramirez JL, Romeo Ramirez JA. Anisakiasis gastrica aguda causada por insuficiente cocción en microondas. *Med. Clin.* 1996; **106**: 317–18.
- 12 Alonso A, Daschner A, Moreno-Ancillo A. Anaphylaxis with *Anisakis simplex* in gastric mucosa. *N. Engl. J. Med.* 1997; **337**: 350–1.
- 13 Audicana T, Fernandez de Corres L, Muñoz D *et al.* Recurrent anaphylaxis caused by *Anisakis simplex* parasitizing fish. *J. Allergy Clin. Immunol.* 1995; **96**: 558–60.
- 14 Moreno-Ancillo A, Caballero MT, Cabañas R *et al.* Allergic reactions to *Anisakis simplex* parasitizing sea food. *Ann. Allergy Asthma Immunol.* 1997; **79**: 246–50.
- 15 Alonso A, Moreno-Ancillo A, Daschner A, López Serrano MC. Dietary assessment in five cases of allergic reactions due to gastroallergic anisakiasis. *Allergy* 1999; **54**: 517–20.