

Gastroallergic anisakiasis: Borderline between food allergy and parasitic disease—Clinical and allergologic evaluation of 20 patients with confirmed acute parasitism by *Anisakis simplex*

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Background: Human subjects can be parasitized by *Anisakis simplex* by eating raw or undercooked fish. Gastric anisakiasis is probably the most frequent clinical entity presenting with severe epigastric pain, vomiting, and diarrhea. In gastroallergic anisakiasis hypersensitivity symptoms predominate.

Objective: We sought to describe clinical features, laboratory data, and gastroscopic findings in gastroallergic anisakiasis.

Methods: We selected 40 patients presenting to the emergency department with an acute allergic reaction, and if we suspected acute parasitism by *A simplex*, a fiberoptic gastroscopy was performed. In 20 patients we could detect one or more nematodes; these patients are referred to as group A. Those in whom no worm could be found are referred to as group B (n = 20). A detailed history, clinical features, gastroscopic findings, laboratory data, and skin prick test responses were compared. **Results:** Long-time intervals of up to 26 hours between fish intake and onset of hypersensitivity symptoms were found (group A, 5.4 ± 6.3 hours; group B, 5.3 ± 2.6 hours). Patients in groups A and B did not differ with respect to allergic symptoms (urticaria, angioedema, erythema, bronchospasm, and anaphylaxis) or the mainly light abdominal symptoms (upper abdominal pain, nausea, vomiting, and diarrhea). No significant differences were found with respect to age, time interval between fish intake and onset of symptoms, white cell and eosinophil counts, specific IgE levels against *A simplex*, or total IgE levels.

Conclusions: The peculiar sometimes long-time interval between fish intake and onset of allergic symptoms render the diagnosis difficult. An early gastroscopy can confirm the diagnosis and prevent complications. We suggest that gastroallergic anisakiasis be considered a distinct clinical entity in which the predominant symptoms are hypersensitivity symptoms and in which the correct diagnosis is not only important in the management of the acute reaction but also in the prevention of further allergic episodes. (J Allergy Clin Immunol 2000;105:178-81.)

Key words: *Anisakis simplex*, gastric anisakiasis, specific IgE, urticaria, angioedema, anaphylaxis, food hypersensitivity, parasitic diseases, skin tests, gastroscopy

Abbreviation used

SPT: Skin prick test

Anisakis simplex is a nematode belonging together with *Contracaecum* and *Pseudoterranova* to the Anisakidae family, Ascaridoidea superfamily, and Ascaridida order. The adult worm parasitizes sea mammals, such as whales, seals, dolphins, and sea lions. In its different larval stages, it can have several intermediate hosts. In sea fish or cephalopods, the worms develop to the third larval stage.¹

Human subjects can be parasitized by eating raw or undercooked fish or seafood that contains the third-stage larvae. Acute gastric anisakiasis first described in 1962 by Van Thiel² is the most frequent clinical entity caused by gastric mucosal penetration of the nematode. The patient feels epigastric pain, nausea, and vomiting, typically within 12 hours after ingestion of parasitized fish. The diagnosis is confirmed by gastroscopy, and symptoms cease after removal of the nematode by gastroscopic means. Most of the cases have been described in Japan with the raw fish-eating habits of its people, but reports of gastric anisakiasis have been published from all over the world.³⁻¹⁴

In recent years the allergenic potential of *A simplex* has been recognized.^{6,15-18} Typically, patients have recurrent hypersensitivity symptoms after intake of various fish but negative skin prick test (SPT) responses and specific IgE for the implicated fish. The involvement of an IgE-mediated response has been proven by means of SPTs and specific IgE for *A simplex*. Therefore *A simplex* allergy has been described as a distinct clinical entity independent of parasitism.

Gastroallergic anisakiasis is a consequence of ingestion of raw or undercooked fish. Here the patients can have abdominal symptoms together with hypersensitivity symptoms, such as urticaria, angioedema, or anaphylaxis. The diagnosis can be suspected by the patient's history, and gastroscopy can be useful to confirm the diagnosis when a nematode can be visualized and removed. In this entity we also find positive SPT responses and specific IgE against *A simplex*.¹⁹⁻²²

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The purpose of this study is to describe clinical features, laboratory data, and gastroscopic findings in a group of 20 patients with confirmed gastroallergic anisakiasis and in another group of 20 patients with suspected acute parasitism but no finding of this nematode by using gastroscopy.

METHODS

Subjects

For 10 months, patients who were attended in the emergency department with hypersensitivity symptoms, such as urticaria, angioedema, acute erythema, bronchospasm, and/or anaphylaxis, were asked to describe gastric or abdominal symptoms and to provide a history of intake of raw or undercooked fish in the 24 hours before the onset of symptoms ($n = 92$). In 40 of these patients, a fiberoptic gastroscopy was performed to rule out an acute parasitism by *A simplex* (Fig 1). Of 40 gastroscopies, we could detect one or more worms in 20 patients. Our microbiology service identified the nematodes as *A simplex*. These patients are referred to as group A ($n = 20$). Those patients in whom no worms could be found are referred to as group B ($n = 20$).

Investigation

In the study we included data obtained in the emergency department and data obtained by an allergologic evaluation. A detailed history was taken. In the emergency department we asked for the type of fish eaten, the mode of cooking, and the time interval between intake of fish and onset of abdominal or allergic symptoms (ie, latency of abdominal-gastric symptoms). We described the different hypersensitivity and abdominal symptoms. Any previous symptoms related to fish or unexplained urticaria or angioedema were noted. A white cell and eosinophil count was performed. We documented data about treatment and response to it. The latency of fiberoptic gastroscopy was defined as the length of time from onset of gastric or allergic symptoms to fiberoptic gastroscopy.

The allergologic evaluation was as follows: total serum IgE was assessed by the IMx-Method (Abbot Diagnostics, Chicago, Ill), and specific IgE to *A simplex* was assessed by CAP-FEIA (Pharmacia, Uppsala, Sweden). Specific IgE was considered positive at levels greater than 0.35 kU/L. These determinations were performed within 24 hours after onset of symptoms. SPTs were carried out within 1 week with *A simplex* antigen (Lab IPI, Madrid, Spain) and with the implicated fish (ALK-Abelló, Madrid, Spain). SPT responses were considered positive with a mean wheal diameter of at least 3×3 mm. Histamine at 1% concentration and saline solution (0.9% NaCl) were the positive and negative controls.

Controls

To assess the prevalence of positive SPT responses and positive specific IgE levels in the region studied, we have at our disposal a control group of 21 patients, 11 patients arriving at the emergency department during the same period of time without allergic or gastrointestinal symptoms, and 10 healthy staff members. None had eaten raw or undercooked fish in the 24 hours before undergoing SPT. SPTs were performed against *A simplex* (positive and negative control: histamine 1% and NaCl 0.9%, respectively).

We also have at our disposal a study of prevalence of specific IgE against *A simplex* in sera from adult blood donors of our region.²³

Statistics

Statistical analysis was performed by using SPSS SV (Program SPSS for Windows Student Version 6.0.1, SPSS Inc, 1989-93).

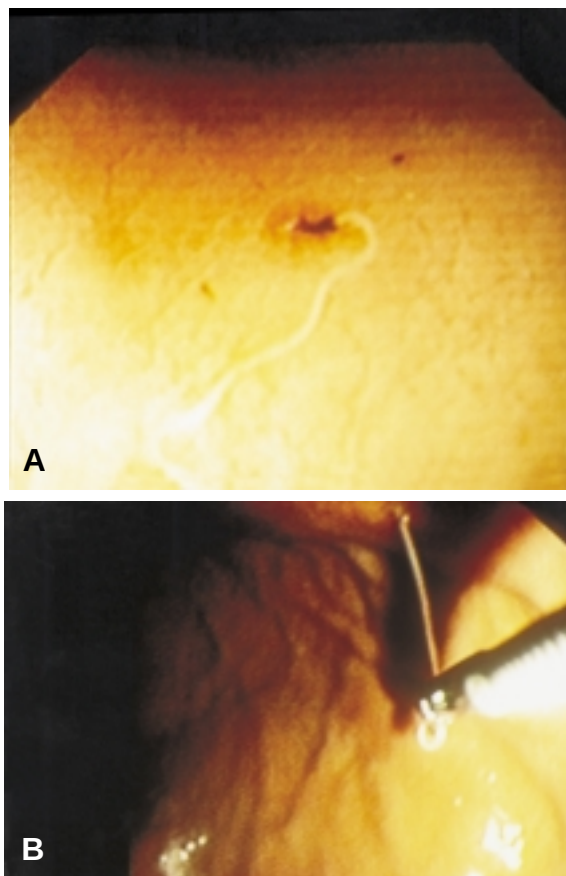


FIG 1. Fiberoptic gastroscopy in the diagnosis and treatment of gastroallergic anisakiasis. **A**, The head of a white filiform nematode (length, 3 cm) is attached to the gastric mucosa, producing a hemorrhagic erosion. **B**, The mobile nematode is extracted by gastroscopic means and afterwards identified as third-stage larva of *A simplex*.

Mean latencies (gastric-allergic symptoms and fiberoptic gastroscopy) were calculated for groups A and B and compared. Mean values for white cell counts, eosinophil counts, total serum IgE levels, and specific IgE levels to *A simplex* were calculated and compared between groups A and B.

The number of patients sensitized to *A simplex* was compared among groups A and B and the control group.

The *t* test for equality of means was used for comparison of age, latencies, white cell counts, and eosinophil counts. Mann-Whitney and Wilcoxon rank-sum tests were used for comparison of total and specific IgE levels in groups A and B.

The Fisher exact test was used for comparison of sensitized patients in groups A and B and the control group.

RESULTS

Mean age was 48.3 ± 15.0 years (mean $\pm$ SD) in group A, 39.7 ± 17.5 years in group B, and 40.5 ± 12.9 years in the control group (no statistical differences). The sex distribution was 10 men and 10 women in group A, 9 men and 11 women in group B, and 8 men and 13 women in the control group.

The fish most frequently implicated were anchovies in

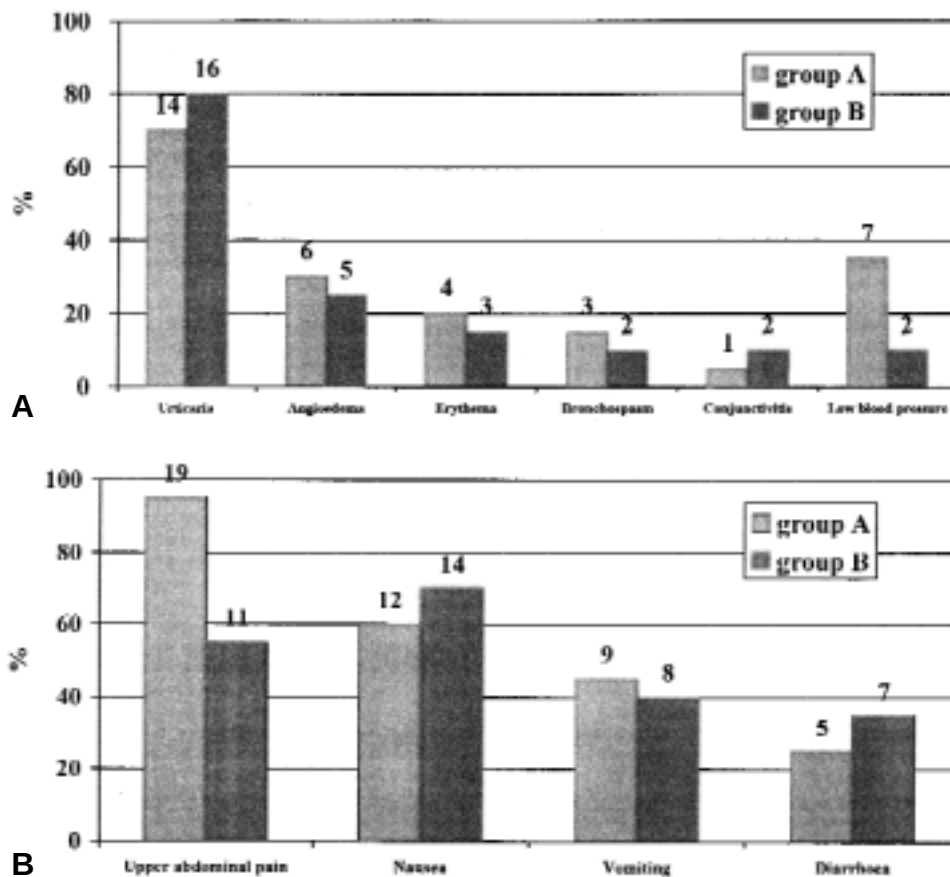


FIG 2. A, Frequency of hypersensitivity symptoms in patients with gastroallergic anisakiasis. **B,** Frequency of abdominal symptoms in patients with gastroallergic anisakiasis. The number of patients is indicated over the bars. Group A, Confirmation of acute parasitism by gastroscopic means (n = 20); group B, no nematode detected.

vinegar sauce in 27 patients and raw anchovies without preparation in another 5 patients. Other implicated fish species and preparations were hake (2 grilled, 2 in batter, and 1 cooked in microwave oven) and sardines (2 raw and 1 grilled).

The frequency of hypersensitivity and abdominal symptoms can be seen in Fig 2, A and B. Low blood pressure was defined as a systolic pressure of less than 100 mm Hg. Anaphylaxis was present in 7 patients in group A and 4 patients in group B (involvement of at least 2 different target organs, laryngeal edema, or presence of a low blood pressure). Diarrhea was classified as an abdominal symptom and was not considered a different target organ.

The time interval between intake of fish and onset of abdominal symptoms was 3.2 ± 2.3 hours (range, 15 minutes-7.5 hours) in group A and 4.9 ± 2.9 hours (range, 30 minutes-12 hours) in group B ($P = .057$).

The time interval between intake of fish and onset of hypersensitivity symptoms was 5.4 ± 6.3 hours (range, 20 minutes-26 hours) in group A and 5.3 ± 2.6 hours (range, 1.5-12 hours) in group B ($P = .98$). Abdominal symptoms preceded hypersensitivity symptoms in 16 patients, abdominal and hypersensitivity symptoms

appeared simultaneously in 15 patients, and hypersensitivity symptoms were the first to appear in 9 patients.

Three of 40 patients had previous allergic episodes with fish, and 4 patients had previous, unexplained acute allergic reactions.

The time interval between onset of abdominal or hypersensitivity symptoms and fiberoptic gastroscopy was 20.3 ± 14.0 hours in group A and 16.4 ± 9.0 hours in group B ($P = .3$).

Twenty-eight of 40 patients received initial treatment with antihistamines, corticosteroids, or epinephrine in the emergency department, and symptoms disappeared within a few hours in most of them. Only 3 patients required prolonged treatment for 2, 3, and 14 days, respectively.

In 17 fiberoptic gastroscopies in group A, only one larva could be detected, in 2 patients 2 and 3 nematodes could be seen, and 1 patient was massively parasitized by 20 worms.²² Most gastroscopies showed signs of acute ulcerations, erosions, and even small hemorrhagic lesions, mostly next to and near the implantation site of the nematode. However, in 6 patients the nematode was found fixed to the gastric mucosa without other macroscopically pathologic findings. In group B 13 patients showed abnormal mucosal changes, as can be seen in Table I.

TABLE I. Gastroscopic findings in gastroallergic anisakiasis

	Group A (n = 20)	Group B (n = 20)
One or more nematodes, n (%)	20 (100)	0 (0)
Erosions or ulcerations, n (%)	14 (70)	10 (50)
Hemorrhagic lesion, n (%)	2 (10)	1 (5)
Gastroduodenitis, n (%)	2 (10)	4 (20)
No (other) findings, n (%)	6 (30)	7 (35)

Group A, Confirmation of acute parasitism by gastroscopic means; group B, no nematode could be detected.

SPT responses were positive against *A simplex* in 19 patients in group A and in 18 patients in group B. In the control group SPT responses against *A simplex* were positive in 4 (19%) of 21 patients ($P < .01$). SPT responses against implicated fish were negative in all cases. Specific IgE against *A simplex* was present in all patients in group A and in 19 of 20 patients in group B.

White cell and eosinophil counts were available only in 16 patients in group A and 18 patients in group B. No statistical differences could be detected for specific IgE, total IgE, white cell count, and eosinophil count (Table II). Six of 16 patients showed white cell counts of greater than $10,000 \times 10^9/L$ in group A and 7 of 18 patients in group B.

Two of 16 patients showed eosinophil counts of greater than $350 \times 10^9/L$ in group A and 2 of 18 patients in group B.

DISCUSSION

Studies from Japan describe urticaria as a symptom appearing in about 10% of patients affected by gastric anisakiasis.^{5,24} Other studies suggested that the gastric symptoms of gastric anisakiasis were the consequence of an allergic mechanism.^{24,25} Animal studies show that the third-stage larva of *A simplex* is able to produce an IgE-mediated response in the host, as well as a recruitment of eosinophils, both of which are typical features of a T_H2 -mediated immunologic response induced by parasites.²⁶⁻²⁸

Thus in the case of gastroallergic anisakiasis, the IgE response documented by SPTs and specific IgE levels are to be interpreted as the cause of the type I hypersensitivity reaction, as well as the physiologic response against parasite invasion.^{6,7,19,26} In other human helminthic infections, such as equinococcosis, ascariasis, toxocariasis, or schistosomiasis, specific IgE has also been related to both parasite infestation and allergic type I hypersensitivity symptoms.^{27,29,30} But in contrast to these entities, in gastroallergic anisakiasis we know the exact moment of infestation.

Although one of the patients of group A did not show a positive SPT response, specific IgE was present in all patients of this group with gastroscopically confirmed gastroallergic anisakiasis. Thus the presence of specific IgE in our patients is a marker not only of acute para-

TABLE II. Laboratory parameters in patients of group A and B

	Group A	Group B	P value
Specific IgE	29.8 (12.4-56.8)*	11.3 (6.6-34.4)*	.08
Total IgE	146 (63.7-370)*	100 (31.3-242)*	.26
White cell count	$10,180 \pm 4355^\dagger$	$10,750 \pm 4285^\dagger$	.7
Eosinophil count	$200 \pm 153^\dagger$	$210 \pm 116^\dagger$	.83

Group A, Confirmation of acute parasitism by gastroscopic means; group B, no nematode could be detected.

*Median specific IgE (against *Anisakis simplex*) and total IgE levels with interquartile ranges (in kilounits per liter).

[†]Mean white cell and eosinophil count with SDs (in cells $\times 10^9/L$).

sitism but also indicates the responsible pathogenic mechanism of the hypersensitivity reaction.^{21,31} In group B we failed to detect either specific IgE against *A simplex* or a positive SPT response in only one patient. It seems that patients of group B could be given the same diagnosis, even if no nematode could be detected. Many reasons support this. First, the inclusion criteria selected patients with a similar history (ie, presence of abdominal together with hypersensitivity symptoms and a history of ingestion of raw or undercooked fish). No significant differences with respect to clinical and laboratory data could be found in either group, and gastroscopic findings in group B were similar to those seen in group A, with the only exception that the worm could not be detected, although some of the gastroscopic findings could have been testimony of the action of the nematode *A simplex*. SPT responses and the presence of specific IgE to *A simplex* are reported to be positive to a varying degree.^{6,7,18,23,24,32} In our control group 19% of subjects were sensitized to *A simplex*, even without a history of hypersensitivity reaction. This result is supported by a study of sera from adult blood donors in our region in whom specific IgE to *A simplex* was found in 16%.²³ It is probable that this high rate of specific IgE and SPT responses is due to the high frequency of (raw or undercooked) fish consumption in our country, and it has already been shown that an acute parasitism by *A simplex* is followed by a specific IgE response to nematode antigens, which is a typical feature of helminth infestation.^{30,31,33}

In series of acute gastric anisakiasis diagnosed by gastroscopy, mucosal edema, erosions, and hemorrhage were common findings.^{3,5} In 178 patients Sugimachi et al³ found a normal mucosa in 15%. The mucosal reaction and the epigastric pain has been related to the penetration of the digestive wall by the worm and has already been postulated to be an allergic reaction.^{24,25} In our study mucosal edema was not a predominant feature, and the following explanation seems reasonable. In gastric anisakiasis the predominant symptom is severe epigastric pain, which is probably caused by a severe mucosal reaction. On the other hand, the patients in our study complained above all of the hypersensitivity symptoms, and nearly all patients described abdominal symptoms only after a pointed inquiry. This can also explain our higher

percentage of near-normal gastroscopic findings. We cannot rule out that penetration of *A simplex* in patients of group B without gastroscopic lesions could have taken place in a lower portion of the gastrointestinal tract. In this respect it is also possible that patients with acute parasitism may present only with allergic symptoms.³⁴

We postulate that patients in group B also had gastroallergic anisakiasis, with self-limiting parasitism caused by the nematode having been vomited or having passed to a lower portion of the gastrointestinal tract.

Only 26 of 40 patients needed drug therapy to manage the allergic reaction, indicating that the symptoms disappeared in many patients before or on arriving at the emergency department. If we consider that only 3 patients needed treatment of more than 1 day's duration, it seems that we are dealing with a mostly acute and self-limited disease. On the other hand, the acute allergic reactions can be life-threatening, with a high percentage of anaphylaxis. Abdominal symptoms disappeared in a few hours after gastroscopic extraction of the nematode. This has already been documented in gastric anisakiasis, in which severe epigastric pain ceases after removal of the worm.³ This therapeutic approach is not only diagnostic and therapeutic but also prevents chronic anisakiasis, which is rare but can be complicated with granuloma formation, penetration, or perforation.^{35,36}

One of the most interesting aspects of this study is the documentation of the time interval between fish ingestion and onset of symptoms. In gastric anisakiasis onset of symptoms has been reported mainly within 12 hours, which is consistent with our results. As a whole, hypersensitivity symptoms appeared with a longer mean latency of 5.3 hours, but patients experienced the onset of allergic symptoms as late as 26 hours after fish intake. This is important to consider because the diagnosis is difficult to suspect the longer the time interval. With long time intervals, it is possible that patients do not relate allergic symptoms to previous intake of fish. Gastric anisakiasis is a well-known differential diagnosis of severe epigastric pain, but as has already been said, our patients displayed only mild abdominal complaints, which were often not spontaneously related by the patient. Because patients may not remember eating fish when they see the specialist, it is important to record this aspect of the patient's history in the emergency department and to ask the patient about abdominal symptoms. Food allergy is one possible cause of acute allergic reactions, and it is normally sufficient to ask about previous episodes and to consider the food eaten in the last 2 hours before the onset of symptoms when an IgE-mediated hypersensitivity reaction is suspected.³⁷ However, in gastroallergic anisakiasis we should be aware that we are dealing with an IgE-mediated hypersensitivity reaction, which is often not immediate, and this fact makes the diagnosis difficult. Although the frequency of parasitism of fish by *A simplex* can vary over time, it is plausible to attribute the high number of diagnoses to the protocol looking for this entity.^{8,38} Here we can underline the importance of the knowledge of this entity not only by

the specialists but also by all physicians in primary care and in the emergency department.

We show that a detailed history is a reliable tool for the diagnosis of gastroallergic anisakiasis, which is supported by a high rate of gastroscopic confirmation and a near-total confirmation by a further allergologic evaluation. We could not identify the white cell or eosinophil counts in the emergency department as a marker of an acute infestation or a predictor of a positive gastroscopic finding. Leukocytosis has been associated with acute gastric anisakiasis, but only 38% of patients in our study had elevated values. Eosinophilia is a typical feature of helminth infestation. Only 4 patients showed elevated values. It is probable that the time interval is too short to detect changes in eosinophil number in most patients because eosinophilia is supposed to peak after 7 to 10 days,^{39,40} and thus in acute gastroallergic anisakiasis, it is not a useful laboratory parameter in the emergency department.

The best treatment for anisakiasis is prophylaxis. Because larvae cannot survive at a temperature higher than 60°C for 10 minutes or lower than -20°C for 24 hours, patients should be told to eat only well-cooked or deep-frozen fish.^{21,41} Nearly all marine fish can be parasitized by *A simplex*, and different countries have their own raw fish specialties, such as sushi or sashimi (mainly in Japan but also in Japanese restaurants all over the world), anchovies in vinegar sauce (Spain), matjess-herring (Netherlands), rollmops (Germany), and other smoked fish specialties. The most frequently implicated fish was anchovies in vinegar sauce, but other raw or undercooked fish preparations were also implicated. Thus it is possible to acquire a live larva of *A simplex*, even in regions or countries where raw fish is not eaten.

We suggest that gastroallergic anisakiasis be considered a distinct clinical entity in which the predominant symptoms are hypersensitivity symptoms and in which the correct diagnosis is not only important in the management of the acute reaction but also in the prevention of further allergic episodes.

In conclusion, gastroallergic anisakiasis is easily diagnosed once you know the peculiar history and clinical features discussed in this study. We encourage allergists in other countries to search for this entity.

REFERENCES

1. Cheng TC. Nematodos secernenta. In: Cheng TC, editor. Parasitología general. Superfamilia heterocheloidea. Madrid: Editorial AC; 1978. p. 649-51.
2. Van Thiel PH. Anisakiasis [abstract]. Parasitology 1962;52:16-7.
3. Sugimachi K, Inokuchi K, Ooiwa T, Fujino T, Ishii Y. Acute gastric anisakiasis. Analysis of 178 cases. JAMA 1985;253:1012-3.
4. Van Thiel PH, Kuipers FC, Rosman RT. A nematode parasitic to herring causing acute abdominal syndromes in man. Trop Geogr Med 1962;2:97-113.
5. Muraoka A, Suehiro I, Fujii M, Nagata K, Kusunoki H, Kumon Y, et al. Acute gastric anisakiasis. 28 cases during the last 10 years. Dig Dis Sci 1996;41:2362-5.
6. Kasuya S, Hamano H, Izumi S. Mackerel-induced urticaria and *Anisakis*. Lancet 1990;335:665.
7. Kasuya S, Koga K. Significance of detection of specific IgE in *Anisakis*-related diseases. Arerugi 1992;41:106-10.
8. Mira Gutierrez J, García Martos P, Hilario Madrid LM, Rodríguez Igle-

- sias MA. Anisakiasis, una parasitosis emergente en nuestro medio. Rev Clin Esp 1995;195:51-4.
9. Lucas SB, Cruse JB, Lewis AAM. Anisakiasis in the United Kingdom. Lancet 1985;1:843-4.
10. Mudry J, Lefevre P, Dei-Cas E, Vernes A, Poirriez J, Débat M, et al. Anisakiase humaine: 5 cas dans le nord de la France. Gastroenterol Clin Biol 1986;10:83-7.
11. Kliks MM. Anisakiasis in the western United States: four new cases reports from California. Am J Trop Med Hyg 1983;32:526-32.
12. Bourrée P, Paugam A, Petithory JC. Anisakidosis: report of 25 cases and review of the literature. Comp Immunol Microbiol Infect Dis 1995;18:75-84.
13. Ikeda K, Kumashiro R, Kifune T. Nine cases of acute gastric anisakiasis. Gastrointest Endosc 1989;35:304-8.
14. Deardorff TL, Kayes SG, Fukumara T. Human anisakiasis transmitted by marine food products. Hawaii Med J 1991;50:9-16.
15. Moreno-Ancillo A, Caballero M, Cabañas R, Contreras J, Martín-Barroso JA, Barranco P, et al. Allergic reactions to *Anisakis simplex* parasitizing seafood. Ann Allergy Asthma Immunol 1997;79:246-50.
16. Del Pozo MD, Moneo I, Fernández de Corres L, Audicana MT, Muñoz D, Fernández E, et al. Laboratory determinations in *Anisakis simplex* allergy. J Allergy Clin Immunol 1996;97:977-84.
17. Audicana MT, Fernández de Corres L, Muñoz D, Fernández E, Navarro JA, del Pozo MD. Recurrent anaphylaxis caused by *Anisakis simplex* parasitizing fish. J Allergy Clin Immunol 1995;96:558-60.
18. Fernández de Corres L, Audicana M, del Pozo MD, Muñoz D, Fernández E, Navarro JA, et al. *Anisakis simplex* induces not only anisakiasis: report on 28 cases of allergy caused by this nematode. J Invest Allergol Clin Immunol 1996;6:315-9.
19. Kasuya S, Hamano H, Izumi S. Gastric anisakiasis with anaphylactoid reaction. ACI News 1989;1:140-1.
20. Daschner A, Alonso A, Vicente J, Suárez de Parga JM, López-Serrano MC. Anisakiasis Gástrica. ¿Son siempre inocuos los boquerones en vinagre? Emergencias 1997;9:173-5.
21. Alonso A, Daschner A, Moreno-Ancillo A. Anaphylaxis with *Anisakis simplex* in the gastric mucosa. N Engl J Med 1997;337:351-2.
22. Daschner A, Alonso-Gómez A, Mora C, Moreno-Ancillo A, Villanueva R, López-Serrano MC. Gastro-allergic anisakiasis with massive parasitism. Rev Esp Alergol Immunol Clín 1997;12:370-2.
23. Muñoz Pereira M, San Martín M, Orma N, Ortega N, Pascual C, Martín Esteban M. Incidencia de IgE específica frente a *Anisakis simplex* y *Ascaris lumbricoides* en población normal y atópica [Abstract]. Rev Esp Alergol Immunol Clín 1996;11:197-8.
24. Asaishi K, Nishino C, Totsuka M, Hayasaka H, Suzuki T. Studies on the etiological mechanism of anisakiasis. 2. Epidemiologic study of inhabitants and questionnaire survey in Japan. Gastroenterol Jpn 1980;15:128-34.
25. Akao N, Ohyama T, Kondo K. Immunoblot analysis of serum IgG, IgA and IgE responses against larval excretory-secretory antigens of *Anisakis simplex* in patients with gastric anisakiasis. J Helminthol 1990;64:310-8.
26. Urban JF, Madden KB, Svetic A, Cheever A, Trotta PP, Gause WC, et al. The importance of Th2 cytokines in protective immunity to nematodes. Immunol Rev 1992;127:205-20.
27. Jarrett E, Mackenzie S. Parasite-induced 'nonspecific' IgE does not protect against allergic reactions. Nature 1980;283:302-4.
28. Allen JE, Maizels RM. Immunology of human helminth infection. Int Arch Allergy Immunol 1996;109:3-10.
29. Warin RP, Champion RH. Urticaria. London: W. B. Saunders; 1974.
30. Ishizaka T, Urban J, Takatsu K, Ishizaga K. Immunoglobulin E synthesis in parasite infection. J Allergy Clin Immunol 1976;58:523-38.
31. Daschner A, Alonso-Gómez A, Caballero MT, Suarez-de-Parga JM, López-Serrano MC. Usefulness of early serial measurement of specific and total IgE in the diagnosis of gastro-allergic anisakiasis. Clin Exp Allergy 1999;29:1260-4.
32. Del Pozo MD, Díez JM, Fernández E, Audicana M, Muñoz D, Fernández de Corres L. Prevalence of sensitization to *Anisakis simplex* (a parasitizing fish nematode) [Abstract]. Allergy 1996;51(Suppl 31):53.
33. Lee TDG, Xie CY. IgE regulation by nematodes: the body fluid of *Ascaris* contains a B-cell mitogen. J Allergy Clin Immunol 1995;95:1246-54.
34. Daschner A, Alonso-Gómez A, Caballero MT, Barranco P, Suarez-de-Parga JM, López-Serrano MC. Gastric anisakiasis: an underestimated cause of acute urticaria and angioedema? Br J Dermatol 1998;139:822-8.
35. Bier JW, Deardorff TL, Jackson GJ, Raybourne RB. Human anisakiasis. Baillieres Clin Trop Med Commun Dis 1987;2:723-33.
36. Matsuoka H, Nakama T, Kisanuki H, Uno H, Tachibana N, Tsubouchi H, et al. A case report of serologically diagnosed pulmonary anisakiasis with pleural effusion and multiple lesions. Am J Trop Med Hyg 1994;51:819-22.
37. Sampson HA. IgE mediated food intolerance. J Allergy Clin Immunol 1988;81:495-504.
38. Orecchia P, Paggi L, Mattiucci S, Di Cave D, Catalani N. Infestation by larvae of *Anisakis simplex* and *Anisakis physeteris* in fish species of the Italian seas. Parassitologia 1989;31:37-43.
39. Petithory JC, Verrier F, Guyet-Rosset P. Etude biologique d'un cas d'anisakiase colique. Revue de la littérature. Path Biol 1992;40:47-51.
40. Podolska M, Tokarski S, Rokicki J. Leukocyte parameters in the course of pig infection with III. larval stage of *Anisakis simplex* [abstract]. Wiad Parazytol 1996;42:197-204.
41. Deardorff TL, Throm R. Commercial blast-freezing kills third-stage *Anisakis simplex* larvae encapsulated in salmon and rockfish. J Parasitol 1988;74:600-3.