Case Report

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Anaphylaxis due to Hypersensitivity to *Anisakis simplex*

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Anisakis simplex · Anaphylaxis · Hypersensitivity

Abstract
Anaphylactic reactions are among the most frequent causes for requests for emergency medical care. It is possible that no clear precipitating factor can be found delaying the onset of adequate treatment and increasing the risk of new episodes of anaphylaxis in the future. Hypersensitivity to *Anisakis simplex*, an intestinal parasite found in fish, is an unusual cause of anaphylaxis but it should always be borne in mind in countries where a great deal of fish is consumed, especially if it is eaten raw or undercooked. 3 cases of anaphylaxis due to hypersensitivity to *A. simplex* are described.

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Anaphylactic reactions represent one of the most frequent causes for requests for emergency medical care. In the first examination of the patient, it is possible that no clear precipitating factor of the reaction can be found, increasing the difficulty of a specific diagnosis. In addition, if such an acute condition exists, it can even increase the life-threatening situation if the beginning of adequate treatment is delayed.

Hypersensitivity to *Anisakis simplex*, an intestinal parasite found in fish, is an unusual cause of this reaction that should always be borne in mind in Spain. This country has one of the highest consumptions of fish worldwide and, in addition, the fish is frequently eaten raw or undercooked. It is precisely under these circumstances when the *Anisakis* larva, which is still alive, is capable of secreting its excretory-secretory antigen which can probably provoke the anaphylactic reaction [1, 2].

We present 3 cases of anaphylaxis due to hypersensitivity to *A. simplex* after the intake of undercooked anchovies. These 3 subjects had previously eaten anchovies without any problems.

Case 1: A 56-year-old woman with no significant medical background presented with malaise, diffuse and itchy cutaneous erythema, dysphagia, dyspnea and thoracic constriction with a subsequent loss of consciousness, 30 min after having eaten *exclusively* anchovies in oil and salt. She was seen at the Emergency and Rescue Municipal Care Service (SAMUR) unit of Madrid which includes a physician, a nurse and paramedic staff. Low blood pressure (70/30 mm Hg) and a lack of verbal response (Glasgow Coma Scale 8) were observed and parenteral adrenaline (0.5 ml), 6-methylprednisolone (80 mg) and dexchlorpheniramine (5 mg) were administered, after which the clinical picture abated and the patient was kept at the hospital centre for observation.

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Case 2: The second case is that of a 48-year-old male Caucasian diagnosed as having hepatic hydatidosis in 1989 who underwent a partial hepatectomy and who had been asymptomatic since then. Coinciding with the intake of beer and anchovies in vinegar sauce, the patient developed diffuse and intense itching, dyspnea at rest, sensation of nausea, abdominal pain and loss of consciousness. The patient was seen 6 min after the onset by the SAMUR medical staff, and the following was observed: coma condition equal to 3 on the Glasgow Coma Scale, mucocutaneous paleness, blood pressure 90/60 mm Hg decreasing to 60/25 mm Hg some minutes later, spontaneous breathing with a breathing rate of 15, heart rate of 120 beats/min, glycaemia of 103 mg/dl, reactive miotic pupils and no signs of apparent neurological focality. No signs of tonicoclonic convulsions were seen. The patient was endotracheally intubated and volume expanders were supplied parenterally, at which time maculopapular erythema appeared on the trunk. The patient was then administered adrenaline (0.5 ml s.c.) and admitted to the intensive care unit of the reference hospital. The electrocardiogram showed normal PR, QRS and QT intervals, a normal sinus rhythm, and there were no T wave abnormalities. An intravenous infusion of epinephrine was initiated (2.5 ml of epinephrine, diluted 1:10,000 at 10-min intervals) and intravenous 6-methylprednisolone and dexchlorpheniramine were also administered. A cranial CT scan was performed and no pathology was observed. He later drank beer without any problems.

Case 3: The third case is a 52-year-old Caucasian woman with no significant medical background who presented on two occasions with reactions after the intake of anchovies in vinegar sauce. On the first occasion, she presented with itchy papulae and maculae. On the second one, she presented with facial angio-oedema, dysphonia and dyspnoea at rest in addition to the same skin lesions. Both reactions required emergency treatment with parenteral adrenaline, 6-methylprednisolone and antihistamines. No problems with anchovies and fish between these two episodes were described.

In the Allergy Service at our hospital, skin prick tests were performed with *Anisakis* extract (1 mg/ml), a battery of fish extracts (hake, salmon, sole, tuna fish and anchovy), common inhalants (grass, *Olea europea* and *Cynodon* pollens; house dust mites *Dermatophagoides pteronyssinus* and *Dermatophagoides farinae*; cat and dog dander) and latex extract. Skin prick tests were performed on the volar side of the forearm with prick lancets (Bayer, Madrid, Spain) with commercial extracts (ALK-Abelló and IPI Lab., Madrid, Spain) and the response was assessed at 15 min and 24 h. A wheal diameter of at least 3 mm, according to the European Academy of Allergy and Clinical Immunology criteria (EAACI), was considered to be positive. In all the cases an exclusively positive prick test for *A. simplex* was observed. In the second case, one positivity was also verified at 24 h.

Table 1. Values of patients 1–3

	Patient 1	Patient 2	Patient 3
Total IgE, kU/l	579	1,467	16,540
Anisakis IgE, kU/l	130	15.7 (CAP 3)	4,670
Anisakis IgE (3 months later), kU/l	27.8	4.2	233
Parasite-specific IgE	negative	*Echinococcus* (21 kU/l; CAP 4)	negative
Fish-specific IgE	negative	negative	negative

Total IgE in serum and specific IgE against *A. simplex*, *Ascaris lumbricoides, Echinococcus* and some fish (hake, salmon, tuna and anchovy) were measured with the CAP technique (scale of 0–6), following the manufacturer's instructions (Pharmacia-Upjohn, Uppsala, Sweden). Total IgE and specific IgE against *A. simplex* were measured 3 months after the related episodes following the same instructions by the same laboratory. The values obtained are shown in table 1.

IgG was determined for *Echinococcus* with the same UNI-CAP system in the second patient, and values over 200 mg/l were obtained. Based on these analytic results, it was decided to perform a complete study in order to rule out an active echinococcosis. The results of the plain thoracic-abdominal x-ray, the protein analysis, and complete analyses including hepatic function were totally normal. The abdominal ultrasonography, although with interposition of air, visualized a normal liver, kidneys, spleen and pancreas head. An abdominal CT scan showed posthepatectomy changes and calcified hydatic cyst in the right hepatic lobe. The determination of parasites in the stool of the 3 patients was negative.

Fish and cephalopod intake was withdrawn from the diet, and the patients have remained asymptomatic since then. In the successive examinations, a decrease in the total IgE and specific IgE against *A. simplex* has been verified.

When there is an anaphylactic reaction, the main aim of the physician is to administer treatment quickly, since such a reaction presents a life-threatening situation that requires rapid and precise action. The mean action time

of the SAMUR in a city such as Madrid, with a very complicated system of traffic, is 8 min, which guarantees this performance.

Anaphylaxis is an allergic reaction in which there is a frequent relationship between food and drug intake, poisoning such as in the case of the hymenopteras, or exercise (anaphylaxis due to exercise) which is frequently, although not always, associated with the previous intake of food [3]. In the first 2 cases, the existence of witnesses and the verification of signs suggesting an erythema-mediated IgE reaction facilitated the onset of adequate treatment with adrenaline, fluid therapy, corticosteroids and antihistamines. But this is not always the case. In this sense, the posterior allergy study is essential to avoid new episodes of anaphylaxis [4].

In these 3 patients, the intake of raw or undercooked fish was the most significant factor directing the study. *A. simplex* is a nematode parasite of sea mammals, which uses fish as intermediary hosts in its larval development. Man suffers from parasitation through the intake of this fish, this condition being manifested either as gastrointestinal disorders, which are known as anisakidosis, or as an IgE-mediated allergic reaction [5]. Although different cases with cutaneous involvement, either urticaria or angio-oedema, have been reported, the anaphylaxis cases are less frequent. In our patients, we reached the diagnosis on the basis of the positivity of the skin tests and the abnormally increased IgE and *Anisakis*-specific IgE values [6, 7], since we did not consider it to be ethically correct to perform a provocation test with parasitized fish and with *Anisakis* when reactions such as those presented by our patients were present.

Finally, the possibility of a cross-reaction between *Echinococcus* (a parasitation which is rare but still present in Spanish rural areas) and *A. simplex* had to be abandoned in the case of patient 2, as has previously been suggested [8], although these cross-reactions are more frequent against Ascaris [9, 10]. Contact with the *Anisakis* larvae in the patient with a history of previous hydatidosis could have induced a reaction similar to that produced by the rupture of a hydatic cyst. In summary, the possibility of hypersensitivity to antigens of the *A. simplex* larvae could be considered as a possible cause of an anaphylactic reaction, especially in places such as Spain where fish is frequently eaten.

References

1 Alonso A, Daschner A, Moreno-Ancillo A: Anaphylaxis with *Anisakis simplex* in the gastric mucosa. N Engl J Med 1997;337:350–351.
2 Moreno-Ancillo A, Caballero MT, Cabañas R, Contreras J, Martín Barroso JA, Barranco P, López-Serrano MC: Allergic reactions to *Anisakis simplex* parasiting seafood. Ann Allergy Asthma Immunol 1997;79:246–250.
3 Patterson R, Hogan MB, Yarnold PR, Harris KE: Idiopathic anaphylaxis. Arch Intern Med 1995;155:869–871.
4 Daschner A, Alonso-Gómez A, Caballero T, Barranco P, Suárez de Parga JM, López-Serrano MC: Gastric anisakiasis: An underestimated cause of acute urticaria and angioedema. Br J Dermatol 1998;139:822–828.
5 Buendia E: *Anisakis*, anisakidosis and allergy to *Anisakis*. Allergy 1997;52:481–482.
6 Kasuya S, Koga K: Significance of detection of specific IgE in *Anisakis* related diseases. Arerugi 1992;41:106–110.
7 Daschner A, Alonso Gómez A, Caballero T, Suárez de Parga JM, López-Serrano MC: Usefulness of early serial measurement of specific and total immunoglobin E in the diagnosis of gastroallergic anisakiasis. Clin Exp Allergy 1999;29:1260–1264.
8 Martín-Barroso JA, Barranco P, Muñoz-Pereira A, Moreno-Ancillo A, Cabañas R, Vicente J, López-Serrano MC: Anaphylaxis to *Echinococcus* versus *Anisakis* sensitization (abstract). Allergy 1997;52(suppl 37):215.
9 Kennedy MW, Tierney JY, McMonagle FA, McIntosh A, McLaughlin D, Smith JW: The secreted and somatic antigens of the third stage larva of *Anisakis simplex* and antigenic relationship with *Ascaris suun, Ascaris lumbricoides* and *Toxocara canis*. Mol Biochem Parasitol 1988;31:35–46.
10 Muñoz Pereira M, SanMartín M, Ornia N, Ortega N, Pascual C, Martín-Esteban M: Incidencia de IgE específica frente a *Anisakis simplex* y *Ascaris lumbricoides* en población normal. Rev Esp Alergol Inmunol Clin 1996;11:217–218.

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