Anaphylaxis due to Hypersensitivity to Anisakis simplex

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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.

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.
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 toxicolonic 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 sinu 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 dexamethasone 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. 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 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 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.

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

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<th>Table 1. Values of patients 1–3</th>
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<td>Total IgE, kU/l</td>
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<td>Anisakis IgE, kU/l (3 months later)</td>
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<td>Anisakis IgE</td>
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<td>Parasite-specific IgE</td>
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<td>Echinococcus (21 kU/l; CAP 4)</td>
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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 parasitization 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 hydatid 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**
