

Isolated Contact Urticaria Caused by Immunoglobulin E-Mediated Fish Allergy

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ABSTRACT: Fish is a common cause of food allergy. The reactions usually occur after its ingestion. In most immunoglobulin E-mediated reactions, the allergens are gastroresistant and heat-stable proteins of low molecular weight (parvalbumin). On the other hand, isolated contact urticaria following the handling of raw fish but without symptoms after its ingestion was found among cooks and professional fish handlers. In these cases, the fish allergens are gastrosensitive and thermolabile, as demonstrated by the decrease in the diameter of the wheal in the skin-prick test using cooked fish. To the best of our knowledge isolated fish contact urticaria in children has not been previously reported. We analyze the features of three pediatric cases of contact urticaria from cod (one of them was sensitized to parvalbumin), with tolerance after ingestion of this fish on oral food challenge.

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Fish allergy is common in Europe [1]. Allergists often prescribe a diet devoid of all fish to children with a clinical history suggestive of adverse reaction and sensitization, without performing the oral food challenge – the gold standard in the diagnosis of food allergy. This clinical practice is performed because of frequent generalized reactions following its ingestion or, more rarely, its inhalation.

Fish allergy may also emerge in a clinically less dangerous form, namely, urticaria or isolated contact dermatitis, more frequently described in individuals having prolonged and repeated skin contact with raw fish, for example, cooks and fishmongers. In these cases fish allergy is the result of hypersensitivity to a thermolabile and gastrosensitive allergen and is limited to the contact site [2-4].

We report here for the first time, to the best of our knowledge, three pediatric cases of isolated contact urticaria caused by immunoglobulin E-mediated cod allergy. These cases present significant differences from adult cases.

PATIENT DESCRIPTIONS

PATIENT 1

N.A., a 5 year old boy, was admitted to our pediatric clinic with a history of allergic rhinitis, atopic dermatitis and fish allergy. At age 2 years he ate grouper and 30 minutes later presented with urticaria localized on the skin affected by atopic dermatitis. Skin-prick tests were positive for cooked grouper (4.5 mm) but negative (2 mm) for cod extract. When he was 5 years old, he presented with urticaria after his elbow came into contact with grouper.

SPTs for raw and cooked mussels, raw shrimp and cod extract (Lofarma[®], Milan, Italy) were negative. SPTs for raw and cooked grouper, raw and cooked sea bream, raw and cooked cod, cooked shrimp, raw and cooked tuna, and raw and cooked cuttlefish were positive (9, 6, 6, 4, 5, 4, 5, 3, 3, 5, 4 mm, respectively). The investigation of serum-specific IgE for fish was performed with ImmunoCAP assay (Phadia, Sweden) and the results were as follows: cod 1.63 kUA/L, sole 1.07 kUA/L, anisakis 0 kUA/L, hake 1.12 kUA/L, swordfish 0.07 kUA/L, plaice 1.20 kUA/L, yellow diamond 0.93 kUA/L, salmon 1.26 kUA/L, European sardine 1.03 kUA/L, mackerel 0.8 kUA/L, tuna 0.44 kUA/L, trout 1.72 kUA/L, shrimp 0.04 kUA/L, sepia 0 kUA/L, c rGad 1 parvalbumin 0.97 kUA/L.

The open OFC with cooked grouper was positive (generalized urticaria and itching of the lips and pharynx). We reached the diagnosis of IgE-mediated allergy to grouper and recommended that he not be fed this fish. The open OFC and the Rub tests with cooked tuna were negative. The family was advised to introduce tuna into the diet.

The open OFC with cooked cod was negative and the Rub test was positive. We reached the diagnosis of IgE-mediated allergy to cod, with contact urticaria as the only manifestation. The child was permitted to eat cod. His parents declined to test his tolerance to other fish. At home he ate cod only twice and canned tuna many times with no adverse reaction. His parents did not feed him any other type of fish for fear of an allergic reaction.

SPT= skin-prick test
IgE = immunoglobulin E
kUA/L = kilounits of antibody per liter
OFC = oral food challenge

PATIENT 2

When we knew A.C. he was 7 years old and did not eat fish, crustaceans or mollusks. In his first 2 years of life he presented atopic dermatitis and when he was 2.5 years old he touched cooked cod with his hands and then touched his face; within a few minutes he developed urticaria and angioedema of the face and lips. The test for serum specific IgE for cod was positive (9.45 kIU/L), as were SPTs for bluefish and white fish. The child had never eaten fish before and did not eat it again. During the next 4 years, every time he touched fish he developed contact urticaria; i.e., his mother said that hives appeared on his cheek where he had been kissed by his brother who had just eaten fish. For this reason he avoided the ingestion of fish until he was 7 years old.

We performed SPTs with natural foods and they were positive for canned (4 mm), raw (5 mm) and cooked tuna (5 mm), raw (10 mm) and cooked cod (6 mm), raw squid (4 mm), and negative for raw and cooked clam, cooked squid, raw and cooked mussel, and raw and cooked shrimp. The open OFC with cooked cod was negative, while the Rub test on his cheeks with this food was positive (contact urticaria and hives appeared not only where the Rub test was performed but also on distal sites, for example the trunk and limbs). IgE-mediated allergy to fish was diagnosed, with contact urticaria as the only clinical manifestation, and he was therefore allowed to eat cod. The ingestion at home of clam, mussel, squid and shrimp has been allowed without performing OFC.

The boy did not particularly like eating fish but he did eat it occasionally in the subsequent 7 years (i.e., until his last telephonic follow-up) without any sign of adverse reaction.

PATIENT 3

N.C., a 2 year old child who suffered from atopic dermatitis, came to our clinic because of perioral urticaria supposedly due to the ingestion of cooked cod. The specific serum IgE for cod (ImmunoCAP, Phadia, Sweden) was slightly positive (0.75 kU/L). The child had a history of other food allergies (eggs and nuts). The SPT with cooked cod was positive (mean diameter of wheals 7 mm); the open OFC resulted in only a small urticaria wheal on his left cheek and a light circumoral erythema, where fish had accidentally touched his skin.

We presumed that the modest clinical reaction was due to skin contact and not food ingestion. Therefore, based on the skin-prick test and oral food challenge results, the child was allowed to ingest cooked cod. To further confirm our hypothesis, the successive ingestions of cod at home have not been associated with adverse events.

DISCUSSION

Fish is the third most frequent food allergen after cow's milk and egg in Europe [1]. Contact urticaria constitutes a common

reaction in patients with systemic fish allergy, even in the pediatric age [4]. Contact urticaria from IgE-mediated fish allergy may also occur in isolated form, despite oral tolerance to fish ingestion; it has been described in food handlers and chefs [2] but was not previously described in the pediatric population. The three cases presented here demonstrate that IgE-mediated fish allergy contact urticaria can occur even in children.

There are other points of interest: namely, all children had atopic dermatitis and this could have caused a first "unusual" contact with the allergen. We say "unusual" because it has been theorized that food allergens that enter the body through the airways and skin (and not through the gastrointestinal route) could result in sensitization [5,6]. Skin injuries from atopic dermatitis could be compared to the macerated skin of the hands of professional fish handlers. However, these are the only similarities between our cases and occupational contact urticaria:

- the three children were not exposed to continuous contact with the allergen
- urticaria spread to sites usually not affected by contact (i.e., the hands), and in at least one case (A.C.) it went beyond the contact site
- the food caused contact urticaria also when cooked; therefore, the offending allergen is heat-resistant, even if gastrosensitive.

Unfortunately, the patients A.C and N.C were observed several years ago and at that time we could not measure the specific IgE for parvalbumin or perform molecular analysis. Gad c 1 was positive in case 1, where the SPTs with commercial extracts of cod and OFC were negative, but the Rub test and SPTs with natural food (cod) were positive. The prick-by-prick test with natural food showed a greater sensitivity than the commercial extract, as already documented with vegetables and milk [7,8]. Nonetheless, it was surprising that the positivity of Gad c 1 and the negativity of SPT with cod extracts occurred concomitantly. The company producing the cod extract used in this study assured us of the presence of parvalbumin. Previous studies [9,10] showed that parents did not introduce the food into the diet of their children even after a negative OFC. This is confirmed by our experience.

CONCLUSIONS

According to our experience, isolated contact urticaria caused by IgE-mediated fish allergy exists even in the pediatric age with characteristics different from those seen in adults. It is a rare manifestation: during a period of 10 years we observed only three cases, and an informal survey with the Italian Association of Pediatric Allergists (APAL, www.apalweb.it) did not reveal other such cases up to April 2011.

In the three cases described we reached the diagnosis of IgE-mediated allergy to cod but dietary restriction was not pre-

scribed to the patients because the contact urticaria was the only clinical sign at OFC. However, it is our opinion that pediatric cases of suspected IgE-mediated allergy to fish with a history of contact urticaria should undergo the OFC in order to verify the presence or absence of symptoms after ingestion of the trigger food and that excessive dietary restrictions should be avoided.

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