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POINT OF VIEW

Loss of tolerance for fishes previously tolerated in children with fish food protein induced enterocolitis syndrome

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Abstract We describe two case reports presenting some novel information on fish FPIES. Fish FPIES to one fish does not always start at the same time to other fish. Additionally, development of tolerance to the index fish do not necessarily imply tolerance to other reactive fish. This reflects on the best management of children with FPIES fish.

Food-protein induced enterocolitis syndrome (FPIES) is probably a non IgE-mediated food allergy characterized by repeated and projectile vomiting, pallor and lethargy, sometimes followed by diarrhea; the symptoms appear within 4–6 h after the ingestion of the offending food and are resolved within a few hours.[1] The prevalence of FPIES caused by fish is variable.[2] In Italy, it is second in order of frequency after cow's milk FPIES and responsible for 12% of cases.[3] It has been reported that children with IgE-mediated fish allergy can tolerate other fishes different from the culprit.[4] In 2015, Miceli Sopo et al.[5] showed that even patients with fish FPIES can tolerate fishes other than the offending one. We take the cue from two children with fish FPIES who lost tolerance to other fishes previously tolerated to discuss the diet management of children with fish FPIES.

Case 1. A three-year-old girl was brought to our clinic because of multiple vomiting episodes after fish ingestion. At the age of seven months, the baby ate cod and hake four times each without adverse reactions. At the age of eight months, she had repeated and projectile vomiting 1–2 h after eating hake at two different times. Then, hake was eliminated from the diet. The girl did not eat more fish until the age of 10 months, when she ate cod and had the same adverse reaction. Cod was eliminated from the diet. Then, she ate sole about 4–5 times without any problems. At the age of 16 months, she had repetitive vomiting 2 h after ingestion of sole. So all fishes were excluded from the diet, except for canned tuna, which she has always tolerated.

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We performed prick-to-prick (PtP) test with raw cod, hake, sole and tuna and skin prick test with commercial extract of cod, the results were negative. We did not measure the serum level of specific IgEs. After we performed an open food challenge (OFC) with cod and no adverse reactions were observed, we assumed that the girl was healed from fish FPIES and allowed any fish reintroduction at home. Four days after, she ate hake and had repetitive vomiting after 2 h. Therefore, she continued a fish free diet, except for canned tuna that the girl continued to tolerate. At the age of five years, she tasted a ''latterino'' (a small lake fish) and had vomiting after 3 h. The girl had not FPIES to other foods and tolerated shellfish.

Case 2. A 30-month-old boy was brought to our clinic because of repetitive vomiting, pallor and lethargy 2 h after eating sole and cod, two times each. These were the only introductions of fishes in the diet of the child at the age of 8–9 months, after this age fishes were excluded from the diet. We diagnosed FPIES caused by cod and sole, and performed PtP tests with raw and cooked cod, sole, salmon, swordfish, anchovies, snapper, and canned tuna: they all resulted negative. We did not measure the serum level of specific IgEs. So therefore we performed OFC with canned tuna and cooked salmon, which were tolerated, and we allowed their consumption. After two months and 3–4 ingestion at home of canned tuna without any problems, the child had repeated vomiting after 2 h after a new ingestion of canned tuna. We performed a new OFC with canned tuna and it failed, tuna was eliminated from the diet. Then, OFC with anchovy (passed), swordfish (passed) and snapper (failed) were performed. After these OFC, the child began to eat cooked salmon and, very rarely, swordfish, at home in small amounts (20–30 g at a time). About nine months from the passed OFC with cooked salmon and five safe ingestions at home, the child presented repeated vomiting after eating salmon and even this fish was eliminated from his diet. Later, the child continued to eat normal amounts (50–100 g) of swordfish and anchovies 1–2 times a week. When the child was four-years-old, an OFC with sole was performed and it failed. The child had not FPIES to other foods and tolerated shellfish.

Miceli Sopo et al.[5] reported that 21% of patients with fish FPIES tolerated fishes other than the offending one. These authors suggested that children with fish FPIES can try to introduce via OFC new types of fishes. However, the two patients described here continued to eat tolerated fishes, other than the offending one, and had later developed symptoms of FPIES also versus these other kinds of fishes. This happened with sole for case 1, and tuna and salmon for case 2. Moreover, case 1 passed an OFC with cod at the age of three years and after four days presented acute FPIES after eating hake. Thus, we cannot assume that the acquisition of tolerance versus an offending fish is a marker of tolerance versus another offending fish, even if the fishes are in the same order, as is for cod and hake (Gadiformes).

The reasons for this clinical evolution are difficult to explain, the pathogenetic mechanism underlying FPIES is not yet clear. It is presumed to be due to an inappropriate adaptive immune response to the protein component of foods, similar to IgE-mediated allergy. Although it is reasonable to assume that these adverse reactions are immune mediated, it has been difficult to identify a causative mechanism of FPIES that is consistent with the nature of the symptoms.[6] Particularly, it is not known which fish allergen is triggering the FPIES. It has usually been observed that the first manifestation of FPIES begins with the first or second introduction of the offending food.[7] In the cases we described, several safe ingestions of fish preceded the onset of symptoms in patients who already suffered from FPIES for another fish. We may suppose that the allergen of the new kind of fish is similar but not equal to that of the offending one; therefore, at first it seems to be tolerated, and after a while the immune system recognizes it as foreign, triggering the adverse reaction. A hypothetical factor could be the frequency of fish ingestion, our two patients have eaten the tolerated fishes a few times.

So, what should the allergist recommend to the child and his family? May he allow the consumption of tolerated fishes? It has always been known that a passed OFC could authorize a free food ingestion, but these cases demonstrated that it is not always true for children with fish FPIES. On the contrary, should the allergist ban the consumption of all fishes? Perhaps our report makes this latter option more likely. Of course, other studies will be needed before the best management of patients with fish FPIES is identified.

In conclusion, the novel information provided by these two case reports is that fish FPIES to one fish does not always start at the same time to other fish. These cases also show that developing acquisition of tolerance to the index fish does not necessarily imply acquisition of tolerance to other reactive fish.

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Authors' contributions

SMS and CF designed the study and wrote the manuscript. GB and AR contributed to data collection. SM performed the interpretation of the results. All authors read and approved the final manuscript. The authors declare that we have contributed significantly to the research and preparation, revision and final production of the manuscript and approve its submission to the Journal. The contents of the manuscript have not been previously published and are not currently submitted elsewhere.

Conflict of interest

None.

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