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Fish allergy: in Cyp c1 we trust

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IgE-mediated fish allergy in patients presenting a suggestive clinical history is usually confirmed by skin prick testing (SPT) and/or *in vitro* fish-specific IgE testing. Basophil activation test (BAT) and fish oral challenge are required at times (1–3). We report herein the case of a girl, clinically diagnosed with fish allergy and whose only positive IgE-binding test was sensitization to rCyp c1.

First-line Cyp c1 IgE testing may improve fish allergy diagnosis.

At the age of 3 months, a meal containing codfish resulted in vomiting a few minutes later. Symptoms recurred when the girl's parents attempted to feed her codfish again at the ages of 9 and 19 months. Three attempts to feed her chicken resulted in similar symptoms. All other foods were tolerated. At the age of 3, codfish SPT (Stallergènes, Antony, France) tested negative; no detectable specific IgE were found for codfish, tuna, chicken, shrimp, egg, or peanut (Bayer Diagnostics; Siemens Medical Solutions Diagnostics, Munich, Germany), and total IgE level was normal. An open oral codfish challenge resulted in severe vomiting. Fish and chicken exclusion was applied thereafter. SPT with either Stallergènes extracts or fresh food and fish

and chicken-specific IgE testing (Phadia, Uppsala, Sweden) were repeated at the ages of 4, 6, 8, and 10. These tests were negative. Accidental consumption of chicken (ravioli, chicken nuggets) or fish (codfish, sole) and another oral codfish challenge resulted in vomiting and abdominal pain. At the age of 10, the child underwent codfish and chicken SPT (Stallergènes), codfish BAT (Bühlmann Laboratories, Schönenbuch, Switzerland), and specific IgE testing for codfish and for the recombinant rCyp c1 (Phadia). SPT and BAT were negative; no codfish-specific IgE was detected. Surprisingly, a small amount of rCyp c1 IgE was present: 0.31 kUA/l, with concentrations above 0.1 kUA/l considered positive.

Because low levels of food-specific IgE may be associated with severe clinical reactions, complementary testing of other fish species eaten in our region was performed. This concerned tuna, trout, sole, anchovy, hake, halibut, mackerel, swordfish, chub mackerel (Phadia). All tested negative. Thus, the clinical diagnosis of fish allergy received a late biologic confirmation when rCyp c1 sensitization was evidenced.

rCyp c1 is a recombinant carp beta-parvalbumin, the major fish allergen, extensively cross-reacting among most species (4). To the best of our knowledge, this is the first case of isolated rCyp c1 sensitization. Such a result may be surprising at first sight, yet it might become a common finding with component-resolved diagnosis development. Indeed, parvalbumin content in the fish ImmunoCAP is lower than in the rCyp c1 ImmunoCAP, yielding a higher sensitivity of the latter. Parvalbumin content and folding may be altered during the process of fish ImmunoCAP production. Finally, parvalbumin accessibility may

be hampered by other components in the fish ImmunoCAP.

This result is important because first step *in vitro* allergy testing does not usually include recombinant beta-parvalbumin (rCyp c1, rGad c1)-specific IgE. Rare cases of IgE-mediated fish allergy may thus lack confirmation. There may also be patients with monosensitivity to other fish parvalbumins. Thus, apart from rCyp c1, other recombinant parvalbumins could be useful in the diagnostic work-up of fish allergy diagnosis.

Parvalbumin sensitization may play a central role in the association chicken and fish allergy in this child. Indeed, alpha-parvalbumin has recently been identified as a chicken meat allergen, involved in allergic reactions which do not cross-react with egg or feathers (5). The protein identity of known carp beta-parvalbumin and chicken alpha-parvalbumin ranges between 50 and 60% (<http://www.expasy.ch>). This hypothesis is difficult to check in our patient, who lacks detectable serum-specific IgE to chicken. Nevertheless, parvalbumin homologs among different species may represent a missing biologic link in some fish and meat allergies (6).

In conclusion, we report here the case of a child presenting with persistent fish and chicken meat allergy whose only IgE-mediation proof was shown by serum rCyp c1 IgE testing. We therefore suggest that beta-parvalbumin-specific IgE should be tested not only when SPT and/or total fish extract IgE testing have already yielded positive results but also as a first-line *in vitro* test for fish-induced adverse reactions.

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