



Letter

Selective allergy to the salmonidae fish family: a selective parvalbumin epitope?

Parvalbumins are the major fish allergens and share sequence identities of 61% to 93%, which support cross-reactivity among fish species.¹⁻⁴ We report an unusual case of selective allergy to fish of the Salmonidae family in which salmon- and trout-specific parvalbumins seem to be the only allergens involved.

A 62-year-old, nonatopic woman presented to our clinic with oropharyngeal itching, angioedema, dysphagia, dysphonia, and generalized exanthema with palmar pruritus after having eaten half a trout (approximately 100 g). In the emergency department, the woman had an oxygen saturation of 91%, blood pressure of 70/40 mm Hg, dizziness, and emesis. She had previously tolerated all kinds of fish, but after the reaction she stopped eating fish.

The results of skin prick tests with extracts of tuna, sardine, whiff, hake, cod, sole, sea bream, and the fish parasite *Anisakis* (Leti Alergia, Barcelona, Spain) were negative. The results of prick to prick tests with boiled fish were positive for salmon (6 mm), trout (6 mm), and whiff (3.5 mm) and negative for tuna, cod, and gilthead. The total IgE level (ImmunoCAP; Phadia, Uppsala, Sweden) was 179 kU/L, and specific IgE tested positive for trout (1.44 kU/L), salmon (1.31 kU/L), hake (0.8 kU/L), and cod (0.45 kU/L) and negative (<0.35 kU/L) for *Anisakis*, whiff, tuna, mackerel, anchovy, herring, cod (rGad c 1), and carp (rCyp c 1) parvalbumins.

In summary, the patient reported anaphylaxis to trout and had positive skin test results and ImmunoCAP results for trout and salmon, 2 Salmonidae species, but sensitization to other fish was absent or discordant. With the suspicion of a selective reactivity to Salmonidae fish, double-blind, placebo-controlled food challenges (DBPCFCs) with cod, gilthead bream, salmon, and trout were performed to provide adequate dietary advice. In both the trout and salmon DBPCFCs, the patient presented 15 minutes after the intake of 10 g of oropharyngeal pruritus and tightness of the throat. Cod and gilthead bream challenge results were negative. She was advised to avoid trout and salmon, but other fish species were allowed. In a follow-up visit 1 year later she reported a good tolerance of different fish (gilthead, sea bass, sole, cod, hake, whiting, whiff, sardine, tuna, swordfish, and anchovy) that she had eaten regularly.

For the *in vitro* studies, salmon, trout, whiff, and cod were extracted at 10% (wt/vol) and stored at -20°C. Salmon, trout, cod, and whiff extracts (5 µg of protein per well in 50mM sodium bicarbonate, pH 9.6) were coated on microtiter plates overnight at 4°C and incubated with sera (1:4 dilution) overnight. The patient's serum showed IgE binding to salmon (0.57 optical density [OD]; pooled negative serum, 0.1 OD) and trout (0.71 OD; pooled negative serum, 0.1 OD), without recognition of cod and whiff.

The IgE immunoblotting was performed under nonreducing conditions. Separated proteins were transferred onto a nitrocellulose mem-

brane and incubated with the patient's serum (1:5 dilution). Bound IgE was detected by peroxidase-conjugated antihuman IgE antibody (1:3,000) with an enhanced chemiluminescence blotting kit (GE Healthcare, Buckinghamshire, United Kingdom). The patient's serum showed specific recognition of a 12-kDa band in salmon and trout (Fig 1). A pooled serum sample of 15 negative controls did not show any reactivity. By mass spectrometry (matrix-assisted laser desorption/ionization tandem time-of-flight) the following peptide sequences were obtained: AADTFNFK, VIDQDASGFIEVEELK, and AGDADGDMIGIDEFAVLVKQ for the salmon band and TFFHTIGFASK, VIDQDASGFIEVEELK, and AGDADGDMIGIDEFAVLVKQ for the trout band. Protein identification performed by searching a nonredundant protein sequence database (National Center for Biotechnology Information) using the Mascot program showed results highly consistent with salmon parvalbumin (confidence >95%).

Most fish allergic patients report clinical reactivity to several fish species due to cross-reactivity of parvalbumins. However, a few cases of selective fish allergy have been reported.⁵⁻⁸ The selec-

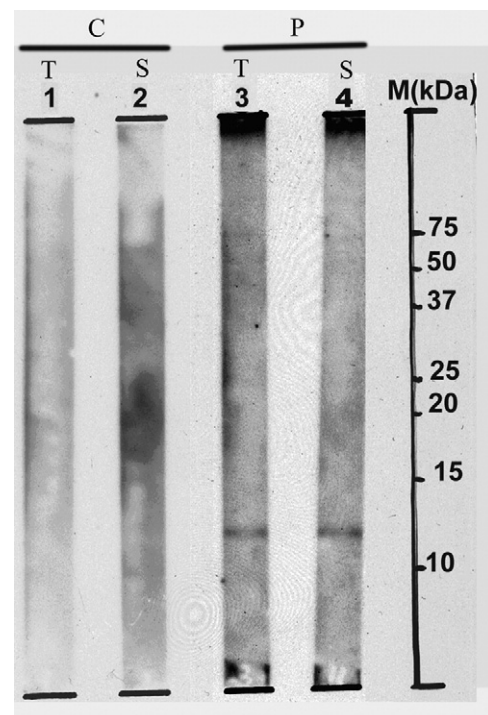


Figure 1. Salmon and trout IgE immunoblot. T indicates trout extract; S, salmon extract; C, pooled control serum; and P, patient's serum. Trout (lane 1) and salmon (lane 2) extracts were incubated with a pooled serum of 15 nonallergic controls. Trout (lane 3) and salmon (lane 4) extracts were incubated with the patient's serum.

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tive reactivity has never been confirmed by oral challenges,⁵⁻⁸ and the allergens involved are different than parvalbumin,⁵⁻⁷ with the exception of a recent report of a selective allergy to salmon and trout.⁸

In our patient, the results of skin tests, CAP, and enzyme-linked immunosorbent assay pointed to a selective IgE-mediated response to trout and salmon. Their clinical relevance was confirmed for the first time by DBPCFC and further supported by the subsequent good tolerance of more than 10 fish species not belonging to the Salmonidae family. Our IgE immunoblotting and mass spectrometry results suggest a specific epitope recognition pattern of Salmonidae parvalbumins, which is supported by the fact that the sequence identity between salmon and trout parvalbumins is higher than with the counterparts of cod, hake, sole, tuna, and whiting,¹⁻⁴ fish species tolerated by our patient. In summary, this case report shows that selective reactions to fish species may be caused by the fish panallergen parvalbumin.

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