Actin as a Possible Cross-Reactive Allergen Between Fish and Poultry

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Fish and chicken are widely consumed [1,2]. Both fish allergy and chicken allergy without associated hypersensitivity to egg and/or bird feather have been reported [1,3]. A new syndrome, fish-chicken syndrome, which involves 3 possible cross-reactive allergens has been proposed [1]. To our knowledge, the present case is the first report of cross-reactivity between fish and chicken due to a protein not yet associated with these foods.

A 43-year-old man diagnosed with mild seasonal pollen-triggered rhinoconjunctivitis experienced several episodes of urticaria, abdominal pain, and dyspnea within a few minutes of eating various types of fish between 1997 and 2002. In 2015, he experienced several episodes of oropharyngeal pruritus, generalized urticaria, and facial angioedema after eating chicken and turkey. He subsequently experienced generalized urticaria, facial angioedema, dysphonia, abdominal pain, vomiting, and dyspnea several minutes after inadvertently eating both types of poultry in meat puddings. Nowadays, he avoids all types of fish and poultry, but tolerates shellfish, mammalian meats, and other foods.

Skin prick tests (SPTs) were performed with a battery of extracts from aeroallergens (pollen, house dust mite, dander, and fungi), meats (chicken, lamb, pig, and cow), fish (hake, cod, sole, anchovy, sardine, salmon, and tuna), *Anisakis simplex*, and shellfish (clam, mussel, squid, and prawn). SPTs were also performed with negative controls (50% glycerinated saline) and positive controls (histamine, 10 mg/mL) (ALK-

Abelló). Prick-by-prick tests were performed with raw and boiled meats (chicken, turkey, lamb, pig, cow, and rabbit), fish (hake, cod, sole, anchovy, sardine, salmon, and tuna), and shellfish (clam, mussel, squid, and prawn). Serum total IgE, specific IgE, and baseline tryptase levels were measured using ImmunoCAP (Thermo Fisher), following the manufacturer's instructions.

SPT results were positive (wheal ≥3 mm wider than the negative control) to olive pollen, chicken meat, hake, and cod and negative to the remaining extracts. Prick-by-prick tests were positive to raw and boiled chicken, turkey, hake, and cod and negative to the remaining foods. Serum total IgE was 48 IU/mL. Serum specific IgE was positive against extracts from olive pollen (4.50 kU_A/L), chicken meat (0.41 kU_A/L), hake (0.96 kU_A/L), and cod (1.32 kU_A/L) and negative to pig, cow, *A simplex*, sardine, anchovy, tuna, salmon, shrimp, mussel, and squid, as well as against the parvalbumins Gad c 1 and Cyp c 1 and the tropomyosins Der p 10 and Pen a 1 (<0.10 kU_A/L). Baseline serum tryptase level was 2.8 µg/L (normal, <11.4 µg/L).

Additionally, in order to ascertain which proteins from poultry and fish were the cause of these allergic reactions, protein extracts from hake, cod, turkey, and chicken were prepared by homogenization in phosphate-buffered saline, dialyzation, and lyophilization. These extracts were studied using SDS-PAGE under reducing conditions (2-mercaptoethanol) [4], transferred onto polyvinylidene difluoride membrane filters (Millipore Corp.), and incubated with patient serum. Immunoblotting studies revealed IgE-binding bands of 42 kDa and 33 kDa in hake, cod, turkey, and chicken extracts (Figure, I). The presence of IgE cross-reactivity between proteins from fish and poultry was studied by means of an immunoblotting-inhibition assay with the patient's serum using cod extract as the solid phase and extracts from turkey and chicken as inhibitors. All the inhibitor extracts were able to completely inhibit IgE-binding in the cod extract (Figure, II).

To identify the fish IgE-binding proteins, the 42-kDa and 33-kDa proteins from cod and hake were manually excised, digested with trypsin, and analyzed by tandem mass spectrometry [5]. Proteins were identified using a nonredundant protein sequence database (National Center for Biotechnology Information). The analysis of the resulting peptides by tandem mass spectrometry identified the 42-kDa band as the fish skeletal α-actin. We were not able to identify the 33-kDa IgE-binding band. Subsequently, we detected α-actin–mediated cross-reactivity between fish and poultry. Finally, in order to confirm sustained tolerance to shellfish, we very cautiously performed an oral food challenge with shrimp, mussel, and squid, which revealed good tolerance. However, the patient declined to undergo oral food challenge with the fish that yielded negative results in cutaneous and serology tests (sardine, anchovy, tuna, and salmon).

The novelty of our report lies in the description of a new cross-reactive IgE-binding protein from fish and poultry. The newly proposed cross-reactive syndrome, fish-chicken syndrome, has been reported in 30 patients to date. It can be triggered by 3 kinds of proteins, namely, parvalbumins (12 kDa), aldolases (40 kDa), and enolases (50 kDa) [1,2].

Actins are highly conserved proteins that are involved in cell motility, structure, and integrity [6]. Skeletal α-actin, which is expressed in skeletal muscle, is one of 6 different actin isoforms that have been identified [7]. Although actin has been reported to be an IgE-reactive molecule in Nile perch [8] and in meat-allergic patients, but with negative SPT results [9], to our knowledge, it has never been described as a cross-reactive allergen in fish or poultry.

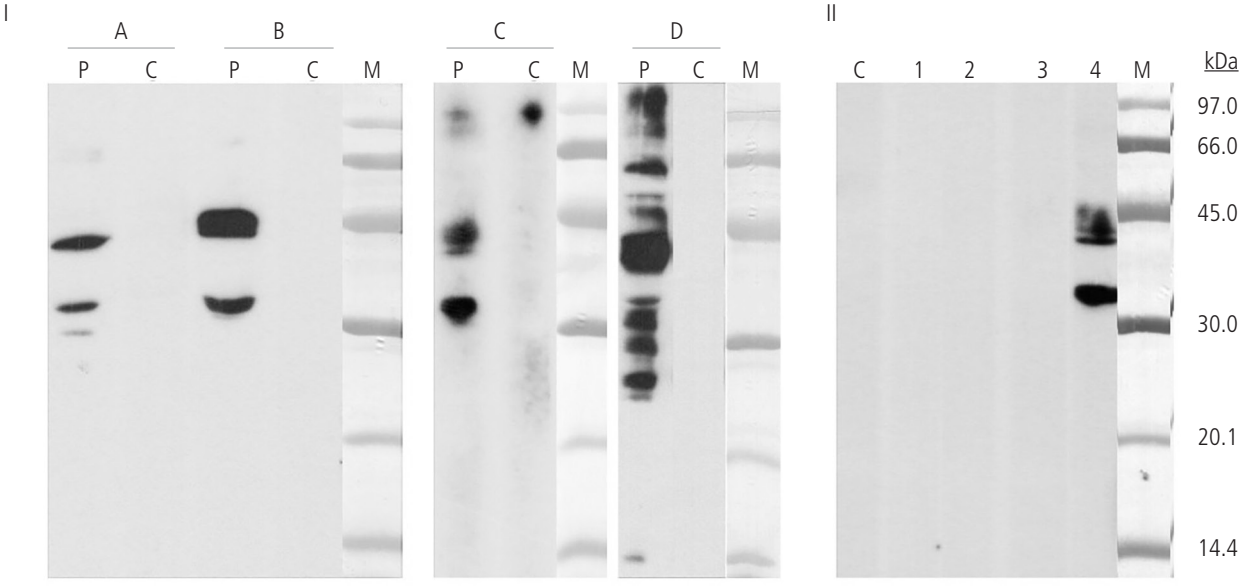

Figure. I, SDS-PAGE Immunoblotting. A) Hake extract B) Cod extract C) Turkey extract D) Chicken extract. Lane P, patient's serum; Lane C, control serum (pool of sera from nonatopic individuals). II, SDS-PAGE Immunoblotting-inhibition. Solid Phase, cod extract. Lanes 1-4, patient's serum preincubated with extracts from cod (1) (positive control of inhibition), turkey (2), chicken (3), and sunflower pollen (4) (negative control of inhibition); Lane C, control serum (pool of sera from nonatopic subjects); Lane M, molecular mass standard.

Actin is a 42-kDa myofibrillar protein that is present at a concentration of ≈150 mg/g in raw chicken breast; enolase and aldolase are sarcoplasmic proteins that are present at a concentration of ≈4 and ≈3 mg/g, respectively. All of these proteins are poorly soluble [10]. Both enolase and aldolase are able to produce protein aggregates that react with serum circulating IgE from fish- and poultry-allergic patients [1]. Therefore, it seems reasonable to conclude that actin, a protein much more concentrated in chicken meat and with similar solubility, will also have the same ability.

In conclusion, to our knowledge, this is the first published case of allergy to skeletal α-actin as a possible new trigger of fish-chicken syndrome. Further studies are necessary to confirm our data on this cross-reactive syndrome.

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Conflicts of Interest

The authors declare that they have no conflicts of interest.

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