

PRACTITIONER'S CORNER CASE REPORTS

Anaphylactic Shock to Mediterranean Silverside (*Atherina boyeri*) Caused by Nonparvalbumin Allergens

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Food allergy is a growing health problem worldwide, with fish being one of the most common triggers of reactions. Global consumption of fish as a component of daily diet has been increasing [1], and the estimated prevalence of fish allergy ranges from 0% to 7%, according to geographical area [2]. The underlying pathophysiologic mechanism is mainly IgE-mediated, and symptoms range from urticaria to anaphylaxis. Sensitization usually starts during childhood and persists lifelong, with avoidance being the only therapeutic option [1,3]. Even non-IgE-mediated reactions (including food protein-induced enterocolitis syndrome) have been associated with fish intake [2,4]. Parvalbumin, an acidic calcium-binding protein that is resistant to heat and digestive enzymes is considered a major fish allergen with high cross-reactivity across fish species [1,5].

Mediterranean silverside (*Atherina boyeri*) is a fish belonging to the Atherinidae family, genus *Atherina*. *A boyeri* is also known as pejerrey and tolerates low-salinity water. It lives in the Mediterranean and other seas. We report the case of a patient with a history of immediate systemic hypersensitivity reaction after ingestion of pejerrey and tolerance to other fish. His allergology study suggested IgE-mediated sensitization to allergens other than parvalbumins. To our knowledge, there is only 1 previous publication reporting 2 cases of allergy to pejerrey with tolerance to other fish [6].

A 49-year-old man with a history of atopy (drug allergy and food allergy to peach), who, immediately after intake of fried pejerrey, experienced dysphonia, dysphagia, itching

in the genital area, malar angioedema, and syncope. In the emergency department, his blood pressure was 60/40 mmHg and oxygen saturation was 95%. He was treated with intravenous hydrocortisone 200 mg and dexchlorpheniramine 5 mg, intramuscular epinephrine 0.5 mg, and fluid therapy. His condition improved within a few hours. Serum tryptase was not measured during the reaction. The patient was subsequently referred to our allergy department. His clinical history ruled out simultaneous use of drugs and the presence of possible cofactors. After the reaction, the patient avoided ingestion of pejerrey and continues to tolerate other fish species.

We performed a skin prick test with a battery of commercial raw fish (tuna, sardine, cod, and hake) and *Anisakis simplex* extracts and prick-by-prick tests with cooked and raw pejerrey. Serum specific IgE to cod, tuna, anchovy, and sardine was determined using the Immulite assay (Siemens). Specific IgE to *A simplex*, hake, and recombinant parvalbumins (rGad c 1 and rCyp c 1) were determined by ImmunoCAP (Thermo Fisher).

Protein extracts from pejerrey body and pejerrey head and viscera were prepared by homogenization in phosphate-buffered saline, dialyzed, and lyophilized. SDS-PAGE immunoblotting was carried out under reducing conditions (2-mercaptoethanol) with pejerrey extracts, as described by Laemmli [7], using a patient serum dilution of 1/3, a secondary antibody dilution of 1/10 000 (SouthernBiotec), and a chemiluminescent detection method (GE Healthcare UK Limited).

The results of the skin prick tests with the fish extracts tested and the *A simplex* extract were negative. Prick-by-prick tests to cooked and raw pejerrey were positive (10 mm and 7 mm, respectively). Serum specific IgE results for *A simplex*, cod, hake, tuna, anchovy, sardine, and recombinant parvalbumins (rGad c 1 and rCyp c 1) were all negative. SDS PAGE immunoblotting with head and viscera extract revealed 2 IgE-reactive bands, a broad band of 60-55 kDa and another of 34 kDa (Figure). However, no bands were detected with the pejerrey body extract.

According to the clinical history and positive *in vivo* and *in vitro* results, the patient was considered to have experienced an anaphylactic reaction to pejerrey with tolerance to other fish species and sensitization to allergens other than parvalbumin. Subsequently, we advised the patient to avoid pejerrey and to check the ingredients listed for foods that might contain it. No restrictions were placed on other fish species.

Parvalbumin has been recognized as the major fish allergen since 1969. Parvalbumin is a low-molecular-weight protein (10-12 kDa) that is water-soluble and calcium-binding in muscle. It is thermally stable and able to preserve its allergenic activity, even under acidic conditions and after pepsinolysis. The high amino acid sequence homology for the parvalbumins of different fish species is responsible for the common cross-reactivity between them. In fact, IgE-binding parvalbumins have been detected in over 90% of fish-allergic patients [5,9].

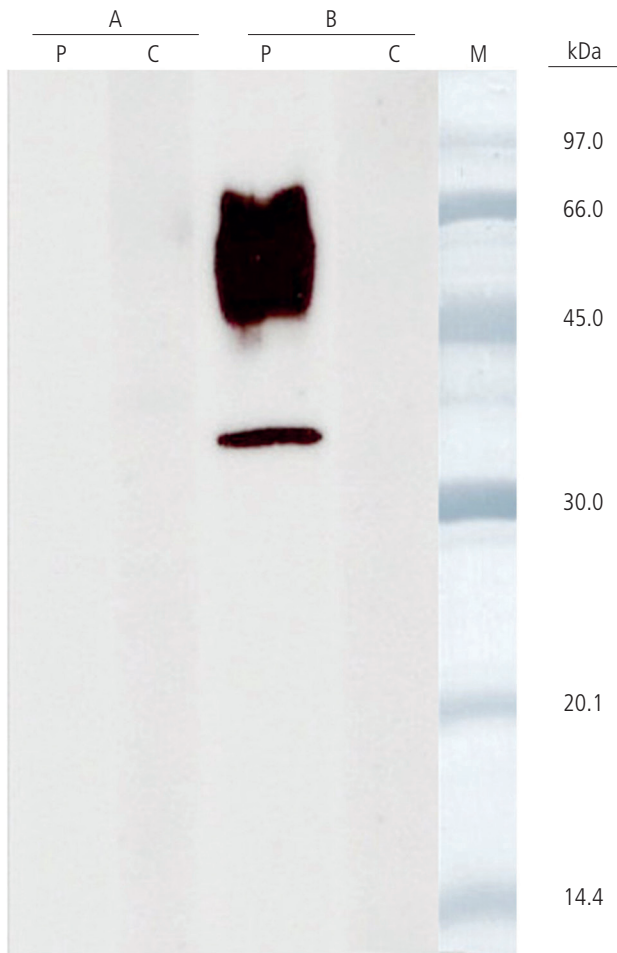


Figure. SDS-PAGE immunoblotting. A, Pejerrey body extract. B, Pejerrey head and viscera extract. Lane P, patient serum; Lane C, control serum (pool of sera from nonatopic individuals). M indicates molecular mass standard.

However, minor allergens, such as fish enolase, aldolase, and gelatine, have been shown to trigger monosensitivity and oligosensitivity via IgE-mediated reactions to specific fish species without sensitization to parvalbumin IgE, and various publications have reported clinical cases of monosensitivity and oligosensitivity to specific fish species, thus highlighting the role of new fish allergens other than parvalbumin [8-10].

In 2009, Kuehn et al [8] published an anecdotal clinical case of an anaphylactic reaction caused by ingestion of marshmallows containing fish gelatine. The *in vitro* study detected protein bands of 110 and 210 kDa corresponding to the hetero α chains and β chain of tuna collagen, whereas parvalbumin was not identified. Kuehn et al [9] also reported the first cases of sensitization to fish aldolase (40-50 kDa) and enolase (20 kDa) in patients with a history of allergic reaction to cod, with a negative *in vitro* study result for parvalbumin. The importance of fish enolase and aldolase as new fish allergens has subsequently been investigated. According to the IgE binding patterns for parvalbumins, fish-allergic patients have been classified into 3 IgE-based clusters, with as many as 28% of patients recognizing only IgE to enolase, aldolase,

and fish gelatine [10]. In 2014, Gonzalez-Mancebo et al [6] reported 2 cases of anaphylaxis to silverside. Using SDS-PAGE immunoblotting and tandem mass spectrometry, the authors identified bands of 28.5 kDa and 38 kDa in pejerrey body; these corresponded, respectively, to triosephosphate isomerase β and glyceraldehyde-3-phosphate dehydrogenase [6].

To our knowledge, we report the third case of anaphylaxis to pejerrey in a patient who tolerated other fish species. SDS-PAGE immunoblotting detected IgE-reactive bands (55-60 kDa and 34 kDa) in the head and viscera extract, although no bands were detected in muscle. Similarly, no IgE to recombinant parvalbumins or binding bands of its molecular weight (12 kDa) were detected. Even though we did not perform an oral challenge test with pejerrey, *in vivo* and *in vitro* studies suggested an IgE-mediated anaphylactic reaction, with recognition of 2 allergens other than parvalbumin.

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Conflicts of Interest

The authors declare that they have no conflicts of interest.

Previous Presentation

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