CASE REPORT

Occupational Asthma Caused by Turbot Allergy in 3 Fish-Farm Workers

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Abstract

We report 3 patients (26, 31, and 33 years) who worked at the same fish farm for several years. They experienced symptoms of rhinoconjunctivitis and bronchial asthma while classifying fish by size. Their asthma gradually worsened to the extent that it became persistent and required daily medication with inhaled corticosteroids and bronchodilators. Symptoms improved during weekends and holidays. All 3 patients could eat turbot. Our study showed that the patients were allergic and that sensitization was probably by inhalation. The allergens were parvalbumin in 1 case and a different allergen in the remaining 2 patients.

Key words: Occupational asthma. Fish allergy. *Psetta maxima*. *Scophthalmus maximus.*

Resumen

Presentamos los casos de 3 pacientes de 26, 31 y 33 años que han trabajado en la misma piscifactoría de rodaballos durante varios años. Los 3 iniciaron con síntomas de rinoconjuntivitis y asma mientras trabajaban clasificando el pescado por tamaño. La clínica de asma fue empeorando llegando a ser persistente con uso diario de medicación para su control (corticoides inhalados y broncodilatadores). Los 3 mejoraban de sus síntomas durante los fines de semana y las vacaciones. Los tres toleraban la ingesta de rodaballo. En nuestro estudio se ha demostrado que los 3 eran alérgicos a rodaballo, siendo la vía de sensibilización la vía respiratoria. Las proteínas responsables de la sensibilización fueron en un caso la parvalbúmina, mientras que los otros dos pacientes reconocieron una proteína diferente de este alérgeno mayoritario del pescado.

Palabras clave: Asma ocupacional, alergia a pescado, *Psetta maxima*, *Scophthalmus maximus.*

Introduction

The turbot (*Psetta maxima* or *Scophthalmus maximus*) is a flat fish that belongs to the Scophthalmidae family. Turbot farming first began in Spain in the 1980s, and the country is now responsible for more than 75% of the world's production.

Although allergy to fish usually occurs after ingestion [1], exposure to fish steam generated by heating seems to trigger symptoms in allergic patients [2]. Likewise, aerosols generated by passive evaporation can cause occupational asthma in workers at food processing plants, such as frozen and smoked fish factories [3,4]. In recent years, the clinical and immunological characteristics of fish allergy have been studied, as has cross-reactivity between species [5-7].

Case Description

Three patients—aged 26, 31, and 33 years—consulted for rhinoconjunctivitis and asthma. They had been working at the same fish farm for between 2 and 12 years, and their symptoms appeared after months or years. Two of the 3 patients associated the onset of these symptoms with handling of turbot. Symptoms started in the morning and worsened as the day went on, although they became less intense or improved during weekends and holidays. Two of the patients began to present cutaneous symptoms on the hands and forearms when they handled turbot or sole without adequate protection. All 3 patients could eat turbot, although 1 did not eat turbot for 2 years.

We carried out skin prick tests with common aeroallergens (*Dermatophagoides pteronyssinus* and *Dermatophagoides*

farinae, *Lepidoglyphus destructor*, epithelium (dog and cat), *Alternaria alternata*, *Plantago lanceolata*, grass mix, *Parietaria judaica*, *Cupressus arizonica*, latex) and prick-prick tests with raw and boiled turbot. We also performed prick tests with turbot extract and turbot food extract, which contains shellfish. Patient number 3 also underwent prick-prick tests with cod (*Gadus morhua*), sole (*Solea senegalensis*), hake (*Merluccius merluccius*), horse mackerel (*Trachurus mediterraneus*), sardine (*Sardina pilchardus*), sea bream (*Sparus aurata*), mackerel shark (*Isurus oxyrhinchus*), and ballan wrasse (*Labrus bergylta*), all of which were administered both raw and boiled.

Turbot extracts were prepared by separating the meat from the raw skin at 10% (w/v) in phosphate buffer for 90 minutes at 5ºC using magnetic stirring. The extract was dialyzed against phosphate buffer and centrifuged, and the supernatant was passed through a 0.2 µm filter before being stored in aliquots at –20ºC until use.

Turbot extract was analyzed by sodium dodecyl sulfate–polyacrylamide gel electrophoresis in 16% polyacrylamide gels under nonreducing conditions before being electrophoretically transferred onto nitrocellulose strips for immunoglobulin (Ig) E immunodetection with the patients' sera, as described elsewhere [8].

Specific IgE was determined against prawn tropomyosin (Pen a 1) using the ADVIA-Centaur platform (Bayer HealthCare Diagnostics Division, Tarrytown, New York, USA) [9]. Specific IgE was determined using the CAP system (Phadia, Uppsala, Sweden) in the third patient against carp (*Cyprinus carpio*) recombinant parvalbumin (rCyp c1).

Peak-flow measurements were recorded in 2 working periods of 1 month separated by a 2-week period without working. Measurements were registered in the morning, afternoon, and evening, with 3 forced expirations on each occasion. The best of the 3 measurements was chosen for the analysis.

All 3 patients underwent nonspecific bronchial methacholine challenge following the method described by Chatham et al [10]. The results were expressed as PC_{20} (concentration of methacholine, in mg/mL, that produced a 20% fall in forced expiratory volume in the first second [FEV_1]). Briefly, successive doses of methacholine were nebulized through a DeVilbiss 464 (DeVilbiss HealthCare, Somerset, Pennsylvania, USA) as follows: 1 breath of 5 mg/mL followed by 4 additional breaths of 5 mg/mL of methacholine, then 1 breath of 25 mg/mL, and finally 4 breaths of 25 mg/mL. Dose-response curves were obtained and the PC_{20} was calculated in each case.

The patient who had not eaten turbot for 2 years also underwent an open oral challenge.

The results of skin testing were positive in all 3 cases for dust mites, *Plantago lanceolata* pollen, and grass pollen, and negative to dog and cat epithelium, fungi, and latex. The results of prick-prick testing were positive to raw and boiled turbot and negative with fish fodder. In the third patient, the results of prick-prick tests with other types of fish were positive except for cod and mackerel shark.

IgE-immunodetection of turbot meat and skin extracts with the patients' sera is shown in the Figure. IgE from patients 1 and 2 recognized the same bands of around 50 kDa and 38 kDa in both extracts, as well as other high molecular mass bands (>75 kDa). In patient 3, we observed a band with an approximate value of 12 kDa, which fits with the molecular weight of parvalbumin, the major fish allergen.

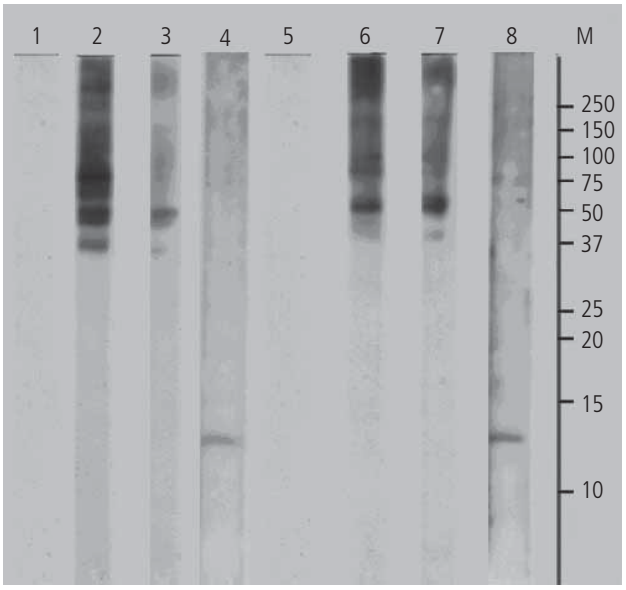

Figure. Lanes 1 to 4, turbot meat (1, negative control; 2, serum from patient number 1; 3, serum from patient number 2; 4, serum from patient number 3). Lanes 5 to 8, turbot skin (5, negative control; 6, serum from patient number 1; 7, serum from patient number 2; 8, serum from patient number 3). M, the position of the markers of molecular weight is indicated in kDa.

Specific IgE testing against prawn tropomyosin gave negative results. Specific IgE testing in the third patient against rCyp C1 revealed a value of 0.67 kU_A/L.

The bronchial methacholine challenge results were positive in all 3 cases with a PC_{20} value of 32, 14.6, and 12.5 mg/mL, respectively.

Peak-flow determinations revealed variations of over 20% for the days the patients worked with turbot and an improvement during weekends, holidays, and sick leaves.

The result of the controlled oral challenge with turbot was negative (well tolerated) in the patient who had not eaten turbot for 2 years.

Discussion

Different types of food are involved in occupational asthma. They can be carried by aerosols, mainly in cooking steam. Allergy to several species of shellfish and fish have been reported in fishermen and cooks. Droszcz et al [5] studied fish farm workers with symptoms of rhinitis and urticaria, and demonstrated that the patients were allergic to fish. Furthermore, generation of bioaerosols in areas where fish is stored and processed seems to facilitate the presence

of allergens in the environment by passive evaporation. Rodríguez et al [4] reported the cases of 2 patients diagnosed with occupational asthma due to fish through specific bronchial induction with aerosolized fish extracts

One of the patients who previously tolerated fish later developed symptoms after ingestion. The work involved cleaning, cutting, and packing different fish species at a frozen fish factory in one case and, at a smoked fish factory in the other. Douglas et al [6] published a study in which people who worked with equipment that generated aerosols containing salmon serum proteins experienced an IgE-mediated response to those proteins. Inhalation of the aerosols was significantly associated with occupational asthma, and the severity of the symptoms was correlated with the distance from the source of the aerosols.

We present 3 cases of rhinoconjunctivitis and occupational asthma in turbot-allergic fish-farm workers. Two of the patients also experienced cutaneous symptoms on contact, although each patient presented a different band pattern in IgE-immunoblotting. We proved an IgE-mediated allergic mechanism through skin testing and determination of serum specific IgE. The route of sensitization seemed to be inhalation. The proteins detected by the patient's sera corresponded only to the major fish allergen—parvalbumin—which was responsible for the allergy in the third case. In patients 1 and 2, other proteins, with an approximate molecular weight of 50 and 38 kDa, were involved. However, the sensitization profile to common aeroallergens observed by skin prick testing was identical in all 3 patients. This profile is very common, and in the opinion of the authors, has no relation with the presence of turbot allergy.

Today, all 3 patients can eat turbot and other fish, and they have not experienced symptoms since leaving their job.

To our knowledge, this is the first report of sensitization to turbot in fish-farm workers; however, we expect more cases to appear in the future. The fact that the 3 patients are smokers may play a role in their condition.

At this fish farm, around 30 people are in direct contact with turbot, mainly to feed them and classify them by size. Consequently, more than a thousand tons per year can be produced. It would be very interesting to study and quantify the allergens that present in this environment, as in studies with other types of fish [11]. This approach would provide useful information on the allergen load needed to sensitize patients and on potential preventive measures.

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Conflicts of interest

A. Ledesma y F. de la Torre work for ALK-ABELLÓ, S.A.

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