Dear Editor,

A 48 year old buyer of luxury foods developed tingling and itching of her ears with a burning sensation of her face, nausea and faintness within 2–3 min of eating of two types of Beluga caviar, foie gras, quail eggs, wheat blinis and champagne at a friend’s dinner party. There was also swelling of the face and a mild constricting sensation of her throat. Her voice was noted to be altered and she had loose motions one hour later and a single vomit 2 h subsequently. An oral antihistamine led to gradual improvement over 2 h although her nausea continued for several days. The reaction was not accompanied by respiratory symptoms, itching of the torso and limbs or skin rash. None of the other diners suffered ill health and to our knowledge there have been only 2 previously reported cases.1,2 However, neither have involved allergy to both ingested and airborne caviar proteins. Allergy to salmon caviar appears to be a more frequent problem3 and there are also rare cases of allergy to king fish caviar.4 The precise allergen responsible for the Beluga caviar allergy was considered to be vitellogenin by Perez Gordo et al.1 In salmon roe allergy, IgE mediated reactivity was detected towards fragments of vitellogenin and to lipovitellin while that in king fish caviar the allergy was to a 33 kDa alpha S1 casein like protein.5 Thus, there is similarity in the fish roe proteins that induce reactivity in those with allergy to different types of caviar. However, given that the skin testing was negative to salmon and herring roe in our patient, it is likely that the specific IgE antibodies here are restricted to species specific epitopes in the sturgeon egg vitellogenin or else other proteins entirely. Regardless, the rarity of Beluga caviar allergy may be related to the infrequent consumption of this tasty but expensive delicacy. The infrequent consumption of fish roe more generally may explain the relative rarity of allergy to fish eggs compared to fish meat allergy.

Recently our patient developed itching and tingling of her lips within 2 h of undertaking one of her regular visits to the caviar factory. She then suffered dyspnea with bronchospasm and cough followed by facial redness and then urticaria on her arms. The reaction was controlled by an oral antihistamine. She now carries a salbutamol inhaler in addition to her anti-histamines and adrenaline auto-injector. This was deemed especially important if she anticipated exposure to high levels of airborne caviar and other fish roe proteins. Despite the negative SPT to salmon and herring roe, she was asked to avoid all fish roe.

Beluga caviar is obtained from the Caspian sea sturgeon, Huso huso and our patient’s reaction was due to an IgE mediated allergy to one or more sturgeon egg proteins or other compounds in the caviar preparation. Allergy to sturgeon caviar is exceptionally rare and to our knowledge there have been only 2 previously reported cases.1,2

Fig. 1. Results of the skin prick testing to the 2 types of caviar consumed.

References

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The patient described in this report has provided full signed consent allowing the publication of her clinical details and her anonymity has been preserved.

Conflict of interest

The authors have no conflict of interest to declare.

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References

Salmon roe, which is also known as salmon caviar, red caviar, or ikura and is frequently consumed in countries such as Japan or Russia, is a delicacy commonly served in sushi-based meals [1,2]. Allergic reactions to salmon roe have been reported in Japan [3,4], and a few cases were recently described in western countries (3 cases in France [5], 2 cases in the USA [2,6]). Nevertheless, studies on the allergenicity of salmon roe are rare [7].

We report the first case of salmon roe anaphylaxis in a young adult in Portugal. A 26-year-old man with a history of mild controlled persistent asthma and persistent, moderate-severe allergic rhinitis who was sensitized to house dust mites was admitted to our emergency department complaining of dyspnea, rhinorrhea, ocular pruritus, epigastric pain, and nausea. The symptoms began a few minutes after the ingestion of a sushi meal comprising rice, salmon, salmon roe, wasabi, soy, and ginger and were treated with intramuscular epinephrine, intravenous corticosteroids, and antihistamines. Uvular edema persisted in the emergency department. The patient denied having eaten other foods, taken any drugs (including nonsteroidal anti-inflammatory drugs), being infected, or having recently exercised. Skin prick tests with commercial food extracts were negative for salmon and other fish, shellfish, soy, rice, total egg, egg white, egg yolk, ovalbumin, and ovomucoid. Skin prick-prick tests were positive for chum salmon (Oncorhynchus keta) roe (17×10 mm) and negative for egg (white and yolk), ginger, salmon, flying fish roe (tobiko), sturgeon roe (caviar), and black scabbard fish roe. Specific IgE (sIgE) was 0.28 kU/L.
for salmon roe extract (ImmunoCAP, Phadia) and negative for extracts of salmon and other fish (<0.10 kU/L). SDS-PAGE immunoblotting (Roxall) with chum salmon roe extract and the patient’s serum revealed a 20-kDa IgE-binding band (Figure). This band was manually excised from the gel, digested with trypsin, and assessed using mass spectrometry following the methods of Pastor et al [8]. Proteins were identified by searching a nonredundant protein sequence database (National Center for Biotechnology Information) using the Mascot program (http://www.matrixscience.com). The resulting peptides identified by mass spectrometry corresponded to the region of vitellogenin that forms lipovitellin. After the allergic reaction, the patient tolerated salmon and other fish roes (tobiko, caviar, and black scabbard fish). The patient eats fish and shellfish regularly with no complaints. We report a case of salmon roe allergy confirmed by positive in vivo and in vitro tests. In this case, no oral food challenge was performed. Yanagida et al [1] reported that a value of 34.6 kU/L of the sIgE to salmon roe has a 95% positive predictive value for a positive oral challenge result. Despite the low level of sIgE to salmon roe detected in the present case, we decided not to perform an oral food challenge test because of the severity of the reaction and the fact that we were able to rule out all other possible triggers. Furthermore, SDS-PAGE immunoblotting had additional value in our etiological investigation, confirming the presence of sIgE to salmon roe in the patient’s serum. Roe from fish or other aquatic species is enclosed in the ovarian membrane, and salmon roe contains 3 major components that are equivalent to hen’s egg yolk proteins, namely, lipovitellin, phosvitin, and β’-component [3]. Nevertheless, there does not seem to be cross-reactivity between salmon roe proteins and hen’s egg [1,3]. These proteins are degradation fragments of vitellogenin, a protein synthesized in fish liver that is carried to the oocytes through the bloodstream [9]. β’-component is a dimer composed of 2 proteins (16 kDa and 18 kDa, respectively) derived from the same polypeptide chain and is associated with cross-reactivity between fish roes. The 20-kDa IgE-reactive protein detected in our study was identified as the lipovitellin from salmon roe, a protein that has been reported to be an allergen both in salmon roe [3,9] and in beluga caviar [10].

To our knowledge, this is the first reported case of salmon roe allergy without concomitant salmon allergy in a Portuguese patient. Allergic reaction to fish roe is rare in western countries; however, given the increase in consumption of fish roe in these countries, salmon roe allergy should be considered when evaluating patients with anaphylaxis after ingestion of sushi.

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Conflicts of Interest

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Previous Presentations

With the exception of protein identification, data from this case report were presented as a poster at the EAACI 2018 annual congress.

References

Rapid Desensitization to Adalimumab Is Associated With Decreased Basophil Sensitivity

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Palabras clave: Adalimumab. Desensibilización rápida. Test de activación de basófilos. CDsens.

Adalimumab is a fully human recombinant monoclonal antibody against TNF-α that is used mainly in inflammatory diseases such as Crohn disease and ulcerative colitis. Immediate hypersensitivity reactions to this molecule have been reported and may be local or systemic, ranging from pruritus to anaphylaxis [1]. Rapid subcutaneous desensitization to adalimumab has been undertaken by several teams and appears to be an effective management approach, especially in patients with no obvious alternative therapeutic options [2-5]. Rapid drug desensitization protocols for patients who experience hypersensitivity reactions consist of incremental, step-by-step administration of the full therapeutic doses of the eliciting drug [6]. Despite the absence of consensus on the appropriate protocol, particularly for subcutaneous drugs, the few cases reported in literature validate the concept. Here, we report that successful desensitization to adalimumab in 2 patients is associated with a decrease in basophil sensitivity, which we monitored using the basophil activation test (BAT).

Patient #1 was a 30-year-old woman with severe Crohn disease diagnosed 12 years ago. She experienced severe urticarial lesions at the injection site within 1 hour of the first injection of adalimumab (40 mg). This was a new course after a 6-year interruption of treatment (colectomy surgery, pregnancy). Patient #2 was a 38-year-old woman with severe ulcerative colitis diagnosed 10 years ago. She reported urticarial lesions at the injection site within 1 hour of the fifth injection of adalimumab (40 mg). For both patients, the results of prick testing with adalimumab were negative (100 mg/mL), although intradermal testing at 1:1000 (injection of 0.02 mL of adalimumab) was positive.

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Anaphylaxis to Beluga caviar

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Abstract

Fish roe is an extremely rare cause of anaphylaxis and although its consumption has increased in recent years. We described the case of a 59-year-old man, who experienced an anaphylactic reaction after consuming caviar. Skin prick-test were performed with Beluga caviar, salmon caviar, cod, salmon, hen egg yolk and egg white, ovalbumin, ovomucoid, shrimp and mold. Only SPT to Beluga caviar was positive. The absence of sensitization to fish and hen egg was confirmed by undetectable specific IgEs to cod, parvalbumin (Gad c 1 and Cyp c 1), egg yolk and egg white, ovalbumin and ovomucoid. An immunoblot was also performed and showed an IgE-reactive band indicated that the patient was sensitized to a 26 kDa protein in Beluga caviar.

In the present case, immunoblotting of the patient’s serum revealed a single IgE-reactive band at 26 kDa band, which does not appear to correspond to the previous cases.

Key words: Anaphylaxis; caviar; food allergy; immunoblot; vitellogenin

Introduction

Fish roe is an extremely rare cause of anaphylaxis and although its consumption has increased in recent years, little has been published on allergic reactions to these caviar products.1–5 Beluga caviar is a luxury delicacy that is eaten as a garnish or spread. Only two cases of Beluga caviar–induced anaphylaxis have been reported in the literature.1 We report herein a new anaphylaxis case to Beluga caviar without allergies to other roes.

Methods

A 59-year-old man, with no atopic history, experienced an anaphylactic reaction after consuming caviar. Until now, he was accustomed to consuming caviar without reaction, once a year for Christmas. Ten minutes after the consumption of approximately one teaspoon of Beluga caviar without any other food or alcohol, he presented a severe anaphylactic reaction with hypotension (60/40 mmHg) and dyspnea, requiring intramuscular epinephrine (0.3 mg) in prehospital care enabling clinical improvement. Tryptase was sampled during the first hour after the onset of the anaphylactic reaction and showed an increase at 16.8 µg/L. The basal tryptase rate was measured 24h later at 5.6 µg/L.

IgE sensitization was investigated by skin prick tests (SPTs), specific IgE measurements (ImmunoCAP® Thermo Fisher Scientific, Wattham, USA) and immunoblotting. SPTs were performed with Beluga caviar (from sturgeon Petrossian, Paris, France), salmon caviar (Petrossian, Paris, France), cod, salmon, hen egg yolk and egg white.

Results

Only SPT to Beluga caviar was positive (wheal 15 mm). In order to rule out irritation causing these results, the same tests were performed in 3 healthy volunteers. Positive controls were 10% histamine chlorhydrate (7 mm) and 9% codeine sulfate (5 mm). Negative control was physiological serum (no reaction).

The absence of sensitization to fish and hen egg was confirmed by undetectable specific IgEs to cod, parvalbumin (Gad c 1 and Cyp c 1), egg yolk and egg white, ovalbumin and ovomucoid (ImmunoCAP® Thermo Fisher Scientific, Wattham, USA).

Since ImmunoCap® to Beluga caviar was not commercially available, specific IgEs were detected by immunoblot. Briefly, a protein extract from Beluga caviar was prepared and proteins separated by Sodium Dodecyl Sulfate (SDS)-PAGE, showing numerous proteins mainly around 25 kDa as well as greater than 70 kDa. Separated proteins were then transferred onto a Polyvinyliden difluoride (PVDF) membrane and the immobilized proteins were incubated overnight at +4°C with the patient’s serum. After washing and incubation with an enzyme-labeled
anti-human IgE antibody, the addition of enzyme substrate allowed detecting bands in the presence of specific IgEs in the patient’s serum. The resulting IgE-reactive band indicated that the patient was sensitized to a 26 kDa protein in Beluga caviar. A control immunoblot performed in the absence of the patient’s serum did not show any nonspecific IgE reactive bands (Figure 1).

**Figure 1.** Coomassie blue-stained-SDS-PAGE with Beluga caviar (A) and corresponding IgE immunoblots with (B) or without (C) patient’s serum. Lane 1: Beluga caviar. M: molecular weight markers in kDa.

**Discussion**

The main component in fish roe is yolk, the latter of which is comprised of 3 major proteins: lipovitellin (21 kDa), phosphvitin (35 kDa) and ß'-component (ß'-c, 18 kDa)). These three proteins derived from the same precursor, vitellogenin, with an apparent molecular mass of 580 kDa, appear as two major bands corresponding to 180 kDa and 120 kDa after SDS-PAGE.6,7 Gonzalez-de-Olano et al. have identified several proteins in salmon roe (18 and 21 kDa), trout roe (18 kDa) and slated hake roe (18 and 30 kDa).5

In their description of the first case of Russian Beluga caviar anaphylaxis, Untersmayr et al. performed an immunoblot with the patient’s serum which revealed four unidentified IgE-reactive bands of 30, 84, 100 and 118 kDa, the latter two being more reactive.1 In the reported case of Iranian Beluga caviar anaphylaxis, immunoblotting showed a broad spectrum of IgE-reactive bands ranging from 23 to 120 kDa, identified as fragments of vitellogenin by mass spectrometry.7 In the present case, immunoblotting of the patient’s serum revealed a single IgE-reactive band at 26 kDa band, which does not appear to correspond to the previous cases (Figure 1). Moreover, we can speculate that this protein is not a fragment of vitellogenin since another reactive band would likely have been found in this instance.

**Conclusion**

To the best of our knowledge, this is the first case of Beluga caviar anaphylaxis described in France. Our patient presented a selective food allergy to Beluga caviar. Both skin prick testing and immunoblotting pointed to an IgE-mediated reaction. The resulting sensitization appeared to be due to a 26 kDa protein, which has not been described previously.

**Conflicts of interest**

S Lefèvre, I. Moumane and E Beaudouin: none
S Jacquenet is employed by Genclis SA, a biotechnology company specialized in allergy

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