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Cross-Reactivity due to Tropomyosin: Case Report

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Summary

Introduction. Tropomyosin is considered to be the major antigen of shrimp and other shellfish, able to provoke IgE-mediated hypersensitivity reactions. This allergen is also known to be cross-reactive, as it is homologous between multiple species.

Case presentation. 27-year-old female had multiple anaphylaxis due to different triggers each time (consumption of shrimps, peanuts and pastry with white wine) and history of childhood asthma. Skin-prick and prick-prick testing showed positive results for shrimp, but were negative for inhalant allergens and peanut. Further testing with ALEX showed increased total serum IgE concentration, as well as sensitization to 19 allergens: strong sensitization to house dust and food mites, fish and seafood, moderate – to cockroaches and slight – to mold and yeast allergen group. Also, strong sensitization to cross-reactive tropomyosin was found. Treatment plan includes avoiding seafood, house dust mites and cockroaches, usage of allergy diary MASK to track symptoms of rhinitis.

Discussion. Tropomyosin is considered to be an invertebrate pan-allergen, due to its highly conserved structure between multiple species. It is known, that childhood asthma is a risk factor for sensitization to HDMs and cockroaches, and children with this condition have high prevalence of environmental allergies, specifically to indoor allergens. Our case report presents patient's sensitization to four tropomyosin homologues between multiple species – shrimp, house dust mites, fish parasite *Anisakis simplex* and cockroach. It is possible that sensitization to all 19 allergens is due to tropomyosin.

Keywords: tropomyosin, anaphylaxis, shrimps, allergens, allergen specific IgE.

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INTRODUCTION

The crustacean shellfish is one of the eight major food allergens, with a prevalence of up to 10.3% in certain areas of the world. Tropomyosin (TM) is considered to be the major antigen of shrimp and other shellfish, which is able to provoke IgE-mediated hypersensitivity reactions [1]. It is known, that TM from cockroaches and house dust mites (HDMs) is highly similar to shellfish TM and cross-reactivity between them was displayed by previous studies. However, it is not known which of these allergens – shellfish or HDMs and cockroaches, can sensitize

allergy patients upon primary exposure [2]. Our case report presents a clinical situation of sensitization to TM homologues across food and respiratory allergens and brings additional insight to pathogenesis of simultaneous multiple allergies.

CASE PRESENTATION

Overall healthy 27-year-old Lithuanian female was admitted to allergist consultation for recurrent anaphylactic shock caused by consumption of shrimps and peanuts, frequent sneezing and stuffy nose. In early child-

Table. Summary of positive allergy test (ALEX) laboratory findings

Allergens group	Sensitization class according to IgE values
House dust and food mites (kU/L)	6.48 (3 class)
Mold and yeast (kU/L)	0.56 (1 class)
Fish and seafood (kU/L)	9.11 (3 class)
Cockroaches (kU/L)	4.06 (2 class)
Cross-reactive allergens	
Tropomyosin	(3 class)
Total IgE (kU/L)	1920

Class of IgE concentrations: 1 class – sIgE concentration is 0.3–1 kU_A/L – low quantity found; 2 class – sIgE concentration is 1–5 kU_A/L – average quantity found; 3 class – sIgE concentration is 5–15 kU_A/L – high quantity found.

hood, patient had numerous pneumonia and was diagnosed with mucoviscidosis few years later. Later this diagnosis was revoked (for the last 10-years dyspnea is absent, bronchitis only occurs after acute viral respiratory infections). In later childhood, patient was referred to an allergist consultation, due to swelling induced by fleas, mosquitos and other insects. At that time, blood serum IgE test was performed and its results showed total serum IgE being increased sevenfold, yet no additional tests followed this finding. As an adult (26-year-old), patient had her first anaphylactic shock, during which she felt acute stomach cramps only a few minutes after consumption of peanuts. One year later, she had acute stomach cramps 30 minutes after consumption of eight shrimps (regular for patient's diet, but in smaller quantity) accompanied by face-neck urticarial rash and weakness. First aid was performed (shots of adrenalin, clemastin and 12 mg dexamethasone) and symptoms faded away few hours later. Following month, similar symptoms occurred after consuming pastry with a glass of white wine. In addition, patient reported nasal obstruction and rhinorrhoea during pollen season. Family history does not present occurrence of any allergies.

Allergy testing was performed two months after anaphylaxis. Laboratory testing showed that serum tryptase and diamine oxidase results were normal. Furthermore, skin prick testing with standard panel of inhalant allergens and prick-prick testing with suspected food was performed. Results for inhalant allergens were negative (evaluated as 0 (0 – negative, 4+ – strongly positive)), for shrimps – positive (evaluated as 3+), for peanuts – negative (evaluated as 0). Additionally, allergy test ALEX was performed, to determine values of total

IgE (IgE) and specific IgE (sIgE) for 282 allergens and components. Test's results showed sensitization to four allergen groups and to one cross-reactive allergen (Table). Total serum IgE was increased by almost twenty times.

Further investigation of sensitization to specific allergens showed 19 positive sIgE – antigen reactions. First positive (strong) reaction was to mite allergens, which include house dust mites and food mites: *D. farinae* (Der f) – 3.54 kU_A/L (2 class), *D. pteronyssinus* (Der p) – 1.01 kU_A/L (2 class) and its allergen component tropomyosin (Der p 10) – 3.76 kU_A/L (2 class), *Acarus siro* (Aca s) – 1.23 kU_A/L (2 class) and *Blomia tropicalis* (Blo t) – 6.48 kU_A/L (3 class). Secondly, positive (slight) reaction was to mold and yeast allergens, which showed relatively low sensitization to *Aspergillus fumigatus* unknown allergen component (Asp f 4) – 0.56 kU_A/L (1 class). Thirdly, fish and seafood allergens group showed (strong) sensitization to *Anisakis simplex* (parasitic Herring worm) allergen component tropomyosin (Ani s 3) – 9.11 kU_A/L (3 class), crab (Chi spp.) – 2.06 kU_A/L (2 class), lobster (Hom g) – 2.88 kU_A/L (2 class), squid (lol spp.) – 1.37 kU_A/L (2 class), *Mytilus edulis* (Myt e) – 3.69 kU_A/L (2 class), oysters (Ost e) – 2.61 kU_A/L (2 class), *Penaeus monodon* allergen component tropomyosin (Pen m 1) – 4.22 kU_A/L (2 class), molluscs (Rud spp.) – 2.24 kU_A/L (2 class). Lastly, cockroach allergen group showed (medium) sensitization to *Periplaneta Americana* allergen component tropomyosin (Per a 7) – 4.06 kU_A/L (2 class).

Treatment plan for the patient includes diet without shrimp, other shellfish, and seafood in general, environmental control to avoid house dust mites and cockroaches. Adrenalin auto-injector and antihistamines were

prescribed for anaphylaxis treatment. Patient has been trained to fill out "MASK-air" allergy diary App for allergic rhinitis symptoms evaluation. Specific immunotherapy treatment for house dust mites will be discussed after allergic rhinitis and allergy symptoms evaluation by MASK after six months' period.

DISCUSSION

Tropomyosin is a 38–41 kDa protein, which is responsible for muscle contraction regulation. It is considered to be an invertebrate pan-allergen, due to its highly conserved structure between multiple species, whereas vertebrate TM is non-allergenic [3, 4]. Protein homologues in shrimps, prawns, lobsters and crabs have the amino acid sequence identity of 91–100%, whereas HDMs TM have 78.5–81.7% and cockroach has 82.4% sequence identity to shrimp's TM. Furthermore, shrimp TM (Pen m 1) has eight IgE-binding epitopes and multiple sequence alignment studies of those epitopes shown that crab (Por p 1) and lobster (Hom p 1) TM have almost identical sequences at all the eight Pen m 1 epitopes. Contrastingly, HDMs (Der p 10 and Blo t 10) TM had overall >80% epitope sequence identity, with the exception of the first epitope, for which sequence identity is 58%. This concludes why TM cross-reactivity is stronger within shellfish allergens compared with cross-reactivity interspecies, which may have late onset clinical symptoms or never occur at all [2].

It is known, that childhood asthma is a risk factor for sensitization to HDMs and cockroaches. Children with this condition have a high prevalence of environmental allergies, specifically to indoor allergens. Interestingly, levels of exposure to HDMs and cockroaches are proportional to possibility of sensitization to these allergens, thus reducing HDMs at children house may be effective protective measure against allergy development [5].

Our case report presents patient's sensitization to four TM homologues between multiple species – shrimp, HDMs, fish parasite *Anisakis simplex* and cockroach. It is important to note that these four antigen – sIgE reactions out of overall 19 positive, had the highest values. According to laboratory testing, our patient is sensitized to other allergens, which are known to contain highly conservative TM protein, thus, confirming the possibility of

TM being responsible for patient's simultaneous multiple allergies. To verify this hypothesis additional testing with allergen component TM should be done for all allergens with established sensitization.

It is important to emphasize, that in our reported case, patient had recurrent respiratory complaints in childhood, which could have caused sensitization to HDMs and/or cockroach TM antigens. Increased total serum IgE in early patient childhood would support this hypothesis. Furthermore, allergic reaction to shrimps began only in adulthood, with shrimps previously being a part of patient's regular diet in lower quantities without any complaints. This sensitization to shrimp TM may have developed as a consequence of primary sensitization to HDMs or cockroach TM, which would explain anaphylactic shock caused by previously regular shrimp consumption, only in patient adulthood and not earlier. ♦

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Santrauka

TROPOMIOZINO LEMIAMAS KRYŽMINIS REAKTYVUMAS: KLINIKINIS ATVEJIS

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Ivadas. Tropomiozinas yra vienas iš pagrindinių krevečių ir kitų vėžiagyvių antigenų, galinčių išprovokuoti IgE sukeltą padidėjusio jautrumo reakcijas. Šis alergenai taip pat yra žinomas kaip kryžmiškai reaktyvus, nes jis yra homologiškas kelioms rūšims.

Klinikinis atvejis. Dvidešimt septynerių metų moteris patyrė sunkią anafilaksiją dėl skirtingų alergenų poveikio (krevečių, žemės riešutų, pyrago ir baltojo vyno). Be to, ji vaikystėje yra sirgusi astma. Atliekant odos dūrio ir dūrio-dūrio mėginius, rezultatai buvo teigiami krevetėms, o ikvėpiamiesiems alergenams ir žemės riešutams – neigiami. Laboratoriniai tyrimai (ALEX, nanotechnologijos) parodė padidėjusią bendrą IgE koncentraciją kraujo serume, taip pat išsijautrinimą 19 alergenų: stiprų išsijautri-

nimą namų dulkeis ir maisto erkėms, žuvims ir jūrų gėrybėms, vidutinį – tarakonams ir silpną – pelėsių ir mielių alergenų grupei. Taip pat nustatytas didelis jautrumas kryžmiškai reaktyviu tropomiozinui. Rekomenduotas gydymo planas: vengti jūrų gėrybių, namų dulkių erkių ir tarakonų, paskirtas simptominis rinito gydymas.

Diskusija. Tropomiozinas yra didysis stabilus ir karščiui atsparus vėžiagyvių alergenai. Voragyviai yra panašūs į vėžiagyvius, todėl galimos kryžminės reakcijos su namų dulkių erkėmis. Yra žinoma, kad astma vaikystėje yra išsijautrinimo namų dulkių erkėms ir tarakonams rizikos veiksnys, o vaikai, sergantys šia liga, yra ypač išsijautrinę patalpų alergenams. Šiuo aprašomuoju atveju nustatytas pacientės išsijautrinimas keturiems tropomiozino homologams tarp kelių rūšių alergenų – krevečių, namų dulkių erkių, žuvyse parazituojančių kirmėlių *Anisakis simplex* ir tarakonų. Galbūt ir kitiems iš nustatytų 19 alergenų išsijautrinimą sukelia kryžmiškai reaguojantis tropomiozinas.

Reikšminiai žodžiai: tropomiozinas, anafilaksija, krevetės, alergenai, alergenai specifiniai IgE.

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