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Case Report

Research Development of Seafood Allergen

Xue Gao*, Yiwei Tang, Defu Zhang and Jianrong Li

College of Chemistry, Chemical Engineering and Food Safety, Bohai University, Jinzhou, 121013, China

***Corresponding author:** Xue Gao, College of Chemistry, Chemical Engineering and Food Safety, Bohai University, Jinzhou, 121013, China

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Abstract

Seafood plays an important role in human nutrition and health. The growing international trade in seafood species and products has added to the popularity and frequency of consumption of a variety of seafood products across many countries. Asian countries have the highest rates of fish consumption in the world, which is higher than world average. Seafood is composed of diverse sea organisms and humans are allergic to many of them. Fish and shellfish are the most common seafood that causes adverse allergic reactions among nations; the symptoms ranged from oral allergy syndromes to urticaria and anaphylaxis. The major identified allergens are parvalbumin in fish and tropomyosin in shellfish. In addition to arginine kinase, sarcoplasmic calciumbinding protein, and myosin light chain have recently been reported in seafood. This article provides an overview of clinical features, diagnosis, species and characteristics of seafood allergy.

Keywords: Seafood; Allergy; Allergen; Prevalence; Clinical symptoms

Introduction

In recent years, there has been a significant amount of media attention on the subject of food allergy. Allergies to foods are a significant public health problem, affecting up to 4% of adults and 8% of children [1,2]. Most allergic reactions to foods can be attributed to relatively few food groups, which include seafood. Among food allergens of animal origin, seafood is a frequent cause of adverse food reactions in hypersensitive individuals. Fish, egg, milk, and crustaceans represent the animal kingdom in the "big eight" group of food allergens [3]. The majority of food allergic patients react to these foods. The growing international trade in seafood products has added to the popularity and frequency of consumption of a variety of seafood products across many countries [4]. Asia is the world's most populous continent, with a population of almost 4 billion people and many emerging economies. It has one of the highest rates of fish consumption in the world, with an estimated average annual consumption of 24.9 kg per capita compared with a world average of 16 kg per capita [5].

Seafood includes vertebrate finned fish such as cod, salmon, and tuna, crustacea such as shrimp, crab, and lobster, and mollusks such as squid, scallop, clams, and snails. Following the reaction of allergen with specific immunoglobulin E (IgE), the mast cell degranulates and releases histamine, leukotrienes and other mediators, causing hypersensitive reactions [6-8]. This article provides an overview of current literature related to the clinical features, diagnosis, and appropriate management of seafood allergy. The purpose for this review article is to provide an overview and discussion of current seafood allergy research.

Clinical features, diagnosis and management of seafood allergy

The main clinical manifestations of allergic reactions to seafood include vomiting and diarrhea while the most extreme form of reaction is life-threatening anaphylactic shock [9]. Various studies have subsequently confirmed that occupational seafood allergy can be manifest as rhinitis, conjunctivitis, asthma, urticaria, and protein contact dermatitis. Reactions are immediate, reported mostly within 2 h; however, late-phase reactions have been reported up to 8 h after ingestion [10]. Importantly respiratory reactions are often seen after ingestion of allergenic seafood and frequently with anaphylactic reactions. The appearance of allergic symptoms results not only from ingestion of seafood, but can also be triggered by inhaling cooking vapours and handling seafood in the domestic as well as in the occupational environment [7,11,12]. Symptoms manifest mainly as upper and lower airway respiratory symptoms and dermatitis, while systemic anaphylaxis is rarely seen with this type of exposure.

Diagnostic methods include skin prick test (SPT) as well as in vitro quantification of specific IgE antibodies using assays such as the Immuno- CAP and immunoblotting to identify the specific IgE binding allergens. However, positive test results are not necessarily proof of clinical sensitivity. Possible cross-reactivity between tropomyosin from crustacean and molluscs with tropomyosin from insects and mites may have clinical significance. While these types of assays contain the majority of possible allergens found in the individual fish species, possible variations of parvalbumin concentrations cannot be taken into account.

In general, management of food allergies, including seafood allergy, still primarily relies on avoidance. Unfortunately, strict avoidance is not always possible. As a result, new approaches to the treatment of food allergy are being investigated and developed. In-vitro assays for the detection of crustacean tropomyosin are available, but cross-reactivities with other invertebrate tropomyosins from insects and mite are reported [13]. The detection of parvalbumin is much more problematic as these allergens show even higher biochemical and immunological variability among the different fish species [14].

Allergens

Tropomyosin was first described as a crustacean allergen in shrimp in 1981. Tropomyosins in invertebrates have a molecular

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weight of between 38 and 41 kD and show great homology in their amino acid sequence. Tropomyosin belongs to a family of proteins associated with the thin filament in muscle, and microfilaments in many nonmuscle cells. Together with actin and myosin, tropomyosin plays a functional role in the contractile activities of these cells. Importantly, tropomyosin is not only a crustacean allergen but has been confirmed in a number of mollusk species [15]. It has become apparent that molluscs such as mussel, oyster, squid, limpet and abalone can be significant food allergens in exposed populations. Tropomyosin has been demonstrated as one of the major allergens in squid, oysters, scallops, snails and abalone. This allergen has been identified as the responsible allergen for cross-reactivity between seafood and mites.

Parvalbumins are globular proteins about 12 kDa in size and are abundant in lower vertebrates such as amphibians and fish. High amino acid homology of 60-90% has been observed between parvalbumin from fish species however studies on cross-reactivity are conflicting and the degree of allergenicity between species has been illustrated to vary significantly [16]. Parvalbumins are resistant to thermal and enzymatic degradation. Gad c 1, is a parvalbumin that was first identified in Baltic cod (*Gadus callarias*). Gad c 1 has been well-studied, characterized, and sequenced. Another parvalbumin, the major allergen in the white muscle of Atlantic salmon, was identified and named Salmo salar (Sal s l) [17]. In the Atlantic cod (*G. morhua*), an oligomeric parvalbumin encoded by a distinct gene was identified as Gad m 1 and found to have greater homology with Sal s 1 than with Gad c 1. Parvalbumins can be found as one of two distinct isoform lineages; α and β. Fish often contain both α and β parvalbumin; however, the majority of allergenic parvalbumin's reported belong to the β lineage. Furthermore, most fish express two or more different β parvalbumin isoforms, which are subsequently named β1, β2, and so forth [18].

In addition, other allergens have been recently identified in shellfish such as sarcoplasmic calcium-binding protein [19], myosin light chain [20] and arginine kinase [21, 22]. Arginine kinase a potential new class of invertebrate pan-allergens have been identified in Pacific white shrimp and Black tiger prawn as Lit v 2 and Pen m 2 respectively [22,23]. However, the clinical significance of these allergens in mollusks is currently undefined. Two other allergens identified in the Pacific white shrimp (Litopenaeus vannamei) are myosin light chain kinase [24] and sarcoplasmic calcium binding protein [25], identified as Lit v 3 and Lit v 4 respectively.

Fish allergen

Tuna is extensively consumed, and many fish-allergic individuals are able to tolerate canned tuna. Cod and herring are a popular choice for fried fish, and mackerel and salmon are also commonly used in mainstream cooking. Extensive cross reactivity between different species of fish including freshwater and saltwater fish has been demonstrated. The Baltic cod was the first food source in the early 1970s ever analyzed for the molecular nature of the offending allergen [26].

Beale et al. [27] identified oligomeric forms of parvalbumin in five highly consumed fish species in Southern Africa. A highly cross-reactive allergenic isoform of parvalbumin was identified from Pacific pilchard which was characterized at molecular level. Isoforms varied between approximately 10-13 kDa. Sera from several subjects also displayed IgE reactivity to 24 and/or 38 kDa proteins in yellowtail, anchovy and hake crude extracts which were assumed to be oligomers of parvalbumin due to the comparable positions of dimeric and trimeric parvalbumin. Hamada et al. [28] purified parvalbumin (a possible candidate for the major allergen) from the white muscle of three species of mackerels (S. japonicus, S. australasicus, and S. scombrus) from Japan. All the purified preparations from three species gave a single band of about 11 kDa and were clearly identified as parvalbumins by analyses of their partial amino acid sequences.

There is a series of case reports showing that fish allergic patients may be sensitized to single fish species due to IgE reactivity to proteins other than parvalbumin [29,30]. Triose phosphate isomerase β has only recently been described in a case report as being an allergen in sole [31]. Yamada et al. [32] characterized IgE-binding components of Yellowfin and Albacore tuna fish from Japan. They identified a specific protein with a molecular weight of approximately 46 kDa that is present in Yellowfin tuna, but absent in Albacore. Their studies indicated that patient sera may contain different tuna fish species IgE-specific antibodies directed against unique species-specific allergens present in Yellowfin and Albacore tuna fish. Espineira et al. [33] developed a rapid and sensitive method for the detection of anisakids in seafood based on PCR. Their method allows detecting the presence of anisakids in fish and determining the particular anisakid species. This method can be applied to all kinds of processed products including those undergoing intensive processes of transformation, for instance, canned foods. They proposed rapid, robust, highly sensitive, and readily adaptable method in routine molecular diagnostic laboratories. Shen et al. [34] reported that octopus Arginine kinase (AK) was purified and confirmed by mass spectrometry for the first time, and its molecular mass was 38 kDa. The full-length gene sequence of octopus AK encompassed 1209 bp and was predicted to encode a protein with 348 amino acid residues.

Shellfish allergen

Shellfish are a non-taxonomic group that includes crustacean and mollusks, which are invertebrates, unlike fish. Crustaceans are classified as arthropods together with arachnids and insects. Over 50 000 living crustacean species are found world-wide and a large number of varieties are consumed raw or cooked. Molluscs is also a large and diverse group, subdivided into the classes Bivalve, Gastropods and Cephalopods and comprises almost 100 000 different species, including several economically important seafood groups such as mussels, oysters, abalone and squid (calamari). Among food allergens of animal origin, shellfish are a frequent cause of adverse food reactions in hypersensitive individuals. Most shellfish species that are known to elicit allergic food reactions belong to the class crustacean and include shrimp, crab, crawfish and lobster, with the genus *Penaeus* being one of the most frequently reported causes of allergic reactions.

Hoffman et al. [35] first isolated two allergens from raw and cooked shrimp, termed antigen I and antigen II respectively. The heat stable antigen II, demonstrated specific IgE binding in the sera of all 11 shrimp-allergic subjects tested. Nagpal et al. [36] isolated two heatstable shrimp allergens from *Penaeus indicus*, called Sa-I and Sa-II. Sa-II had a molecular weight of 34 kD similar to that of shrimp antigen II. The number of amino acid residues of SA-II was estimated

at 301 amino acid residues, based on the molecular weight of 34 kD and the amino acid composition. Daul et al. [37] first identified Pen a 1 as the shrimp muscle protein tropomyosin based on the amino acid sequence homology of a HPLC-purified 21-residue peptide obtained by endopeptidase Lys-C digestion of Pen a 1; significant homology (60–87%) with tropomyosins from various species was observed. The greatest homology (87%) was with tropomyosin from the fruit fly *(Drosophila melanogaster)*, reflecting the phylogenic relationship between these two arthropods. An ELISA test kit has been developed and is currently in market for the detection of crustacean tropomyosin [38], but its ability to detect molluscan tropomyosin is not known. Sinanoglou et al. [39] developed an ELISA for the detection of tropomyosin from squid, octopus, and cuttlefish with a detection limit of 0.05 ppm.

Leung et al. [40] demonstrated in vitro that sera from nine crustacean allergic patients had IgE binding to antigens from all 10 mollusk species tested. However, in vitro cross-antigenicity does not necessarily indicate clinical cross allergenicity. Jirapongsananuruk et al. [41] demonstrated that shrimp allergy can be species-specific. Some studies reported clinical reactivity of 38% between shrimp and other crustacean members, 14% between crustacea and mollusks, and 49% between mollusk members. Yu et al. [23] characterized a new shrimp allergen, Pen m 2 (MW=40 kDa), by means of two-dimensional immunoblotting and MALDI-TOF. Pen m 2 was recently determined to have AK activity. This allergen was recognized by 94 % of patients. In 2008, Shiomi et al. [20] described a 20-kDa allergen in shrimp (Penaeus monodon), which was identified as a sarcoplasmic calcium-binding protein (SCP) recognized by 50 % of studied patients.

In a recent multicentre study on more than 100 Italian shrimp-allergic adult patients investigated by immunoblot analysis and rPen a 1-specific IgE measurements, only 41% were tropomyosin reactors, whereas IgE reactivity at molecular weights > 60 kDa was detected in 52% of cases [42]. Guillen D et al. measured IgE specific for arginine kinase (rPen m 2) and sarcoplasmic calcium-binding protein (rPen m 4) in sera from a group of shrimp-allergic patients. Shrimp arginine kinase and sarcoplasmic calcium-binding protein are minor allergens sensitizing only 10% -15% of Italian shrimp-allergic patients, but are clinically relevant. Hemocyanin (Hcs) is a clinically relevant high molecular weight shrimp allergen possibly cross-reacting to house dust mite [43]. Hcs were identified as heat-stable, non-cross-reactive, high-molecular-weight allergens from Macrobrachium rosenbergii shrimp. Since circulatory organs are not always removed during food preparation, high concentrations of Hcs may be present along with shrimp meat, which contains the known cross-reactive tropomyosin protein [44, 45].

Conclusion

Allergic reactions to seafood are a common cause of food allergy in many regions of the world. Seafood allergy is an important clinical problem of increasing prevalence. Assessment by an allergist is very important for appropriate diagnosis and treatment. As our understanding of the mechanisms involved and the identification of seafood allergens and potential cross-reacting allergens advance, our approach to diagnosis and management of this difficult problem will continue to improve. Although these areas of technological developments are still in their infancies, it is likely that they will have a significant impact on more precise clinical implications for correct diagnosis, management and immunotherapy of seafood allergy.

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Refernces

1. Simonne AH, Gollub EA. Decoding food labels: tools for people with food allergies. University of Florida IFAS Extension 2007; 1-12.
2. Ozol D, Mete E. Asthma and food allergy. Curr Opin Pulm Med 2008; 14: 9-12.
3. Poulsen LK, Hansen TK, Nørgaard A, Vestergaard H, Stahl Skov P, et al. Allergens from fish and egg. Allergy 2001; 56: 39-42.
4. Lehrer SB, Ayuso R, Reese G. Seafood allergy and allergens: a review. Mar Biotechnol 2003; 5: 339-348.
5. SOFIA. Food and agriculture organization of the United Nations corporate document repository. http://www.fao.org/sof/sofia/ indexen.htm. Accessed March 2010.
6. van der Ventel ML, Nieuwenhuizen NE, Kirstein F, Hikuam C, Jeebhay MF, et al. Differential responses to natural and recombinant allergens in a murine model of fish allergy. Mol Immunol 2011; 48: 637-646.
7. Jeebhay MF, Robbins TG, Lehrer SB, Lopata AL. Occupational seafood allergy: a review. Occup Environ Med 2001; 58: 553-562.
8. Chegini S, Metcalfe DD, Sampson HA, Simon RA. Food allergy: adverse reactions to foods and food additives. Malden (MA): Blackwell Science 2003; 487-510.
9. James JM, Crespo JF. Allergic reactions to foods by inhalation. Curr Allergy Asthma Rep 2007; 7: 167-174.
10. Villacis J, Rice TR, Bucci LR, El-Dahr JM, Wild L, et al. Do shrimp-allergic individuals tolerate shrimp-derived glucosamine? Clin Exp Allergy 2006; 36: 1457-1461.
11. Taylor AV, Swanson MC, Jones RT, Vives R, Rodriguez J, et al. Detection and quantitation of raw fish aeroallergens from an open-air fish market. J Allergy Clin Immunol 2000; 105: 166-169.
12. Goetz DW, Whisman BA. Occupational asthma in a seafood restaurant worker: cross-reactivity of shrimp and scallops. Ann Allergy Asthma Immunol 2000; 85: 461-466.
13. Sakai S, Matsuda R, Adachi R, Akiyama H, Maitani T, et al. Interlaboratory evaluation of two enzyme-linked immunosorbent assay kits for the determination of crustacean protein in processed foods. J AOAC Int 2008; 91: 123-129.
14. Faeste CK, Plassen C. Quantitative sandwich ELISA for the determination of fish in foods. J Immunol Methods 2008; 329: 45-55.
15. Taylor SL. Molluscan shellfish allergy. Adv Food Nutr Res 2008; 54: 139-177.
16. Lim DL, Neo KH, Yi FC, Chua KY, Goh DL, et al. Parvalbumin—the major tropical fish allergen. Pediatr Allergy Immunol 2008; 19: 399-407.
17. Lindstrom CD, van Do T, Hordvik I, Endresen C, Elsayed S. Cloning of two distinct cDNAs encoding parvalbumin, the major allergen of Atlantic salmon (Salmo salar). Scand J Immunol 1996; 44: 335-344.
18. Van Do T, Hordvik I, Endresen C, Elsayed S. The major allergen (parvalbumin) of codfish is encoded by at least two isotypic genes: cDNA cloning, expression and antibody binding of the recombinant allergens. Mol Immunol 2003; 39: 595-602.

19. Lopata AL, Lehrer SB. New insights into seafood allergy. Curr Opinion Allergy Clin Immunol 2009; 9: 270-277.

20. Shiomi K, Sato Y, Hamamoto S, Mita H, Shimakura K. Sarcoplasmic calcium-binding protein: identification as a new allergen of the black tiger shrimp Penaeus monodon. Int Arch Allergy Immunol 2008; 146: 91-98.

21. Ayuso R, Grishina G, Bardina L, Carrillo T, Blanco C, et al. Myosin light chain is a novel shrimp allergen, Lit v 3. J Allergy Clin Immunol 2008; 122: 795-802.

22. Garcia-Orozco KD, Aispuro-Hernandez E, Yepiz-Plascencia G, Calderon-de-la-Barca AM, Sotelo-Mundo RR. Molecular characterization of arginine kinase, an allergen from the shrimp Litopenaeus vannamei. Int Arch Allergy Immunol 2007; 144: 23-28.

23. Yu CJ, Lin YF, Chiang BL, Chow LP. Proteomics and immunological analysis of a novel shrimp allergen, Pen m 2. J Immunol 2003; 170: 445-453.

24. Ayuso R, Lehrer SB, Reese G. Identification of continuous, allergenic regions of the major shrimp allergen Pen a 1 (tropomyosin). Int Arch Allergy Immunol 2002; 127: 27-37.

25. Ayuso R, Grishina G, Ibanez MD, Blanco C, Carrillo T, et al. Sarcoplasmic calcium-binding protein is an EF-hand-type protein identified as a new shrimp allergen. J Allergy Clin Immunol 2009; 124: 114-120.

26. Elsayed SM, Aas K. Characterization of a major allergen (cod) chemical composition and immunological properties. Int Arch Allergy Appl Immunol 1970; 38: 536-548.

27. Beale JE, Jeebhay MF, Lopata AL. Characterisation of purified parvalbumin from five fish species and nucleotide sequencing of this major allergen from Pacific pilchard, Sardinops sagax. Mol Immunol 2009; 46: 2985-2993.

28. Hamada Y, Nagashima Y, Shiomi K, Shimojo N, Kohno Y, et al. Reactivity of IgE in fishallergenic patients to fish muscle collagen. Allergol Int 2003; 52: 139-147.

29. Hassan M, Wanis I, Maryam AN. Delayed clavulanic acid–induced anaphylaxis in a patient undergoing bariatric surgery. Ann Allergy Asthma Immunol 2014; 113: 324-325.

30. Asero R, Mistrello G, Roncarolo D, Casarini M, Falagiani P. True monosensitivity to a tropical sole. Allergy 1999; 54: 1228-1229.

31. Perez-Gordo M, Pastor-Vargas C, Cases B, Las-Heras MD, Sanz B, et al. New allergen involved in a case of allergy to Solea solea, common sole. Ann Allergy Asthma Immunol 2010; 104:352-353.

32. Yamada S, Nolte H, Zychlinsky E. Identification and characterization of allergens in two species of tuna fish. Ann Allergy Asthma Immunol 1999; 82: 395-400.

33. Espineira M, Herrero B, Vieites J, Santaclara F. Detection and identification of anisakids in seafood by fragment length polymorphism analysis and PCR-RFLP of ITS-1 region. Food Control 2010; 21: 1051-1060.

34. Shen HW, Cao MJ, Cai QF, Ruan MM, Mao HY, et al. Purification, Cloning, and Immunological Characterization of Arginine Kinase, a Novel Allergen of Octopus fangsiao. J Agric Food Chem 2012; 60: 2190-2199.

35. Hoffman DR, Day ED Jr, Miller JS. The major heat stable allergen of shrimp. Ann Allergy 1981; 47: 17-22.

36. Nagpal S, Pajappa L, Metcalf DD, Rao S. Isolation and characterization of heat-stable allergens from shrimp *(Penaeus indicus)*. J Allergy Clin Immunol 1989; 83: 26-36.

37. Daul CB, Slattery M, Morgan JE, Lehrer SB. Common crustacea allergens: Identification of B cell epitopes with shrimp-specific monoclonal antibodies; in Kraft D, Sehon A (eds): Molecular Biology and Immunology of Allergens. Boca Raton, CRC Press 1993; 291-294.

38. Poms RE, Klein CL, Anklam E. Methods of allergen analysis in food: A review. Food Add Contam 2004; 21: 1-31.

39. Sinanoglou VJ, Batrinou A, Konteles S, Sflomos K. Microbial population, physicochemical quality, and allergenicity of molluscs and shrimp treated with cobalt-60 gamma radiation. J Food Prot 2007; 70: 958-966.

40. Leung PS, Chow WK, Duffey S, Kwan HS, Gershwin ME, et al. IgE reactivity against a cross-reactive allergen in crustacea and mollusca: evidence for tropomyosin as the common allergen. J Allergy Clin Immunol 1996; 98: 954-961.

41. Jirapongsananuruk O, Sripramong C, Pacharn P, Udompunturak S, Chinratanapisit S, et al. Specific allergy to Penaeus monodon (seawater shrimp) or Macrobrachium rosenbergii (freshwater shrimp) in shrimp-allergic children. Clin Exp Allergy 2008; 38: 1038-1047.

42. Asero R, Mistrello G, Amato S, Ariano R, Colombo G, et al. Shrimp allergy in Italian adults; a multi center study showing a high prevalence of sensitvity to novel high molecular weight allergens. Int Arch Allergy Immunol 2012; 157: 3-10.

43. Giuffrida MG, Villalta D, Mistrello G, Amato S, Asero R. Shrimp allergy beyond Tropomyosin in Italy: clinical relevance of Arginine Kinase, Sarcoplasmic calcium binding protein and Hemocyanin. Eur Ann Allergy Clin Immunol 2014; 46: 172-177.

44. Surapon P, Orathai J, Thitinun T, Siribangon B, Richard EG. Identification of hemocyanin as a novel noncross-reactive allergen from the giant freshwater shrimp Macrobrachium rosenbergii. Mol Nutr Food Res 2011; 55: 1492-1498.

45. Guillen D, Fiandor A, Del Pozo V, Pedrosa M, Phillips-Angles E, et al. Anaphylaxis caused by hemocyanin contained in shrimp cephalothorax. Ann Allergy Asthma Immunol 2014; S1081- 1206: 00697-00698.

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