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Shadi Sadeghian

shadi.sadeghian@sickkids.ca

University of Toronto

Vicky Le Blanc

University of British Columbia

Case Report

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Incomplete clinical cross-desensitization to lobster following successful shrimp oral immunotherapy in a pediatric patient: ***a case for species-specific crustacean OIT***

Dr. Shadi Sadeghian[1], Dr. Vicky Le Blanc[2, 3]

[1] Department of Pediatrics, SickKids Hospital, University of Toronto, Toronto, ON

[2] Division of Allergy, Department of Pediatrics, Faculty of Medecine, University of British Columbia, Vancouver, BC

[3]British Colombia Children's Hospital, Vancouver, BC

Corresponding author: Shadi Sadeghian, shadi.sadeghian@sickkids.ca

Abstract

Background: Crustacean allergy is rarely outgrown, and avoidance of all crustacean species is usually advised, given that clinical cross-reactivity is high. Oral immunotherapy (OIT) with shrimp is an emerging option, and a recent case series (Schoos et al., World Allergy Organ J 2024) has suggested that a low-dose oral food challenge (OFC) allows many children to start directly at maintenance dosing (300 mg of food protein). To our knowledge, whether shrimp OIT protects against other crustaceans in pediatrics, particularly the species that caused the index reaction, has not been described.

Case presentation: A 13-year-old male presented following an episode of anaphylaxis to lobster 4 years earlier, with concurrent sensitization to shrimp, lobster, and crab. During an OFC at 12 years of age, he developed oral pruritus and uvular edema at 300 mg of shrimp protein; he therefore continued this daily dose, bypassing the OIT build-up phase. During 12 months of OIT maintenance, he had only mild intermittent oropharyngeal symptoms, in the context of exercise as a co-factor. After 12 months of shrimp OIT, serum-specific IgE decreased for shrimp (1.59 to 0.97 kU/L), lobster (1.39 to 0.89 kU/L), and crab (0.92 to less than 0.35 kU/L), and the lobster skin prick wheal decreased. He subsequently tolerated 4 g of shrimp protein during an exit OFC. Two months after liberalizing shrimp from his diet, a lobster OFC was discontinued at a cumulative 1430 mg of lobster protein because of oropharyngeal pruritus, nausea, abdominal pain, nasal congestion, and flushing, which resolved with cetirizine. Lobster OIT was therefore started at daily maintenance dose of 300 mg of lobster protein.

Conclusions: Shrimp OIT was effective in this adolescent, but desensitization to shrimp did not confer full protection against lobster. Tolerance of the treated species should not be assumed to extend to the index species, and a supervised oral food challenge to that species is advisable before the diet is liberalized. More specific component resolved diagnostics may help in risk-stratifying those patients most likely to have species-specific sensitization.

Key words: oral immunotherapy, crustacean allergy, cross-reactivity, cross-desensitization

Background:

Shellfish allergy affects an estimated 1.1% of the Canadian population (1.9% by self-report) [1]; within this category, crustaceans (shrimp, prawn, crab, lobster) account for most reactions, including anaphylaxis [2,3]. Seafood allergy seldom resolves; a Canadian cohort reported resolution rates of approximately 10% [4]. Despite this, as the landscape of evidence for disease-modifying options such as oral immunotherapy (OIT) for food allergy has expanded, there is little data for shellfish in particular [5]. As such, strict food avoidance plus an epinephrine autoinjector remains standard of care in Canada [6], which carries dietary, social, and quality of life costs [2], particularly in cultures whereby shellfish is a mainstay in the diet.

The widely quoted clinical estimate is that about 75% of patients allergic to one crustacean react to another [7], so blanket avoidance of all crustaceans is the classical advice. Tropomyosin is the well-known major crustacean allergen responsible for driving this estimate, given it is highly conserved across shrimp, crab, and lobster. The rationale for this is supported both *in vivo* and *in vitro*; Lobster tropomyosin's (Pan s 1, Hom a 1) share significant sequence homology with shrimp tropomyosin, and it has been found that preincubating serum from crustacean-allergic patients with recombinant shrimp tropomyosin removed IgE reactivity to lobster muscle extract [8].

However, other implicated allergens have been identified and are often left unconsidered, including arginine kinase, myosin light chain, sarcoplasmic calcium-binding protein, troponin C, and triosephosphate isomerase [2,3]. The literature has also started to suggest that sensitization overstates clinical reactivity: extract-based skin and serum tests for shrimp have high sensitivity but poor specificity (82% and 22.2% in one challenge-based cohort) [9], and species-specific tolerance is documented. This introduces further gray area when pan-crustacean skin testing is done, following index reaction to one single species.

The current landscape of crustacean immunotherapy takes advantage of the fact that shrimp has the highest reaction threshold of the priority allergen [10], meaning many patients can ingest a typical OIT maintenance doses on day one. A case series conducted by BC Children's Hospital collated 17 children aged 3 to 17 years undergoing low-dose OFC to 300 mg of shrimp protein, followed by ongoing shrimp 300 mg daily as maintenance OIT, with no documented OIT-related anaphylaxis [11]. Similarly, in the MOTIF phase 2 trial (12 participants, 7 to 55 years), following build-up to 1000 mg maintenance, 58.3% of patients achieved desensitization to a cumulative 4043 mg of shrimp protein, with no epinephrine use, and 7 of 8 achieved sustained unresponsiveness after 6 weeks of avoidance [12]. Practical barriers specific to shellfish OIT include taste aversion, sourcing (especially for species such as lobster and crab), and inconsistent cross-reactivity [13]. Current Canadian guidelines support OIT as a patient-centered option delivered through shared decision making, with personalization of protocols [14].

Current published shrimp OIT reports have been limited in timeframe and information regarding cross-reactivity; many stop at shrimp desensitization, and to our knowledge, none describe challenge-proven outcomes for a second crustacean species after shrimp OIT. This matters most when the index reaction was to a species other than the one used for OIT, particularly given significant practical benefits of using shrimp as the dosing food, including sourcing and cost. As such, in this case report we aim to describe an adolescent with lobster anaphylaxis who (a) started shrimp OIT at maintenance dose, (b) achieved tolerance of 4 g of shrimp protein, and (c) developed dose limiting symptoms during a subsequent lobster OFC, showing only partial cross-desensitization, to draw practical lessons on cross-desensitization.

Case Presentation:

Our patient is a 13-year-old male, followed at the BC Children's Hospital Allergy Clinic, who was referred for tertiary allergy assessment following an index episode of anaphylaxis in August 2022 after eating 2-3 bites of lobster tail. Symptoms included emesis, drooling, voice change, and dyspnea, corresponding to a World Allergy Organization (WAO) 2024 grade 3 reaction [15]. He had interestingly tolerated prawns and crab without symptoms only a few weeks prior the index reaction. He had similarly tolerated mollusks, fish, and all other priority allergens (milk, egg, wheat, peanut, tree nuts, sesame, soy).

With regard to our patient's atopic profile, he has a history of allergic rhinoconjunctivitis sensitized to house dust mite, grass, tree, and weed pollens.

Initial evaluation

Initial evaluation in December 2022 revealed serum specific IgE (ssIgE) to shrimp 1.02 kU/L; crab and lobster less than 0.35 kU/L. Skin prick tests with fresh food completed in the community prior to referral were reportedly positive to shrimp, crab, and lobster. He had continued strict avoidance of all crustaceans, carried an epinephrine autoinjector, and experienced no accidental exposures

In April 2024, at age 11, the family was counseled on the option of oral immunotherapy to protect against accidental exposures, and potentially liberalize his diet, which they enthusiastically opted to pursue. Given the cost and practical obstacles of lobster OIT, it was decided to further investigate his shrimp sensitization and use this food as the dosing agent for OIT.

Shrimp Oral Immunotherapy

In order to accurately characterize the patient's shrimp tolerance, in November 2024 (age 12), a graded shrimp OFC was completed. 15 minutes after reaching 300 mg of shrimp protein, the patient developed oral pruritus, mild throat soreness, and mildly edematous uvula. The challenge was stopped, and one dose of bilastine 20 mg was given; symptoms resolved within 15 minutes and no epinephrine was required.

A shrimp allergy was therefore confirmed, and the patient was advised to continue on daily ingestion of 300 mg of shrimp protein (1.5 g of cooked shrimp) as maintenance OIT dose. Continued avoidance of all other crustaceans and shrimp outside of OIT was advised.

Adverse events during OIT were limited to occasional mild oral pruritus in the first months of therapy, in the presence of exercise as a co-factor. Adherence was excellent, and he experienced no anaphylaxis, no epinephrine use, no emergency visits, and no symptoms of eosinophilic esophagitis.

After 12 months of maintenance OIT, he tolerated 4 g of shrimp protein without symptoms. He was therefore advised to continue with regular shrimp ingestion to maintain tolerance, at least 2-3 times weekly. He reported one occasion of unsupervised intake of small amounts of crab (about one sushi roll) without reaction.

Serial allergy testing

Aeroallergen skin prick tests in November 2024 showed sensitization to grass pollen (10 x 15 mm), weed pollen (5 x 9 mm), tree pollen mixes (3 to 4 mm), and dust mite mix (4 x 4 mm); dog, cat, and mold were negative. Serial crustacean ssIgE and skin prick test results before and after shrimp OIT are shown in Table 1.

Table 1 Serum specific IgE and skin prick test results before and after shrimp oral immunotherapy

Test	November 2024 (before OIT)	April to May 2026 (after shrimp OIT)
Shrimp ssIgE (kU/L)	1.59	0.97
Lobster ssIgE (kU/L)	1.39	0.89
Crab ssIgE (kU/L)	0.92	less than 0.35
Shrimp skin prick wheal (mm)	5 x 7[a]	4 x 5[a]
Lobster skin prick wheal (mm)	5 x 12[a]	5 x 5[a]
Crab skin prick wheal (mm)	3 x 5[a]	2 x 2[a]

ssIgE, serum specific immunoglobulin E; OIT, oral immunotherapy. Skin prick test wheals are reported as width x length (mm). From 2024 to 2026, shrimp ssIgE decreased by 39%, lobster ssIgE by 36%, and crab ssIgE became undetectable.

[a]Skin prick tests in 2024 and 2026 used commercial extracts

Lobster OFC:

At age 13, in May 2026, representing the 2 month-mark after completing shrimp exit OFC, a lobster OFC was completed. The goal was to determine whether his shrimp desensitization had conferred protection against lobster, which was the culprit for his initial anaphylaxis reaction.

The plan was to conduct OFC with grilled lobster tail, and planned doses 30, 100, 300, 1000, and 3000 mg of lobster protein at 15-minute intervals.

Table 2 Graded lobster oral food challenge: doses, timing, and observed symptoms

Step	Time	Lobster tail (g)	Lobster protein (mg)	Observations
1	09:08	0.15	30	None
2	09:30	0.5	100	Mouth itch 2/10, resolved in 5 minutes

3	09:49	1.6	300	Itchy mouth and right cheek flushing (resolved in 6 minutes); mild nausea 14 minutes after the dose; interval extended
4	10:25	1.6	300 (planned 1000)	Dose repeated by shared decision; mild, tolerable symptoms
5	10:56	3.7	700	Increased oropharyngeal pruritus, nausea, nasal congestion, mild flushing; challenge stopped at the family's request

OFC, oral food challenge. Doses were given as grilled lobster tail. Steps 4 and 5 were reduced from the planned 1000 mg and 3000 mg of lobster protein by shared decision-making. The cumulative dose ingested was 1430 mg of lobster protein (7.55 g of lobster tail).

The patient tolerated a cumulative dose of 1430 mg of lobster protein prior to developing dose-limiting reaction (mild flushing, oral pruritus, nausea, nasal congestion). His vital signs were stable throughout: oxygen saturation 97%, heart rate 54-70 beats per minute; no emesis, urticaria, or respiratory compromise. Reaction was responsive to cetirizine 10 mg orally; no epinephrine was required. The emergence of reaction at a threshold above a typical OIT maintenance dose, suggested partial (but incomplete) cross-desensitization.

The family wished to start lobster OIT the same day at 300 mg of lobster protein (1.5 g of grilled lobster) once daily. Shrimp ingestion also continued at least weekly. Crab was liberalized in the context of negative investigations, absence of clinical reaction, and tolerance of a small amount.

Discussion:

Our case presentation integrates various questions and gaps in the realm of shellfish and crustacean allergy management, which are particularly striking when compared to other more commonly studied food allergens (such as cross-reactive tree nuts). The central question it raises is why desensitization to shrimp did not fully extend to lobster, the latter being the species responsible for the index reaction.

Experience with tree nut OIT suggests that cross-desensitization depends on the degree of shared epitopes. For instance, it is well known that cross-desensitization between walnut and pecan is still observed when only one of the two foods is included in OIT regimen [16]. Walnut is the logical treatment food in this pair, and this is what is done often in practice: *in vitro,* walnut completely blocks IgE binding to pecan, whereas pecan only partly blocks binding to walnut in some patients, indicating that pecan carries a subset of walnut determinants [17]. Extending this to crustaceans, treating with the species that carries the broader epitope set, or with the index species itself, may give more complete protection. However, it's important to note that unlike tree nuts, whose clinically relevant allergens are concentrated in a few seed storage protein families, crustaceans are whole animals with a broader and more heterogeneous allergen repertoire [3,18].

Tropomyosin, a muscle protein that is highly conserved across species, accounts for much of the IgE cross-reactivity within the class [3,8,19]. However, allergen content of crustaceans varies between species, and even within a species. A proteomic comparison of black tiger and whiteleg prawns found prominent presence of species-specific allergen variants, with myosin light chain, arginine kinase, and sarcoplasmic calcium-binding protein present more abundantly than tropomyosin [20]. In another study, transcriptomic analysis of 5 commonly eaten shrimp species identified up to 39 previously unreported allergens [18]. Within a single shrimp species, tropomyosin abundance varied by up to 13-fold depending

on geographic origin [21], and in a freshwater crayfish, allergen distribution differed by body part [22]. Complimenting these findings, from a clinical perspective, studies have found that tropomyosin is recognized by only 50 to 80% of shrimp-allergic patients [23]. In fact, in an Italian multicenter study 53% of shrimp-allergic patients did not react to tropomyosin [24]. A recent case report in an adult further suggests that species-selective allergy exists: the patient had challenge-proven selective lobster allergy, and their isolated serum did not recognize purified shrimp tropomyosin [25]. Together, these data suggest that assuming crustacean-wide allergy after reaction to one species may not be necessary.

While the evidence above points towards the existence of clinically relevant allergens beyond tropomyosin, it is possible these commonly exist in addition to tropomyosin sensitization, rather than these being mutually exclusive. Various features within our patient's history suggest a sensitization pattern representative of both tropomyosin and non-tropomyosin sensitization: the first IgE profile was discordant with history (shrimp positive, lobster negative), he is house dust mite sensitized, and on a lobster OFC our patient was able to ingest 1430 mg lobster protein before dose-limiting reaction (in contrast to anaphylaxis at the index event). In addition, from a biomarker perspective, following shrimp OIT, lobster ssIgE fell 36%, the lobster skin prick test wheal shrank from 5 x 12 to 5 x 5 mm, and crab ssIgE became undetectable.

Competitive inhibition assays between shrimp and lobster extracts, or validated component-resolved testing, could identify in advance which patients need species-specific OIT [26,27]. Component tests have outperformed extract-based sIgE for shrimp (area under the curve 0.77 to 0.96 versus 0.70 to 0.75), although the most informative component differed between populations [27]. Unsurprisingly, they are not yet a substitute for challenge: in 204 children challenged with shrimp, tropomyosin sIgE predicted the outcome no better than shrimp sIgE, and the authors concluded that the oral food challenge remains essential [28]. Future component panels would also need to include species-specific allergens, such as lobster-specific tropomyosin's (Hom a 1 in American lobster and Pan s 1 in spiny lobster), myosin light chain (Hom a 3), and troponin C (Hom a 6) [8,29]. Until better predictors are available, tolerance of the treated species should not be assumed to extend to the index species, and a supervised challenge to the index species is advisable before crustaceans are liberalized.

Conclusion:

This case shows that shrimp OIT started directly at a maintenance dose can be safe and effective in an adolescent with crustacean allergy, but that desensitization to shrimp does not guarantee protection against the species responsible for the index reaction. After 12 months of shrimp OIT, our patient tolerated 4 g of shrimp protein and showed falling lobster and crab sensitization, yet still developed dose-limiting symptoms during a lobster OFC, although these were milder than his index reaction. We therefore suggest a supervised OFC to the index species before the diet is liberalized. Prospective studies reporting challenge-proven outcomes for untreated crustacean species, together with validated component-resolved and inhibition testing, are needed to identify which patients require species-specific OIT.

List of Abbreviations

IgE: immunoglobulin E

OFC: oral food challenge

OIT: oral immunotherapy

ssIgE: serum specific immunoglobulin E

WAO: World Allergy Organization

Declarations

Ethics approval and consent to participate: Single-patient case report describing routine clinical care; formal research ethics board not required.

Consent for publication: Written consent provided by the patient and his parent for dissemination of his case

Availability of data and materials: Data sharing is not applicable; no datasets were generated or analyzed. All relevant clinical data are included in the article

Competing interests: VL has participated in clinical trials for RAPT Therapeutics and ALK-Abello and has received a speaker honorarium from Novartis. SS declares that they have no competing interests.

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Authors' contributions

• SS: conceived the report, reviewed the chart, and drafted the manuscript

• VL: provided clinical care, performed the oral food challenges, supervised the work, and critically revised the manuscript

• All authors read and approved the final manuscript

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