

### Oral allergy syndrome in shrimp and house dust mite allergies

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#### Clinical Implications

- Pollen food allergy syndrome is due to cross-reactivity between plant inhalant and food allergens, causing self-limited oropharyngeal mucosal symptoms. Clinicians should be aware of mite shrimp allergy syndrome with similar symptoms due to cross-reactivity of invertebrate inhalant and food allergens.

#### TO THE EDITOR:

Pollen food allergy syndrome (PFAS) is a condition characterized by symptoms localized in the oropharyngeal mucosa that are self-limited. It results from IgE cross-reactivity between inhalant allergen sensitization and labile food proteins due to highly conserved homologous protein structures, and it is also known as a class 2 food allergy (FA).<sup>1</sup> This is in contrast to class 1 FA, in which sensitization occurs primarily through the gastrointestinal tract, but also through the skin and airway. In class 1 FA, symptoms can result in life-threatening anaphylaxis.<sup>1</sup> The term “oral allergy syndrome” was the previous terminology used to describe PFAS.

PFAS is a common manifestation of FA in adolescents and adults, coinciding with a higher prevalence of allergic rhinitis (AR) in this age group.<sup>2</sup> Although PFAS has been described, there is little data on shellfish cross-reactivity with animal inhalants, like house dust mite (HDM) tropomyosin. Inhalant exposure to tropomyosin is considered the primary sensitizer for shellfish allergy.<sup>3,4</sup> In fact, oropharyngeal symptoms are frequently reported among adult shellfish allergic patients and in challenge-proven shrimp-allergic and -tolerant patients.<sup>3,5</sup> However, it is not known whether symptoms in patients with oropharyngeal symptoms to shellfish are self-limited, similar to PFAS or whether they are the initial presentation of a systemic reaction. Here, we report a series of pediatric and adult patients with self-limited symptoms localized in the oropharyngeal mucosa during a shrimp oral food challenge (OFC).

Four patients aged 17–41 years seen at the Food Allergy Clinic of Texas Children’s Hospital and Baylor College of Medicine from July 2014 to June 2016. They were noted to have symptoms by history consistent with PFAS. All 4 patients had AR and 2 patients had asthma. The 2 patients with asthma began allergen immunotherapy to pollen and HDM after the diagnosis of shrimp allergy. Their symptoms by history were all localized to the oropharyngeal mucosa and included immediate lip swelling/tingling/itching, tongue swelling/tingling/itching, throat swelling, and difficulty swallowing. All patients had skin prick test (SPT; >3-mm wheal considered as positive) and specific IgE (sIgE) testing for shrimp and HDM and the components at the time of the OFC. An sIgE level of >0.10 kU<sub>A</sub>/L was considered as a positive test. There were no data available on SPT nor on sIgE to shrimp at the time of shrimp allergy diagnosis. All 4 patients

underwent a shrimp OFC using a medium-sized shrimp (11 g per 1 shrimp), to reassess and confirm the diagnosis of shrimp allergy. The challenge protocol includes 5 doses starting with 2 g or one-fifth of a shrimp with doubling doses every 15 to 20 minutes until a final dose of 32 g or approximately 3 shrimp is consumed.

Patient 1 complained of itchy throat after ingesting 4 g (two-fifths of a medium-sized shrimp) that resolved immediately but recurred after ingestion of 8 g (two-thirds of 1 shrimp). No other symptoms occurred, and she was closely observed with no intervention. She proceeded to complete the OFC, ingesting a total cumulative dose of 64 g (6 medium shrimp). Patient 2 complained of difficulty swallowing after ingestion of 8 g of shrimp (two-thirds of 1 shrimp). This symptom resolved after drinking water, and the patient was able to complete the entire OFC. Patient 3 complained of itching and a tingling lip sensation after ingestion of 4 g (two-fifths of 1 shrimp). No lip or tongue swelling was noted on physical examination. Symptoms resolved before the next dose of 8 g (two-thirds of 1 shrimp), and the patient completed the entire OFC with no further symptoms. Patient 4 complained of itchy lips and throat after the first 2-g dose (one-fifth of 1 shrimp) that persisted after the next dose of 4 g (two-fifths of 1 shrimp). Symptoms resolved with no complaints after ingestion of 8 g (two-thirds of 1 shrimp) but then complained of nausea after the 16 g (1½ of 1 shrimp) that resolved after drinking water. He completed the OFC with no progression of symptoms. None of the patients had symptoms at doses less than 2 g.

Patient 1 had a negative SPT to shrimp extract and cooked shrimp but a positive SPT to fresh shrimp and HDM. Patients 2 and 3 had positive SPTs to both shrimp extract and HDM, whereas patient 4 had a positive SPT to shrimp extract, cooked and fresh shrimp but a negative SPT to HDM. Three patients had elevated sIgE to shrimp, but all patients had elevated sIgE to at least 1 HDM protein component (cysteine protease/Niemann-Pick type C2 [NPC2] family/tropomyosin). The sIgE results were compared with 8 patients with systemic symptoms after shrimp ingestion, and there was no significant difference in the median sIgE levels to shrimp and its components as well as to HDM components between groups. This was likely due to small sample size (Table 1).

To our knowledge, this is the first series that reports symptoms consistent with PFAS or mite shrimp allergy syndrome (MSAS) observed by a supervised OFC with no progression to a systemic reaction. Since the OFC, 3 patients continued to ingest shrimp without reports of systemic reaction. Two patients admit that they still have fear every time they eat shrimp. One patient was lost to follow-up (patient 2).

The invertebrate tropomyosin is a pan-allergen that is heat stable and implicated in cross-reactivity among crustaceans, mollusks, HDM, and cockroaches because of its high amino acid sequence homology (82% to 100%) among invertebrates.<sup>6,7</sup> There may be a subgroup of shrimp-allergic patients who may only present with oropharyngeal symptoms due to inhalant tropomyosin sensitization and are not at risk of anaphylaxis, so this is an important clinical distinction. For clinicians, the confusion is in differentiating oral symptoms due to MSAS from a prelude to a class 1 FA. Being able to distinguish MSAS from class 1 FA would be helpful for clinicians to properly guide patients on outcomes,

TABLE I. Demographic data, clinic history, OFC symptoms, SPT, and sIgE results of patients

| Characteristics                                                                    | Patient 1                 | Patient 2                              | Patient 3                                      | Patient 4                           | Median sIgE*<br>(25th, 75th percentile) |
|------------------------------------------------------------------------------------|---------------------------|----------------------------------------|------------------------------------------------|-------------------------------------|-----------------------------------------|
| Age at diagnosis                                                                   | 3 y                       | 6 y                                    | 12 y                                           | 5 y                                 |                                         |
| Age at OFC                                                                         | 17 y                      | 36 y                                   | 41 y                                           | 41 y                                |                                         |
| Atopic conditions                                                                  | Asthma, allergic rhinitis | Asthma, allergic rhinitis              | Allergic rhinitis                              | Allergic Rhinitis                   |                                         |
| History of reaction                                                                | Lip swelling and itching  | Throat swelling, difficulty swallowing | Lip and throat itching, tingling, and swelling | Lip and throat itching and swelling |                                         |
| Symptoms during OFC                                                                | Itchy throat              | Difficulty swallowing                  | Itchy and tingling sensation of lips           | Itchy lips and throat; nausea       |                                         |
| Skin prick test (SPT) to shrimp                                                    | Negative                  | Positive                               | Positive                                       | Positive                            |                                         |
| Skin prick to prick to fresh shrimp                                                | Positive                  | Not done                               | Negative                                       | Positive                            |                                         |
| Skin prick to prick to cooked shrimp                                               | Negative                  | Negative                               | Negative                                       | Positive                            |                                         |
| SPT to house dust mite                                                             | Positive                  | Positive                               | Positive                                       | Negative                            |                                         |
| Total IgE (kU <sub>A</sub> /L)                                                     | 1391                      | 1110                                   | 32                                             | 55                                  | 582.5 (43.5, 1250.5)†                   |
| Specific IgE (sIgE) to shrimp                                                      | 33.1                      | 52.8                                   | <0.10                                          | 3.32                                | 18.21 (1.66, 42.95)†                    |
| sIgE to <i>rPen a 1</i> (kU <sub>A</sub> /L; tropomyosin)                          | 22.5                      | 33.8                                   | <0.10                                          | 0.27                                | 11.39 (0.14, 28.15)†                    |
| sIgE to <i>rPen m 2</i> (kU <sub>A</sub> /L; arginine kinase)                      | 26.9                      | 16.8                                   | <0.10                                          | 0.16                                | 8.48 (0.08, 21.9)†                      |
| sIgE to <i>rPen m 3</i> (kU <sub>A</sub> /L; myosin light chain)                   | 0.11                      | 1.5                                    | <0.10                                          | 3.44                                | 0.81 (0.06, 2.47)†                      |
| sIgE to <i>rPen m 4</i> (kU <sub>A</sub> /L; sarcoplasmic calcium binding protein) | <0.10                     | 2.43                                   | <0.10                                          | <0.10                               | 0.33 (0, 1.54)†                         |
| sIgE to <i>rPen m 6</i> (kU <sub>A</sub> /L; troponin C)                           | <0.10                     | <0.10                                  | 0.12                                           | <0.10                               | 0 (0, 0.06)†                            |
| sIgE to <i>Der p 1</i> (kU <sub>A</sub> /L; cysteine protease)                     | 84.9                      | 38.6                                   | 2.56                                           | <0.10                               | 20.58 (1.28, 61.75)†                    |
| sIgE to <i>Der p 2</i> (kU <sub>A</sub> /L; NPC2 family)                           | 97.5                      | <0.10                                  | <0.10                                          | <0.10                               | 0 (0, 48.75)†                           |
| sIgE to <i>Der p 10</i> (kU <sub>A</sub> /L; tropomyosin)                          | 84.9                      | 46.1                                   | <0.10                                          | 0.25                                | 23.18 (0.13, 65.5)†                     |

OFC, Oral food challenge.

\*Median IgE was compared with 8 patients with systemic symptoms after shrimp ingestion: total IgE = 679.5 (563, 840.5); shrimp sIgE = 10.8 (4.54, 55.9); *rPen a 1* = 5.55 (1.79, 54.86); *rPen m 2* = 5.29 (0.13, 22.3); *rPen m 3* = 0 (0, 0.84); *rPen m 4* = 0 (0, 1.02); *rPen m 6* = 0.22 (0, 7.55); *Der p 1* = 2.8 (0, 23.4); *Der p 2* = 20.45 (0, 69.25); *Der p 10* = 7.03 (3.02, 43.5).

†*P* > .05 compared with patients with systemic symptoms after shrimp ingestion.

risks, and treatment, including the need for epinephrine. It has been hypothesized that HDM tropomyosin causes primary sensitization followed by allergic reactions on shrimp ingestion. However, primary sensitization to heat-labile proteins may also result in mild and self-limited symptoms, as in PFAS. Patients with sensitization to heat-stable proteins such as lipid transfer protein often have a higher risk of systemic reaction. Currently, the shrimp protein components available for testing are all heat-stable proteins except for arginine kinase (*rPen m 2*), which is a heat-labile protein and was elevated in 3 of our 4 patients. Other minor shrimp component proteins may also play a role because the homology between shrimp and HDM/cockroach is very high.<sup>8</sup> Moreover, tropomyosin was not found to be the major allergen involved in mite-sensitized individuals.<sup>9</sup> Further studies involving a larger number of patients with inhibition studies and blinded food challenges to determine the significance of cross-reactions should be performed to describe and understand more about MSAS between animal and food allergens.

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No funding was received for this work.

Conflicts of interest: The authors declare that they have no relevant conflicts of interest.

Received for publication February 11, 2018; revised March 22, 2018; accepted for publication April 15, 2018.

Available online May 8, 2018.

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2213-2198

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<https://doi.org/10.1016/j.jaip.2018.04.035>

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