

Shrimp allergy: Gastrointestinal symptoms commonly occur in the absence of IgE sensitization

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Clinical Implications

- Of 38 shrimp-sensitive patients, 8 (21%) suffered exclusively from gastroenterological symptoms that were delayed in time after shrimp ingestion and had no or minimal IgE antibodies. These patients resemble infants with food protein–induced enterocolitis syndrome (FPIES) and may represent an adult FPIES counterpart.

TO THE EDITOR:

Shellfish allergy affects 2% of the adult US population and up to 3.1% of adults, aged 41–60 years.¹ Reactions include classical immediate hypersensitivity symptoms, such as urticaria, angioedema, dyspnea, and, in some cases, anaphylaxis. Some patients are able to consume shellfish, but later they experience only gastrointestinal symptoms such as nausea, abdominal cramps, diarrhea, and vomiting. These patients resemble infants and young children with food protein–induced enterocolitis syndrome (FPIES).²

As part of a study of T-cell epitopes to shrimp tropomyosin,³ 38 individuals with a history of reactions to ingestion of shrimp were recruited through flyers and newspaper and television advertisements. The major species of shrimp ingested by patients in Utah and specifically in the Wasatch front (the area of greatest population density in Utah) at the time of this investigation was the giant tiger shrimp (*Penaeus monodon*). We determined this information by phone calls to local fish markets and to fish importers in California. All of these patients were interviewed in person by the first author.

Percutaneous testing was performed using extracts of shrimp (*Litopenaeus setiferus*, *Farfantepenaeus aztecus*, and *Farfantepenaeus duorarum*), crab, lobster, mollusks, and fish species, saline as a negative control and histamine as a positive control (Greer Laboratories, Lenoir, NC). Serum total and specific IgE levels were measured using the ImmunoCAP system. The Institutional Review Board at the University of Utah approved the protocol.

Of the 38 subjects, 30 had histories of immediate reactions, including pruritus, erythema, and angioedema, within minutes of shrimp exposure. Of the 30, 22 (73%) had positive immediate skin prick tests and elevated IgE antibody levels to shrimp, other shellfish and shrimp tropomyosin, and these results have been reported separately as part of a report on T-cell tropomyosin epitopes.³ Only 7 (23%) of these 30 patients suffered from gastrointestinal symptoms, including 1 with only nausea and 6 with emesis, abdominal pain, or diarrhea. Remarkably, some patients suffered from severe anaphylaxis with vascular collapse in the absence of gastrointestinal symptoms.

A total of 8 (21%) of the shrimp-sensitive patients suffered exclusively from gastroenterological symptoms, including nausea,

vomiting, abdominal pain, and diarrhea (Table I). These patients differed strikingly from the prior group in that they were able to ingest shrimp without immediate consequences, and most suffered from abdominal symptoms only hours later. The clinical pattern is well exemplified by patient 4. She ate approximately 12 shrimp around 9:30 PM. She awakened 4.5 hours later with nausea, crampy abdominal pain, and ensuing emesis and diarrhea. Over the next 15 hours, she vomited at least 10 times and had 8 episodes of diarrhea. She was then anorectic for the following 2 days. She subsequently experienced approximately 5 more comparable reactions with similar onset, length, and severity. Although she suspected food poisoning, her husband tolerated the shrimp ingestion on all of these occasions.

Table I summarizes the characteristics of the subjects and the reactions they experienced. Of the 8 subjects, 7 were female. The first episodes began early in life before age 21 in 4 subjects, and only in 2 subjects during childhood (below age 13). Some subjects had tolerated shellfish ingestion early in life only to experience symptoms in their 50s and 60s. Most subjects discovered the relationship between shellfish ingestion by trial and error; subject 2 had many reactions early in life. Overall, the symptoms were stereotypic with abdominal pain, nausea, emesis, and diarrhea. In some cases, the diarrhea was impressive, and subjects were confined to the bathroom for hours. Worthy of mention is the absence of skin symptoms, such as urticaria or angioedema, or respiratory symptoms, such as rhinitis or wheezing. Although shrimp was implicated most frequently, all shellfish appear capable of provoking these reactions. After shellfish ingestion, symptoms occurred on average approximately 2 hours after ingestion with a range from 30 minutes to 5 hours. In some instances, symptoms continued as long as 24 hours; the average length of symptoms was approximately 8 hours. Most subjects were not atopic, although subjects 6–8 suffered from allergic rhinitis and conjunctivitis (and asthma in subject 8). Many ate considerable amounts of shrimp before a reaction; subject 5 ate 8 jumbo shrimp and enjoyed them before becoming ill 5 hours later. Subject 6 ate 15–20 shrimp before becoming ill. Subject 8 graded her abdominal pain at 7/10 (in comparison to childbirth at 10/10). Presently, most avoid all shellfish. However, subject 1 tolerates oysters, and subject 5 is able to eat crab without symptoms.

Results of analyses for skin testing and total IgE and IgE antibodies are shown in Table II. Only results for shellfish are shown; tests for IgE antibodies to tuna, salmon, mackerel, and trout were uniformly negative. Only 1 individual (subject 1) had a positive percutaneous test to shrimp. This subject failed to show elevated IgE antibodies to shellfish, and she and subject 3 had low total IgE protein levels. Subject 7 also had a minimal increase of IgE antibodies to shrimp and crab, and clinically had reactions to ingestion of these foods with delayed onset. None of the remaining subjects had positive skin tests or elevated IgE antibody levels. The absence of evidence for IgE reactivity distinguishes these patients from those who developed typical food allergy as adults with positive skin tests especially to shellfish.⁴

Our data indicate that a surprisingly high proportion of adult patients with histories indicative of shrimp reactivity experience

TABLE I. Patient and reaction characteristics

Patient	Age	Gender	Age at onset	No. of reactions	Symptoms	Shellfish implicated	Onset of symptoms after ingestion	Length of symptoms (h)
1	69	F	19	2	Abdominal pain, emesis	Shrimp	2-4 h	9-24
2	57	F	Before age 12	Many, up to 100	Abdominal cramping, diarrhea	Scallops, shrimp	20 min	2
3	38	F	13	5	Emesis, abdominal pain, diarrhea	Shrimp, crab	2 h	Many hours. At age 15 missed 2 days' school
4	36	F	35	6	Emesis, abdominal pain, diarrhea	Shrimp	4 h	15
5	65	F	62	2	Nausea, emesis, abdominal pain	Shrimp	5 h	2-3
6	23	M	20	6	Abdominal pain, diarrhea	Shrimp, mussels, scallops, lobster	1 h	2-3
7	65	F	19	6	Emesis, diarrhea	Shrimp, crab avocado	2-3 h	4-6
8	41	F	21	5	Nausea, emesis, abdominal pain	Shrimp, scallops, abalone, clam	0.5-3 h	4-24

TABLE II. IgE protein and antibody levels

Subject	Prick test	Total serum IgE (IU/mL)*	IgE antibodies to					
			Shrimp	Lobster	Crab	Clam	Oyster	Scallop
1	+	3	<0.35	<0.35	<0.35	<0.35	<0.35	<0.35
2	—	22	<0.35	<0.35	<0.35	<0.35	<0.35	<0.35
3	—	4	<0.35	<0.35	<0.35	<0.35	<0.35	<0.35
4	—	114	<0.35	<0.35	<0.35	<0.35	<0.35	<0.35
5	—	69	<0.35	<0.35	<0.35	<0.35	<0.35	<0.35
6	—	163	<0.35	<0.35	<0.35	<0.35	<0.35	<0.35
7	—	107	0.47	<0.35	0.62	<0.35	<0.35	<0.35
8	—	138	<0.35	<0.35	<0.35	<0.35	<0.35	<0.35

Bold indicates statistical significance.

*International units per mL.

only gastrointestinal symptoms in the absence of or minimal evidence of IgE sensitization. The existence of late reactions to shellfish ingestion is mentioned in a current review,⁵ but the marked propensity for the gastrointestinal tract in the absence of cutaneous or respiratory symptoms and IgE sensitization is not. Even the scholarly textbook review of food allergy⁶ fails to mention this form of shellfish reactivity in adults. Seemingly the most comparable syndrome is FPIES.⁷ Yet in these adult patients, sensitivity persists over decades whereas in children with FPIES it commonly wanes. Overall, the occurrence of these patients indicates the existence of a food-related clinical syndrome evidently not IgE related. Our findings are in agreement with the case report on an adult who experienced symptoms strikingly similar to our patients⁸ and the comprehensive report on 31 patients with adult non-IgE-mediated gastrointestinal food adverse reactions.⁹ Overall, these studies support the conclusion that this is an adult form of FPIES. The original purpose of our study was the identification of shrimp tropomyosin-derived T-cell epitopes,³ and the finding of the patients reported here was a serendipitous observation from the study of subjects who responded to advertisements seeking subjects with allergy to shrimp. The report of Tan and Smith⁹ indicates that although FPIES-like reactions occur commonly to shellfish, other foods

such as bony fish, chicken, and peanuts are implicated. It seems likely that the spectrum of foods implicated in this syndrome will expand as knowledge of its existence increases. Lastly, our study is limited by its retrospective nature, the lack of objective double-blind food challenges, and the absence of a pathophysiological mechanism for these reactions.

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