Food protein–induced enterocolitis syndrome in response to salmon roe and trout roe

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Clinical implications herein, we describe the first case in the medical literature of food protein–induced enterocolitis syndrome in response to specific fish roe. (J Allergy Clin Immunol Global 2023;2:122-3.)

Key words: *FPIES, roe, salmon, trout, non-IgE, delayed*

Adult-onset food protein–induced enterocolitis (FPIES) is an increasingly described phenomenon.[1] FPIES presents with symptoms including profuse emesis and diarrhea without cutaneous or respiratory symptoms, which appear 1 to 4 hours after ingestion of a culprit food.[2-4] This can result in significant morbidity, as subsequent volume loss may progress to hypovolemia, lethargy, and circulatory shock.[4] Although typically a diagnosis of childhood, common culprits for adult-onset FPIES include crustaceans.[2,4]

Although it has been clearly delineated that IgE sensitization is not the perpetrator in acute FPIES reactions,[2] the precise pathophysiology remains unclear. Complicating matters, there has been significant overlap described between FPIES and IgE-mediated food allergy, with presence of elevated food-specific IgE being associated with persistent FPIES beyond childhood.[4] In addition, there have been conflicting reports regarding the importance of food-specific T cells, as well as questions regarding the possibility of type IV hypersensitivity playing a role.[4]

Fish roe are typically enveloped in the ovarian membrane and are commonly used as ingredients in foods such as sushi.[5,6] Although IgE-mediated reactions to fish roe have been documented both in those with preexisting fish allergy and in those without it,[5,7,8] there have been no published cases of FPIES reactions to fish roe.

We describe the case of a 54-year-old female with recurrent episodes that are clinically convincing for FPIES secondary to salmon roe and trout roe.

Abbreviation used
FPIES: Food protein–induced enterocolitis

CASE PRESENTATION

A 54-year-old female anesthesiologist presented with recurrent episodes of delayed profuse emesis and diarrhea following the ingestion of trout roe and salmon roe. Her medical history was unremarkable, she took no regular medications, and she had no preexisting history of food allergy.

The initial episode occurred following a multicourse restaurant meal. The meal contained multiple different food proteins. At the end of the 90-minute meal, she became severely nauseated. After vomiting in the restaurant restroom, she returned home, where she experienced 3 hours of profuse emesis, followed by intense chills, diaphoresis, and delayed watery diarrhea. There was no concern for angioedema, urticaria, or dyspnea. She did not seek medical care, and her symptoms resolved over the following hours. She was well the next day. No other diners who shared her meal developed symptoms of any kind.

The patient then had 4 identical episodes over the next 18 months, all after multicourse meals. The patient and her husband, both physicians, did a literature search and arrived at a suspected diagnosis of FPIES. The patient and her husband (author of this article A.B.) contacted a coauthor (H.K.), who concurred. However, identifying the triggering protein for the patient's suspected FPIES proved elusive. She regularly consumes fish, shellfish, eggs, meats, and dairy without reaction.

Her subsequent episode finally provided a clear cause-and-effect relationship in identifying trout roe and salmon roe as the culprit. The patient consumed avocado and egg on toast (a meal that she consumes regularly without issue) along with added trout roe garnish. Afterward, she developed a presentation identical to her previous 5 episodes. A thorough review of her prior triggering meals (through personal and online photos and menus) clearly identified trout roe or salmon roe as the only ingredient common to all 6 meals.

Serum-specific IgE to all potential allergens present during reactions were drawn, and component-resolved diagnostics for peanut and egg was performed (Table I). Given the presence of gluten at each of these meals, a celiac disease workup was included (Table II). These investigations yielded slightly positive IgE in response to a number of foods that the patient continues to eat (ie, false-positive results); negative IgE to fish, crustaceans, and mollusks; and a negative result of workup for celiac disease in a non–IgA-deficient patient.

REVIEW AND DISCUSSION

FPIES represents a unique form of food allergy that is believed to be distinct from IgE-mediated allergy owing to potential T-cell

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Written and verbal informed consent was obtained from the patient presented in this case regarding publishing of their case details, as well as any applicable visual elements pertaining to this case.

Disclosure of potential conflict of interest: A. Brant is the spouse of the patient described in this case report, and he documented the entirety of the clinical history. The rest of the authors declare that they have no relevant conflicts of interest.

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TABLE I. Serum-specific IgE levels and total serum IgE blood work results

Category	Result (kU/L)	Reference range (kU/L)
Total serum IgE	**154**	<114
Milk, egg, and wheat		
HEW IgE level	**0.15**	<0.10
Ovalbumin	<0.10	<0.10
Ovomucoid	<0.10	<0.10
CM IgE	<0.10	<0.10
Wheat IgE	**0.19**	<0.10
Legume and tree nut		
Peanut IgE (total)	**0.57**	<0.10
Ara h1	<0.10	<0.10
Ara h2	<0.10	<0.10
Ara h3	<0.10	<0.10
Ara h8	<0.10	<0.10
Ara h9	**0.13**	<0.10
Soybean IgE	<0.10	<0.10
Sesame IgE	**0.19**	<0.10
Walnut IgE	**0.13**	<0.10
Hazelnut IgE	**0.17**	<0.10
Cashew IgE	<0.10	<0.10
Almond IgE	<0.10	<0.10
Fish, crustacean, mollusk, and beef		
Codfish IgE	<0.10	<0.10
Salmon IgE	<0.10	<0.10
Tuna IgE	<0.10	<0.10
Shrimp IgE	<0.10	<0.10
Scallop IgE	<0.10	<0.10
Beef IgE	<0.10	<0.10

Serum-specific IgE levels were determined using the Quest Diagnostics Immunoassay. Interpretation of serum-specific IgE level (kU/L): <0.10, absent/undetectable; 0.10-0.34, very low; 0.35-0.69, low; 0.70-3.49, moderate; 3.50-17.4, high; and ≥17.5, very high. Abnormal laboratory results are bolded.
ARA h, Arapis hypogaea; *CM*, cow's milk; *HEW*, hen's egg white.

TABLE II. Results of the investigations for celiac disease

Investigation	Result	Reference range
Serum IgA level	2.74 g/L	<0.47-3.10 g/L
TTGA IgA level	<1 U/mL	<4 U/ml

TTGA, Tissue transglutaminase antibody.

recognition of certain allergens.[2-4] This debated explanation is favored by many, as it provides an explanation for the absence of typical symptoms of anaphylaxis and the delayed timing of reaction.[1,4]

Despite the prevalence of IgE-mediated fish allergy, only a small number of case series have described IgE-mediated fish roe allergy. The potential culprit in 1 such study was hypothesized to be vitellogenin in salmon (*Oncorhynchus keta*) roe, an apparently non–cross-reactive protein also present in hen's egg.[7,8] This was thought to represent sensitization to a unique antigen present in the roe itself but not present in the fish flesh.[8] In addition to this, anaphylaxis in response to fish roe may be quite species-specific, as sporadic case reports describe patients developing allergy to only 1 specific species of roe.[5,8]

One weakness in our case report stems from the lack of hospital-based oral provocation testing to confirm this allergy. This case was in keeping with proposed diagnostic criteria by Nowak-Wegrzyn et al, with delayed vomiting 1 to 4 hours after ingestion of a culprit food in the absence of other IgE-mediated symptoms, coupled with delayed diarrhea 5 to 10 hours after ingestion, pallor, and lethargy.[1] As FPIES is a clinical diagnosis, we believed that provocation testing in the setting of a convincing history was unnecessary and potentially dangerous, particularly in this patient's case. In addition, both the patient and her husband are physicians and were thus able to provide an exceptionally detailed and convincing history.

This case is believed to represent *de novo* FPIES in response to salmon roe and trout roe. Interestingly, this patient regularly consumes trout, salmon, and roe from other fish (including masago, tobiko, and ossetra caviar) with a complete absence of reactivity. This is in line with the aforementioned cases of roe anaphylaxis, in which patients have been able to tolerate the fish from which the roe originated and roe from other species without issue.[6,8] Salmon and trout are both members of the family Salmonidae,[9] perhaps explaining potential cross-reactivity in our case.

CONCLUSION

The relevance of this case is based not only on its uniqueness but also on its additional potential for further delineation of the mechanisms underlying FPIES reactions. It is clear that the reactions described by us were specific to 2 species of fish roe and demonstrated no cross-reactivity with flesh from either fish species. This could be explained by the culprit vitellogenin, which is present in roe but not in fish itself, and perhaps by reaction to a very specific linear epitope shared between salmon and trout vitellogenin. As FPIES is a poorly understood phenomenon, additional unique cases advance our body of knowledge and propel us forward in understanding the immunologic mechanisms underpinning it.

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