

Letter to the Editor

Food protein-induced enterocolitis syndrome can occur in adults

To the Editor:

Food protein-induced enterocolitis syndrome (FPIES) is a rare and potentially severe^{1,2} non-IgE-mediated food allergy. It is traditionally considered to be a pediatric disease, typically presenting during infancy, although it has been reported among older children as well.^{3,4} While most cases of FPIES resolve by age 3 years,^{1,5} there have been reports of persistence beyond age 4 years.⁶ Symptoms often persist among patients with atypical FPIES, which is associated with the presence of specific IgE to implicated food¹; however, the mechanisms and natural history of these disorders have not been clearly delineated. The most common causes of FPIES in childhood are cow's milk and soya milk.^{1,3} A wide range of solid foods have also been reported to cause FPIES in children, notably rice.^{1,3,5,7,8} Although some authors refer to a similar allergy to shellfish in adults,³ to the best of our knowledge there are no reports of FPIES in adults confirmed by oral food challenge test.

A 53-year-old man was referred to our center following 2 episodes of diarrhea and vomiting (in 2008 and 2011), which occurred approximately 4 hours after eating scallops (Mollusca: Bivalvia: Pectinidae). The patient reported a further similar episode occurring more than 20 years ago, with symptoms starting approximately 2 hours after eating clams (Mollusca: Bivalvia). We estimated that in 2008 he ingested ~60 g and in 2011 ~17 g of scallops. The patient's wife had eaten both dishes and did not experience any adverse reaction. Symptoms resolved within few hours without any specific treatment on all 3 occasions. Of note, the patient reported 3 further episodes of "food poisoning" 20 years or more previously, during one of which scallops were ingested. He had no other known scallop or clam exposure, but he has had other molluscs including mussel and oyster, other crustaceans including prawn, lobster, and various vertebrate fish without adverse reaction.

We assessed the patient's sensitization status by using the measurement of specific serum IgE and skin prick tests. Investigations revealed negative specific IgE (<0.35 kU/L) for scallop, shrimp, lobster, crab, blue mussel, squid, and tropomyosin (rPen a 1), and a conclusively negative skin prick test result to poached and raw scallop (wheal diameter 0 mm). We proceeded to carry out a graded open food challenge test with poached scallop, using 2.5 g, 5.5 g, 12 g, and 34 g (total ~12.5 g protein). The doses were administered at 30-minute intervals. Ninety-five minutes after the final dose, the patient vomited twice; this was followed 15 minutes later by profuse blood-stained diarrhea, pallor, and hypotension (77/52 mmHg). In view of the dramatic onset and severity of symptoms, IgE-mediated anaphylaxis was initially suspected, and the patient was treated with epinephrine 0.5 mg intramuscularly, chlorphenamine 10 mg intravenously, and rapid normal saline infusion (1700 mL). He recovered completely within 90 minutes of treatment, during which time he experienced only hypotension but did not have any further gastrointestinal symptoms.

Investigations carried out 1 hour after the onset of symptoms showed a raised white blood cell count ($14.8 \times 10^9/L$; normal

range, $4-11 \times 10^9/L$; baseline level, $6.3 \times 10^9/L$) with neutrophilia ($11.0 \times 10^9/L$; normal range, $2-7.5 \times 10^9/L$; baseline level, $4.02 \times 10^9/L$). Mast cell tryptase (4.1 $\mu g/L$), eosinophil count, and platelet count were within normal range. These laboratory findings in combination with the presence of delayed onset of predominantly gastrointestinal symptoms, hypotension, and lack of specific IgE to the incriminated food suggest that the diagnosis is likely to be FPIES to scallops.

We have advised the patient that if he experiences any severe reactions due to accidental exposure in future, he should call the emergency medical services immediately for rapid intravenous fluid administration and, if necessary, parenteral corticosteroids. Although the patient may have responded to epinephrine, the clinical improvement was likely to be due to rapid intravenous fluid administration rather than epinephrine. Hence, we are of the opinion that epinephrine autoinjector prescription is not indicated in this case. This is in agreement with the practice in infants and children; in this age group, epinephrine autoinjectors are not routinely prescribed for self-treatment.^{1,4} FPIES is not thought to be mediated by mast cells, and antihistamines are not recommended either.¹

In view of the patient's previous reaction with clams and the fact that there is significant cross-reactivity among molluscs,⁹ we have advised him to avoid all molluscs, although oral challenges to other molluscs he has tolerated previously (eg, mussels and oysters) were not carried out.

One of the potential limitations is that we carried out an open rather than a double-blind placebo controlled food challenge. However, although double-blind placebo controlled food challenge is the best way to diagnose food allergy, open food challenge in this case was sufficient because of the clear-cut objective signs of reaction. We are not aware of any previous report of FPIES to scallop or any crustaceans, but there are reports of FPIES in children with other molluscs such as clam⁸ and various fish.⁷ This case suggests that FPIES can persist through to adulthood, or it may possibly develop after an initial period of immune tolerance to the specific food.

The differential diagnosis of gastrointestinal symptoms following seafood ingestion usually includes gastroenteritis, scombrotoxin poisoning, and allergy to *Anisakis simplex*.⁹ However, this case suggests that FPIES should be considered as part of the differential diagnosis in adult patients with gastrointestinal symptoms (with or without hypovolemic shock) that occur within hours of seafood ingestion. As with other forms of FPIES, allergy to more than 1 food is possible, and so closely related foods should be introduced into the diet only under specialist supervision.

In conclusion, we report the first case of FPIES in an adult patient that was confirmed by oral food challenge, indicating that FPIES can occur not only in children but also among adults. In children there is often a significant delay in making this diagnosis,^{1,5} and it may therefore be important to consider the possibility of FPIES in adult patients with acute onset of gastrointestinal symptoms hours after ingesting a food, particularly if this has occurred on more than 1 occasion.

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REFERENCES

1. Sicherer SH. Food protein-induced enterocolitis syndrome: case presentations and management lessons. *J Allergy Clin Immunol* 2005;115:149-56.
2. Jones KD, Noimark L, Osborn M, Warner JO, Boyle RJ. A case of severe atypical food protein-induced enterocolitis syndrome. *Allergy* 2010;65:1061-3.
3. Sampson HA, Anderson JA. Summary and recommendations: classification of gastrointestinal manifestations due to immunologic reactions to foods in infants and young children. *J Pediatr Gastroenterol Nutr* 2000;30:S87-94.
4. Leonard SA, Nowak-Węrzyn A. Food protein-induced enterocolitis syndrome: an update on natural history and review of management. *Ann Allergy Asthma Immunol* 2011;107:95-101.
5. Mehr S, Kakakios A, Frith K, Kemp AS. Food protein-induced enterocolitis syndrome: 16-year experience. *Pediatrics* 2009;123:e459-64.
6. Busse P, Sampson HA, Sicherer SH. Non-resolution of infantile food protein-induced enterocolitis syndrome (FPIES) [abstract]. *J Allergy Clin Immunol* 2000;105:S129.
7. Zapatero Remon L, Alonso Lebrero E, Martin Fernandez E, Martinez Molero MI. Food-protein-induced enterocolitis syndrome caused by fish. *Allergol Immunopathol (Madr)* 2005;33:312-6.
8. Hayashi D, Aoki T, Shibata R, Ichikawa K. [Case of food protein-induced enterocolitis syndrome caused by short-neck clam ingestion]. *Arerugi* 2010;59:1628-33.
9. Woo CK, Bahna SL. Not all shellfish "allergy" is allergy! *Clin Transl Allergy* 2011;1:3.

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