CASE REPORT
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Food Protein-induced Enterocolitis Syndrome Due to Cuttlefish in a Child with Anaphylaxis to Crustaceans

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ABSTRACT

Shellfish is defined as any edible marine invertebrate and refers to crustaceans and mollusks. Crustaceans belong to the phylum Arthropods. Mollusks belong to the phylum Mollusca.

This report illustrates a rare case of a 6-year-old girl with challenge-proven acute food protein–induced enterocolitis syndrome (FPIES) to cuttlefish (phylum Mollusca, class Cephalopoda), anaphylaxis to crustaceans (phylum Arthropoda), and tolerance to other mollusks, including clams and mussels (phylum Mollusca, class Bivalvia). The association of IgE-mediated food allergy and acute FPIES seen in this case is rare.

To our knowledge, this is the first case of FPIES to cuttlefish reported in a child.

This challenge highlights the need for further research into the allergens and mechanisms underpinning FPIES at a molecular level, enabling a better understanding of cross-reactivity patterns and the development of diagnostic and predictive tests to assist in clinical practice.

Keywords: Anaphylaxis; Cuttlefish; Enterocolitis; Pediatrics; Shellfish

INTRODUCTION

Shellfish is defined as any edible marine invertebrate and refers to crustaceans and mollusks. Crustaceans belong to the phylum Arthropoda and include prawn, crab, and lobster species. Mollusks belong to the phylum Mollusca and are divided into 3 classes: bivalve (e.g., clam, scallops, mussels, oysters), gastropods (e.g., snail, abalone, lumped), and cephalopods (e.g., squid, octopus).[1]

Case Presentation

A 6-year-old female was referred to our Allergy Unit for two episodes of facial urticaria, angioedema, vomiting, and dyspnea 1 hour after eating seafood spaghetti cooked with shrimp, prawn, clam, mussel, and squid at 5 years of age. After these episodes, she had not eaten any more shellfish, but she continued to eat and tolerate bony fish. Her family was eager to find out whether she would tolerate shellfish species, as shellfish was part of their diet. She tolerated all other food groups and had no other allergic comorbidities or health issues.

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A prick-by-prick (PbP) test to boiled shrimp, prawn, lobster, clam, mussels, squid, cuttlefish, and octopus was performed. Only PbP for boiled shrimp and prawn resulted positive (3-mm wheal). Serum-specific immunoglobulin E (IgE) to shrimp and prawn was 2.54 kUA/L and 3.01 kUA/L, respectively (ImmunoCap, Phadia, Uppsala, Sweden).

The positive cut-off point was set at 0.1 kUA/L.[2] The diagnosis of anaphylaxis to crustaceans was established, and an epinephrine autoinjector was prescribed. Despite a negative skin test for bivalves and cephalopods, the patient's mother asked us to carry out an oral food challenge (OFC) to those foods in the hospital setting for fear of reactions. OFCs with a cumulative dose of 75 g of boiled clam (11 g of clam protein, equal to 0.36 g/Kg) and 94 g of boiled mussels (11 g of mussel protein, equal to 0.36 g/Kg) were conducted on 2 consecutive days with 2 hours of observation after the final dose, and they resulted negative. She was advised to reintroduce clams and mussels.

Six months later, she underwent an OFC with cuttlefish. She ate a cumulative dose of 77 g of cuttlefish (11 g of protein, equal to 0.36 g/Kg), and after 2 hours, in the absence of clinical manifestations, she was discharged with the indication to liberalize the diet for cuttlefish. However, on the way home (3.5 hours after the last dose), she developed 6 episodes of vomiting and pallor without drowsiness or cutaneous or respiratory clinical manifestations. The family did not seek urgent medical advice, and she recovered in about 1 hour. Food protein–induced enterocolitis syndrome (FPIES) to cuttlefish was suspected. She met the major and one minor criteria for FPIES based on the 2017 consensus,[3] and the challenge was deemed inconclusive.[1]

The family agreed to a diagnostic OFC for cuttlefish, which was performed 4 months later. An intravenous line was placed before starting the OFC. She ate 7 g of cuttlefish (1 g of cuttlefish protein, 10% of the full age-appropriate serving dose). After 2 hours, in the absence of clinical manifestations, another 70 g (10 g protein, 90% of the full age-appropriate serving dose) was given. After 1½ hours from the last dose, she experienced 2 episodes of vomiting within 30 minutes and became pale and lethargic. The vital signs were normal (blood pressure, 95/66 mmHg; body temperature, 36° C; heart rate, 98 beats per minute; oxygen saturation, 100% in room air). Prompt rehydration with saline solution was started and a single dose of intravenous ondansetron was administered. She fully recovered within a few hours.

The complete blood count was evaluated before starting the OFC (T_o), at the time of the reaction (before administering ondansetron) (T_1), and 4 hours after the reaction onset (T_2) (Table 1). The neutrophil count increased from 3098 cells/mm^3 at T_o to 6962 cells/mm^3 at T_2. The diagnosis of FPIES to cuttlefish was confirmed as she met the major criterion and 3 minor criteria (i.e., pallor, lethargy, and increased neutrophil count of >1500 cells/mm^3 above the baseline) of the 2017 consensus criteria for challenge outcome assessment in FPIES[3].

We advised the patient to avoid cephalopods based on FPIES to cuttlefish and crustaceans due to IgE-mediated food allergy. She continued eating and tolerating bivalve mollusks, which she had already tolerated. Written informed consent for the publication of the clinical details was obtained from the patient's parents.

Table 1. Blood cell count values at T_o (before starting the oral provocation test), T_1 (at the moment of reaction), and T_2 (at 4 hours from the reaction)

Parameters, unit of measure	T_o	T_1	T_2
Hemoglobin (g/L)	13.7	12.9	12.3
Leukocytes (cells/mm^3)	6081	5740	10270
Platelets (10^3 cells/mm^3)	201	194	201
Neutrophils (cells/mm^3)	3098	2904	6962
Lymphocytes (cells/mm^3)	3071	2405	2444
Monocytes (cells/mm^3)	299	212	462
Eosinophils (cells/mm^3)	217	132	297

mm: millimeter

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This report illustrates a rare case of a 6-year-old girl with challenge-proven acute FPIES to cuttlefish (phylum Mollusca, class Cephalopoda), anaphylaxis to crustaceans (phylum Arthropoda) and tolerance to other mollusks (calm and mussel [phylum Mollusca, class Bivalvia]).[1]

The association of IgE-mediated food allergy and acute FPIES seen in this case is rare[4], and the underlying biological mechanisms of these two entities differ widely.[5] While there have been significant advances in our understanding of the allergens involved in IgE-mediated food allergy at a molecular level, this aspect is still unknown for FPIES. In this case, one would assume that two different allergens in shellfish trigger two differential immune responses.

To our knowledge, this is the first case of FPIES to cuttlefish reported in a child. Indeed, shellfish accounts for a negligible proportion of acute FPIES cases in children, and the literature is limited to small cohorts and case reports.[4,6,7] In contrast, shellfish are the leading cause of acute FPIES in adults.[8–10] Whether this is due to different dietary habits (e.g., children not eating shellfish in many countries) or differential pathophysiological mechanisms requires further investigation.

In patients with acute FPIES to shellfish, tolerance to other shellfish species is widely variable, and previous reports include both patients who react to multiple shellfish families (suggesting a shellfish panallergen involvement), as well as patients only reacting to a particular species or class, as in our case.[4,6–10]

This case illustrates the great difficulty in predicting acute FPIES before a particular food is introduced into a child's diet, which is a common challenge in clinical practice. This is due to our lack of understanding of the predisposing factors for FPIES (which would help identify patients at risk), the lack of diagnostic or predictive biomarkers, the vast list of foods potentially involved in FPIES (many of which are perceived as uncommon allergens), and the multiple patterns of disease.[11]

This challenge highlights the need for further research into the allergens and mechanisms underpinning FPIES at a molecular level, enabling a better understanding of cross-reactivity patterns and the development of diagnostic and predictive tests to assist in clinical practice.

At present, food challenges under supervision remain the gold standard for acute FPIES diagnosis. In children with acute FPIES to a particular food within a food group (e.g., shellfish, fish, grains, or legumes), OFCs are the only means to determine tolerance to other foods within the group. As illustrated by this case, individual dietary habits, preferences, and nutritional status need to be balanced with the potential risk of reactions at the challenge in clinical decision making.

STATEMENT OF ETHICS

The code of the event report issued by Meyer Children's University Hospital is IR904-20-46755. Written informed consent for publication of the clinical details was obtained from the patient's parents.

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CONFLICT OF INTEREST

The authors declare that they have no conflict of interest to disclose in relation to this paper.

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