



Letters

Suspected severe acute food protein–induced enterocolitis syndrome caused by cow’s milk through breast milk



Food protein–induced enterocolitis syndrome (FPIES) is a non-IgE-mediated gastrointestinal food hypersensitivity characterized by profuse vomiting that is frequently associated with pallor and/or lethargy that appears within 1 to 3 hours after ingestion of the offending food. Severe cases with protracted emesis develop dehydration, hypotension, and acidosis.

A less frequent chronic form of FPIES exists, which is characterized by vomiting, diarrhea, or both and accompanied by poor growth. This form is most common in formula-fed infants younger than 4 months.¹

Breast milk has been proposed to have a protective effect based on the presence of IgA and on its content of highly digested foods; moreover, the amount of the food present in breast milk may not be enough to elicit symptoms.^{1,2} Few cases of cow’s milk (CM) or soy-induced FPIES in exclusively breastfed infants have been reported.^{3–6} A recent population-based study⁷ in Australia reported that 5% of infants had FPIES reactions while they were exclusively breastfed, although food challenges (FC) were not performed to confirm the diagnosis. All cases were caused by CM.

We describe the case of an exclusively breastfed infant who developed acute, severe FPIES induced by CM through breast milk.

An exclusively breastfed 2-month-old boy was admitted to the pediatric intensive care unit for acute onset of vomiting, followed 1 hour later by pallor and lethargy. He was found to be tachypneic (37 breaths per minute) and tachycardic (230 beats per minute), with blood pressure in normal range (104/66), and his temperature was 35.9°C. On exam, he was pale, hypotonic, and lethargic. Laboratory work up was significant for metabolic acidosis (pH 7.10; P_{CO_2} , 47; bicarbonate, 14 mmol/L; base excess, –14; lactic acid, 7 mmol/L), elevated white blood cell count ($21.17 \times 10^9/L$) with neutrophilia (neutrophil count, $9.71 \times 10^9/L$) and thrombocytosis (platelets, $505 \times 10^9/L$). Methemoglobin fraction was 1.5% (range, 0%–1.5%), C-reactive protein level was 0.12 mg/dL, and procalcitonin level was 0.09 ng/mL.

Initially, sepsis was suspected, and empiric antibiotic therapy with ampicillin, cefotaxime, and metronidazole was started. Several boluses of normal saline, 0.09%, were also administered.

Within a few hours of treatment, values returned progressively to baseline and the patient recovered.

Blood, cerebrospinal fluid, and stool culture results were ruled out. Abdominal ultrasound showed free intraluminal liquid and mucosal gut thickening, both findings compatible with enterocolitis. There was no evidence of intussusception. Neurologic study (cerebral ultrasonography and electroencephalography) results were also normal.

Forty-five minutes before this clinical episode the infant was breastfed, 1 hour after his mother had CM with corn flakes for breakfast.

Previously to this acute episode, the patient presented persistent abdominal distention and occasionally mucus stools and irritability mostly during the night. He had never received CM formula.

His family was significant for asthma with sensitization to dust mites, seafood allergy, and celiac disease in the mother. She followed a gluten- and seafood-free diet.

Concerned for acute FPIES as the cause of the infant’s illness, the patient’s mother was advised to avoid dairy products, and the patient was given an elementary formula for 2 weeks. Then, breastfeeding was restarted in the hospital setting, given the severity of the previous reaction and the possibility that food other than CM could be implicated. The infant tolerated the feeding without recurrence of symptoms and he has thrived on a diet of exclusive breastfeeding until 6 months of age.

We suspected acute CM-induced FPIES based on the clinical manifestations of vomiting, pallor, hypotension, and hypothermia, as well as the laboratory findings of metabolic acidosis, neutrophilia, and thrombocytosis. Clinical evaluation was compatible with acute FPIES. The previous chronic, clinical manifestations presented by the infant, abdominal distention, mucus stools and irritability, which resolved once his mother eliminated CM from her diet, also suggested this diagnosis.

FC were not performed after the patient was discharged given the severity of the clinical picture.

Although CM is the most frequent food involved in FPIES, reports of CM-induced FPIES through breast milk are scarce and most of them refer to chronic or less severe, acute FPIES than the case we present.^{3,4,6} Sopo et al³ suggested that the most probable initial presentation of FPIES through breast milk is the chronic form, which is not easy to diagnose. This may lead to severe, acute reactions if patient is exposed to greater amounts of the offending food, even through breast milk.

In infants with CM/soy-FPIES, breastfeeding should be encouraged and, if necessary, an extensive hydrolyzed formula is recommended.⁸ Nursing mothers do not have to avoid trigger foods while breastfeeding unless food-induced FPIES through breast milk has been documented. We decided to maintain breastfeeding given its benefits and the mother’s strong motivation to sustain it. While exclusively breastfeeding we recommended she avoid only CM.

At 6 months of age, the patient started complementary foods at home. Since children with CM- or soy-induced FPIES can have an increased likelihood of reacting to a solid food, recent international guidelines recommend starting with low- and moderate-risk fruits and vegetables, such as apple, pear, carrot, potato,

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pumpkin, and broccoli.⁸ If an infant tolerates a variety of these foods, then subsequent introduction might be more liberal. We followed these recommendations and the patient has not presented other episodes of FPIES; he is thriving within normal ranges. Only banana and legumes are being avoided since his mother noticed mucus stools and irritability in the infant when she ate these foods while breastfeeding.

In summary, we report a case of suspected acute FPIES to CM in an infant. We could not confirm it with reintroduction of CM in the maternal diet or by oral FC, given the severity of the clinical picture. Acute FPIES through breast milk may happen and can be potentially severe. In these rare cases, we believe that an individualized therapeutic approach should be made regarding maintenance of breastfeeding and foods that the mother should avoid during this period.

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Aldolase A new Crustacea allergen

Crustacean allergy is one of the most frequent causes of food allergic reactions, not just by ingestion but also by inhalation.¹ Tropomyosin is considered the major allergen and is responsible of most crustacean allergic reactions. We present a near-fatal case of anaphylaxis attributable to allergy to Crustacea with exclusive sensitization to an infrequent shellfish allergen: aldolase.

A 33-year-old patient with tree nut allergy and a history of mild bronchial asthma attributable to allergy to home dust mites was undergoing exclusive treatment with salbutamol when needed. Four years previously, he presented with facial erythema, nausea, and tachycardia after ingesting marzipan with almonds. Skin prick tests were performed at another medical center with positive results for tree nuts and Pru p 3. Since then he has followed a tree nut-free diet, although he tolerates foods with trace amounts of tree nuts.

In September 2014, he presented with facial erythema, nausea, generalized hives, inspiratory stridor, hypotension, and loss of consciousness immediately after the ingestion of shrimp, tomato, rape, bread, and clams, requiring adrenaline, intubation, and an intensive care unit stay of 2 days. He had no history of nonsteroidal anti-inflammatory drug intake or physical exercise. He has since tolerated all other foods ingested that day (tomato, rape, and bread) and all types of fish and vegetables, except for crustaceans and mollusks, which he has not eaten again.

Complementary Exploration

Food Skin Prick Tests

Food skin prick tests were positive for Pru p 3 and extracts from walnut, hazelnut, peach, and apple and negative for *Penaeus* species tropomyosin (Roxall, Bilbao, Spain) and extracts from megrim, monkfish, cod, anchovy, clam, mussel, and prawn. The results of prick by prick testing with shrimp (*Penaeus notialis*) obtained at a local market (first pricking the fresh food with the lancet and then pricking the patient's skin) were positive (5 × 5 mm).

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References

- [1] Järvinen KM, Nowak-Węgrzyn A. Food protein-induced enterocolitis syndrome (FPIES): current management strategies and review of the literature. *J Allergy Clin Immunol Pract*. 2013;1:317–322.
- [2] Leonard S, Nowak-Węgrzyn A. Food-induced enterocolitis syndrome. *Pediatr Clin North Am*. 2015;62:1463–1477.
- [3] Miceli Sopo S, Monaco S, Greco M, Scala G. Chronic food protein-induced enterocolitis syndrome caused by cow's milk proteins passed through breast milk. *Int Arch Allergy Immunol*. 2014;164:207–209.
- [4] Kaya A, Toyran M, Civelek E, Mirishoglu ED, Kirsacioglu CT, Kocabas CN. Food protein-induced enterocolitis syndrome in two exclusively breastfed infants. *Pediatr Allergy Immunol*. 2016;27:749–750.
- [5] Tan J, Campbell D, Mehr S. Food protein-induced enterocolitis syndrome in an exclusively breast-fed infant, an uncommon entity. *J Allergy Clin Immunol*. 2012;129:873.
- [6] Monti G, Castagno E, Liguori S, et al. Food protein-induced enterocolitis syndrome by cow's milk proteins passed through breast milk. *J Allergy Clin Immunol*. 2011;127:679–680.
- [7] Mehr S, Frith K, Barnes E, Campbell D, FPIES Study Group. Food protein-induced enterocolitis syndrome in Australia: a population-based study 2012–2014. *J Allergy Clin Immunol*. 2017;140:1323–1330.
- [8] Nowak-Węgrzyn A, Chehade M, Groetch ME, et al. International consensus guidelines for the diagnosis and management of food protein-induced enterocolitis syndrome: executive summary: Workgroup Report of the Adverse Reactions to Foods Committee, American Academy of Allergy, Asthma & Immunology. *J Allergy Clin Immunol*. 2017;139:1111–1126, e4.



Total IgE and Serum Specific IgE

The patient's total IgE level was 31 IU/mL. The patient's serum specific IgE had extracts from peanut, cashew, pistachio, hazelnut, almond, chestnut, mussel, clam, megrim, sole, *Anisakis* species, langust, lobster, and shrimp (<0.1 kU/L) and extracts from apple (0.32 kU/L), walnut (0.51 kU/L), and the following components: rPru p 3 (0.79 kU/L), rAra h 9 (0.32 kU/L), rJug r 3 (0.27 kU/L), rDer p 10, and rPen a 1 (<0.1 kU/L) (ImmunoCAP System, ThermoFisher, Waltham, MA).

Other Tests

Oral challenge tests with clam, almond, walnut, peanut, pistachio, hazelnut, apple, and peach were tolerated. We dismissed an oral challenge test with shrimp because of the severity of the clinical reaction presented.

Protein extracts from raw and boiled (100° C for 15 minutes) Northern brown shrimp body (*Penaeus aztecus*) were prepared by homogenization in phosphate buffered saline, dialyzation, and lyophilization.

Sodium dodecyl sulfate–polyacrylamide gel electrophoresis immunoblotting under electrophoretic reducing conditions (with 2-mercaptoethanol) was performed (Fig 1). An IgE-binding band of 38 kDa was detected in both raw and boiled *P aztecus* extracts. The immunoblot with *Penaeus monodon* tropomyosin (Pen m 1) tested negative (data not shown). IgE-binding band was extracted from the gel, and protein was identified as previously described² as fructose 1,6-biphosphate-aldolase from *P aztecus*.

Skin prick testing was performed with the *P aztecus* extract used in immunoblotting assay obtaining positive results (6 × 8 mm). Skin prick testing with this extract gave negative results in 10 dust mite allergic patients.

Discussion

Our patient presented with a life-threatening anaphylaxis after the ingestion of shellfish attributable to fructose