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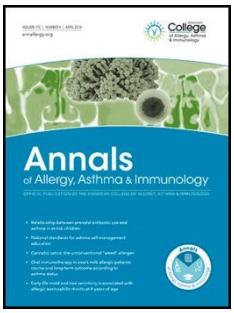

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Tittle: Suspected Severe Acute Food Protein-Induced Enterocolitis Syndrome caused by Cow's Milk Through Breast Milk

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

There is a less frequent chronic form of FPIES, presenting with vomiting, diarrhea or both, accompanied by poor growth. This form is most common in formula-fed infants younger than 4 months (1).
It has been proposed that breast milk may 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 study in Australia reported that 5% of infants had FPIES reactions while they were exclusively breast-fed. All cases were caused by CM (7).
We describe the case of an exclusively breast-fed infant who developed acute, severe FPIES induced by CM through breast-milk.

An exclusively breast-fed 2 month-old boy was admitted to the Pediatric Intensive Care Unit (ICU) presenting pallor, tachycardia, tachypnea and lethargy. Blood pressure was within normal range. One hour before he had emesis. He was afebrile. Blood tests showed metabolic acidosis (pH 7,10, pCO2 47, HCO3 14 mMol/L, base excess -14, lactic acid 7mMol/L), elevated white blood cell count (21.170 $x10^9$/L) with neutrofilia (9.710 x, $x10^9$L) and trombocytosis (platelets 505 $x10^9$L). Methemoglobin fraction was 1,5 % (range: 0-1,5), C-reactive protein 0,12 mg/dl and procalcitonin 0,09 ng/ml.

Initially sepsis was suspected and empiric antibiotic therapy with ampicillin, cefotaxime and metronidazole was started. Several bolus of normal saline 0,09% were also administered.

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

Blood, cerebrospinal fluid and stool cultures were negative. Inborn errors of metabolism were discarded. Abdominal ultrasound showed no data of intussusception but free intraluminal liquid and mucosal gut thickening, both findings compatible with enterocolitis. Neurologic study (cerebral ultrasound and electroencephalogram) was also normal.

His mother presented with bronchial asthma with sensitization to dust mites, seafood allergy and celiac disease. She followed a gluten and seafood free diet. Forty-five minutes before this clinical picture, the infant was breast-fed one hour after she had CM with corn flakes for breakfast.

Previously to this acute episode, his mother reported that the patient presented persistent abdominal distention and occasionally mucus stools and irritability mostly at nights. He had never received CM formula.

Clinical picture, laboratory findings and clinical evolution were indicative of an episode of acute and severe FPIES.

Patient's mother was recommended to avoid dairy products and the patient was placed on an elementary formula for two weeks. Then, breastfeeding was re-started at our Hospital setting given the severity of the previous reaction and the possibility that other food than CM could be implicated. He did not developed acute clinical manifestations at that moment. He is already 6 months old and he has not presented chronic or acute symptoms compatible with FPIES. He is thriving adequately while being exclusively breastfed.

Although CM is the most frequent food involved in FPIES, reports of CM-induced FPIES through breast milk are scarce (3,4,6). As suggested by Sopo et al (3), the most probable initial presentation of FPIES through breast milk is the chronic form, which is not easy to diagnose. This may lead to acute reactions if patient is exposed to greater amounts of the offending food, even through breast milk.

We suspected that CM was involved in this case of acute FPIES given the previous chronic, although mild, clinical manifestations referred by the patient's mother: abdominal distention, mucus stools and irritability that resolved once the mother eliminated CM from her diet. We decided to maintain breastfeeding given its benefits and the mother's high motivation to sustain it. While exclusive breastfeeding we recommended her to avoid only CM but not soy, since soy-induced FPIES is not as prevalent in our country as in others as the United States (US) (8). Regarding solid foods, rice is a cereal responsible for most

cases of solid-food induced FPIES in Australia and the US (2,7) but not In Spain, where fish is the most frequent solid-food involved in FPIES and it usually manifests in older infants and children (8,9). We advised the patient's mother to continue to eat rice and corn, as well as fish.

This patient is about to start complementary foods. We advised to avoid banana since her mother noticed mucus stools and irritability in the infant when she ate this fruit. First solid foods to be introduced will be lower and moderate-risk foods as apple, pear, carrot, potato, pumpkin and broccoli following international guidelines (10).

In infants with CM/soy-FPIES, breastfeeding should be encouraged and if necessary, an extensive hydrolyzed casein-based formula is recommended, although up to 10-15% of infants may not tolerate it and require an aminoacid based formula (1). It is not recommended that mothers avoid trigger foods when nursing unless a reaction after breast-feeding has been documented, as in this case.

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 food challenge, 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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