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CASE REPORT

Food protein-induced enterocolitis syndrome to trivial oral mucosal contact

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Abstract Food protein-induced enterocolitis syndrome (FPIES) is a non-immunoglobulin E (IgE)-mediated gastrointestinal food hypersensitivity, mostly in infants. Patients usually present very ill and often misdiagnosed as acute gastroenteritis, sepsis, ileus, metabolic disorders, necrotizing enterocolitis, or severe gastroesophageal reflux disease. We present a case of an infant who had three acute FPIES episodes: the first was at 5 months of age after chewing on a cellophane wrapper, the second was due to sweet potato, and the third was due to rice cereal. It was realized that in the first episode, the wrapper was covering a rice cake. Evaluation at 7 months of age, while asymptomatic, showed normal complete blood count, low serum immunoglobulin E level, and negative allergy skin prick tests, indicating non-IgE sensitivity. *Conclusion* This case of FPIES has peculiar features in that it occurred in an exclusively breastfed infant and by non-ingestant oral contact with a trivial quantity of rice allergen.

Keywords Food protein-induced enterocolitis syndrome · FPIES · Enterocolitis · Food allergy · Rice allergy · Sweet potato allergy

Introduction

Food protein-induced enterocolitis syndrome (FPIES) is a severe gastrointestinal food hypersensitivity, with typical presentation of acute repetitive vomiting, lethargy, and pallor [5, 8]. Hence, it is often misdiagnosed as acute gastroenteritis, sepsis, ileus, metabolic disorder, or necrotizing enterocolitis [7]. It primarily affects infants, but cases have been reported in older children and a few adults [4, 12]. The most commonly implicated foods are cow's milk, soy, and rice [8, 10]. We present a case of FPIES to exposure to a trivial amount of rice by indirect contact in an exclusively breastfed infant.

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Case report

A 5.5-month-old male, who was exclusively breastfed, developed acute projectile vomiting within 30 min after chewing on a piece of cellophane wrapper. Vomiting occurred every 15 min for 2 h and was associated with pallor, and lethargy, and foul-smelling mucousy diarrhea occurring 1 h after vomiting. The parents (a physician and a veterinarian) suspected he had an acute "stomach virus" and hydrated him with oral fluids. All symptoms resolved within 72 h. He was strictly breastfed and had no previous direct exposure to any other food. Two weeks later, the mother introduced pureed sweet potato (approximately a tablespoon) for the first time, and within 2 h, he developed acute symptoms similar to the previous episode, resolving within 72 h. The sweet potato was prepared at home by the mother without adding any other ingredients.

One week later, the pediatrician recommended introduction of solid foods, starting with rice cereal which the mother mixed with breast milk. Within 2 h of ingesting just a few sips, he developed an acute episode similar to the previous two, and symptoms resolved within a few days. Then it was realized that in the first episode, the wrapper he chewed on was covering a rice cake. Strict exclusive breastfeeding was recommended, and the infant was referred to us for allergy/immunology evaluation.

At our evaluation, he was 7 months old, fed breast milk only, appeared healthy, with normal vital signs, including height and weight, and without any abnormal physical

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findings. Family history revealed asthma in the father. Skin prick tests with seven food extracts (sweet potato, cow's milk, egg white, egg yolk, peanut, wheat, and soybean) were all negative, ruling out immunoglobulin E (IgE)-mediated hypersensitivity. Rice was not included in the tests for fear of a severe reaction. Laboratory tests, while he was asymptomatic, showed white blood cell count of 12.7×10^9 L, eosinophils 6 %, neutrophils 20 %, lymphocytes 69 %, hemoglobin 12 g/dL, hematocrit 34.3 %, platelets 382 k/μL, and serum total IgE level 3 kU/L (normal <10 kU/L).

In our patient, the presentation of three separate episodes was most compatible with FPIES, with rice and sweet potato as the culprit. We recommended continued breastfeeding and strict avoidance of rice and sweet potato from the diet of both the infant and mother. For supplementation, amino acid formula (Neocate Infant, Nutricia) was prescribed as a nutritionally adequate hypoallergenic diet. Also, gradual introduction of other baby foods was recommended. At 9 months of age, he was growing well with normal physical examination. There was no recurrence of symptoms or other illnesses, and he was ingesting banana and apple without any symptoms. By 12 months of age, he was able to eat various fruits, wheat, corn, dairy, and soy products. At 15 months, he had an accidental ingestion of cheese puffs (a commercial snack common in the USA; its label lists unknown quantities of corn meal, rice, sunflower, corn oil, aged cheddar cheese, whey, and buttermilk), but no adverse reaction occurred.

During the most recent follow-up at 19 months of age, the mother reported that the child has been strictly avoiding rice and sweet potato. He has also been striving well and tolerates a variety of fruits, vegetables, wheat, corn, dairy, soy, and various meats. In the future, we might consider a titrated supervised challenge to sweet potato after 2 years of age. Because his first reaction was to a very trivial exposure to rice, an intentional challenge with rice will probably not be considered before 3 or 4 years of age.

Discussion

Patients with acute FPIES usually present very ill with repetitive vomiting, diarrhea, dehydration, hypotension, and hypothermia, associated with leukocytosis, neutrophilia, and thrombocytosis [5, 7, 8]. Symptoms resolve by symptomatic supportive treatment and elimination of the causative food which is usually identified through the history of diet preceding acute episodes. Continued minor exposures can result in chronic symptoms, often misdiagnosed as severe gastroesophageal reflux disease and can lead to failure to thrive, anemia, hypoalbuminemia and eosinophilia [6].

The available information on the pathogenesis of FPIES points to a food-related acute hypersensitivity reaction that is not IgE mediated. Several immunologic cells seem to participate in the pathogenesis, but the specific mechanism remains to be elucidated [1]. Because the underlying hypersensitivity mechanism of FPIES is not clear, the diagnosis is based on the typical clinical presentation rather than on a specific test [1, 2]. Allergy percutaneous testing and serum-specific IgE are generally negative, and patch testing reliability in FPIES has not been proven [6]. A wide variety of causative foods has been reported, with cow's milk, soy, and rice being the most common [8, 10]. The causative foods in our patient were rice and sweet potato. The latter was reported in only very few cases [3, 10]. FPIES has occurred in a few exclusively breastfed infants and was related to maternally ingested food [9, 13]. In our patient, the episodes occurred from his first trivial exposure, suggesting probable previous sensitization by food excreted in breast milk. The fact that the first reaction in our patient was after chewing on a wrapper covering a rice cake indicates that the allergen threshold in FPIES can be very low. An association of FPIES with enterotoxigenic *Escherichia coli* and methicillin-resistant *Staphylococcus aureus* has been reported, suggesting that in some cases, enteral infections may play a role in the development of FPIES [11].

The natural history of FPIES can vary from few to several years [7]. Resolution may be discovered through accidental exposure or by a carefully titrated oral challenge under supervision. The starting dose should be individualized, and extra caution needs to be practiced against early challenge testing. Though our patient did not react to the rice-containing cheese puffs, we elected not to subject the child to an intentional rice challenge, particularly since the quantity and nature of processed rice in that product were unknown.

This particular case demonstrates three key points. First, food sensitization in FPIES can occur through breast milk. Second, the method of exposure to the allergen can be unusual. Third, the allergen threshold can be very low, even by trivial oral mucosal contact.

Consent

Written informed consent for publication of this case report was obtained from the patient's parents.

Conflict of Interest We declare that there are no conflicts of interest.

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