

A Case of Food Protein-Induced Enterocolitis Triggered by Wheat

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Food protein-induced enterocolitis syndrome (FPIES) is an under-recognized and frequently misdiagnosed non-IgE-mediated gastrointestinal food hypersensitivity disorder. We describe the first case of FPIES only to wheat confirmed by an oral food challenge (OFC). The male patient, who was breast fed for the first 2 months, and then was feeding with cow's milk-based formula until he became 4.5 months old, was given a *tarhana* soup (wheat and yoghurt) for the initial food trial. Two hours later, he started retching and vomited consecutively, suffering from watery diarrhea. He was taken to a medical center, where he was diagnosed acute gastroenteritis. He suffered from three more episodes after feeding wheat-containing foods. When the patient was 12 months old, an OFC with wheat was performed. Two hours after he had been challenged, he vomited repetitively, became lethargic, his systolic blood pressure dropped from 95 to 80 mm Hg and stool examination revealed eosinophils and leukocytes, which were negative before the challenge. The serum eosinophil count decreased from 460 to 270 μL and the neutrophil count increased from 2,200 to 10,500 μL at 6 h. The skin prick test with wheat extract, prick to prick test with whole wheat and serum-specific Ig E for wheat were negative. We conclude that FPIES can emerge with food in connection with eating habits or culture. In view of its potentially serious clinical course, it is critical to consider this diagnosis in young children presenting with acute onset of gastrointestinal symptoms or shock.

Introduction

FOOD PROTEIN-INDUCED enterocolitis syndrome (FPIES) is an under-recognized and frequently misdiagnosed non-IgE-mediated gastrointestinal food hypersensitivity disorder.¹ It manifests as profuse repetitive vomiting, often with diarrhea that leads to acute dehydration, lethargy,² and even shock.¹ Subjects with typical FPIES are generally younger than 9 months at the initial diagnosis. Repeated exposure to food triggers causes diarrhea and/or repetitive vomiting within a few hours. The removal of the offending protein from the diet results in resolution of symptoms, and/or a standardized oral food challenge (OFC) elicits diarrhea and/or vomiting within 24 h after administration of the food.² Early literature on FPIES focused on cow's milk and soy, the 2 most common causes of FPIES.³ However, the range of food proteins documented to cause FPIES has expanded to include meats, vegetables, and grains.^{4,5} In this study, we report a case of FPIES triggered only by wheat and discuss the literature.

Case

The male patient, who was breast fed for the first 2 months and then was fed with cow's milk-based formula

until he became 4.5 months old, was given a traditional Turkish soup called *tarhana* (made with wheat flour and milk-based yoghurt) for the initial food trial. Two hours later, he started retching and vomited consecutively, suffering from watery diarrhea. As he became infirmed, he was taken to a medical center, where he was diagnosed acute gastroenteritis (AGE) and hospitalized for 3 days. He was mildly dehydrated. At that time, his total white blood cell count (WBC) was 9,300/ μL with an absolute neutrophil count of 4,900/ μL and an eosinophil count of 186/ μL . Three days after he was discharged, he was fed with a mixture of yoghurt and baby biscuits (cow's milk, soya, sugar, egg, and cornstarch). He was taken to the same clinic with similar complaints and was hospitalized for repetitive vomiting, diarrhea, and 5%–10% dehydration for the second time. Laboratory tests showed metabolic acidosis (pH: 7.23, HCO_3^- : 7.7, and base excess: –20) and elevated WBC (39,000/ μL) with neutrophilia (neutrophils: 31,824/ μL). Stool examinations were normal. The patient's condition improved within 2 h of intravenous saline replacement.

One month later, he was given a mixture of peach and the same baby biscuits for the third food trial; a similar, but even more serious medical picture emerged, compared to the previous 2 consults. The patient was hospitalized with the complaints of repetitive vomiting, diarrhea, lassitude, and

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rapid breathing and diagnosed hypovolemic shock and acute renal failure secondary to AGE. Laboratory tests showed serum pH: 7.0 (normal 7.35–7.45), WBC: 34,400 μ L (normal 6,000–17,500) (69% neutrophil, 0.2% eosinophil), platelet: 977,000 μ L (180,00–510,000), Hb: 15.4 g/dl (normal 10.5–13.5), urea: 104 mg/dl (normal 15–44), creatinine: 1.71 mg/dl (normal 0.3–0.7), uric acid: 13.6 mg/dl (normal 3.6–8.2), and urine density: 1030. In addition to fluid and bicarbonate replacement, an antibiotic therapy was given, as sepsis could not be excluded. Sweat tests for cystic fibrosis, tandem mass and organic acid analysis of urine for other metabolic diseases proved normal. The patient was clinically stable until he was given some lentil soup pretreated with wheat flour (lentil, wheat flour, and oil) just on the day of his planned discharge. He vomited again and started diarrhea, which resolved within 2 h by fluid replacement. The patient was referred to our clinic at this stage when he was 10 months old by the pediatric gastroenterology department for a possible food allergy. He was in good general condition, his weight was 8.6 kg (10–25 percentile), and his height was 71 cm (25–50 percentile). There was no history of atopic diseases either for him or his family. Test results were WBC: 13,400/ μ L (neutrophils 27.9%, eosinophil 4.3%), serum total IgE: 161.9 U/mL. Anti-gliadin IgA and anti-tissue transglutaminase IgA were negative in the serum. Skin prick tests for wheat, cow's milk, barley, rye, rice, oats, corn, soy, peanuts, eggs, fish, and peach, and wheat-specific IgE (0.06 kUA/L, negative <0.35) in the serum proved negative. The patch test was prepared from a wheat flour suspension (1 g in 10 mL of normal saline).⁶ This was applied directly to the skin on filter paper, covered with Finn chambers for 48 h, and read at 48 and 72 h. Wheat flour patch testing was positive at 72 h.⁷ Based on the current history of the patient, wheat-induced enterocolitis was considered. Wheat, barley, rye, and foods containing them were excluded from the diet. In the interim, egg, rice, lentil, corn, potato, pear, and peach were introduced under observation and were well-tolerated. As he was already fed by cow's milk-based formula feeding without any complaints, the mentioned process was not applied to milk. After 2 months, when the patient was 12 months old, an OFC with wheat was performed to confirm the diagnosis. Before the challenge, an intravenous line was placed. According to FPIES OFC protocol,⁸ gradual (during 1 h) administration of food protein 0.06–0.6 g/kg body weight in 3 equal doses, generally not to exceed total 3 g of protein or 10 g of total food (100 mL of liquid) for an initial feeding, was recommended. We therefore calculated the total food protein according to this protocol. We used pudding as the vehicle, which consisted of wheat flour (10 g), sugar (20 g), and milk (80 mL). Two hours after he had been given milk pudding, he vomited repetitively, his systolic blood pressure dropped from 95 to 80 mm Hg, he became lethargic. He did not develop diarrhea, but the stool examination 6 h after the challenge revealed eosinophils and leukocytes, which were negative before the challenge. No blood was detected in stools either macroscopically or microscopically. The serum eosinophil count decreased from 460 to 270 μ L and the neutrophil count increased from 2,200 to 10,500 μ L at 6 h. After fluid replacement of 20 mL/kg, lethargy was improved in 1 h. His all signs returned to normal. Discharge recommendations included strict wheat grain avoidance. In addition, we eliminated barley and rye because of their close taxonomic relation to wheat.

Discussion

There are increasing reports of FPIES induced by food other than cow's milk and soy.⁹ We describe a case of FPIES only to wheat confirmed by an OFC. Up till now, wheat FPIES has been reported in 3 cases.^{10–12} In 2 of them, there were other food allergens besides wheat that were responsible for FPIES. We think that our case is an interesting solid FPIES because he tolerated milk, soy, and rice, but reacted only to wheat, which is previously reported in only 1 case.¹² Our case fulfilled the diagnostic criteria of FPIES both by history (4 distinct episodes and healthy intervals in between) and the challenge test (repetitive vomiting, increase in absolute neutrophil count >3,500 μ L, appearance of fecal neutrophil and eosinophil).⁸ Although neutrophilia is typical in the FPIES episode, our patient has a baseline high serum total IgE level and eosinophilia. This may be a sign of development of atopic diseases in the future.

Today, among solid foods and grains, FPIES is mostly associated with rice although some other cases and/or case series have been reported with chicken, turkey, lamb, fish, beef, hen's egg, short neck clam, rabbit meat, grains other than rice, legumes, fruits, and vegetables.^{4,5,9,13–15} Countries' eating habits and culture are also important in different triggering foods in FPIES.^{13,14} In Turkey, wheat and wheat products are consumed a lot. In fact, in the process of starting supplementary food, traditional tarhana soup is given even before rice or vegetable soups, which are considered to be less allergenic. Diagnosis of FPIES may be delayed as in our case. Solid food FPIES is typically diagnosed at a later age than cow's milk FPIES or soy FPIES between 4–8 months, consistent with the timing of introduction of solids.^{4,16} Delayed diagnosis of solid FPIES in particular may be due to the perception that grains, such as rice, oats, and vegetables have low allergenic potential and are not usually suspected as triggers of allergic reactions.⁴

Rice and oats are the most frequent grains reported in the etiology of solid FPIES.⁴ The coexistence of FPIES to rice and oats might also be explained by the taxonomic relationship between rice and other grains. All cereals are genetically related and come from the same subfamily, *Festucoideae*.¹⁷ However, wheat, rye, and barley are closely related and are genetically more distant from rice and oats.¹⁷ Because of the close taxonomic relationship between wheat, barley, and rye, we removed barley and rye from the diet without a challenge. We planned to wait till the age of 3 to evaluate the development of tolerance in our patient.

Although the IgE antibody to the causal food is typically not detected in FPIES, there are reports of children with FPIES with detectable IgE to the causal protein either at presentation or during follow up. These children referred as "atypical FPIES" had a more prolonged course of FPIES and some of them progressed to typical IgE-mediated sensitivity.^{2,4,14,18,19}

We conclude that FPIES can emerge with food in connection with eating habits or culture. In view of its potentially serious clinical course, it is critical to consider this diagnosis in young children presenting with acute onset of gastrointestinal symptoms or shock. The diagnosis is made on the basis of clinical criteria and/or a standardized OFC.

Author Disclosure Statement

No competing financial interests exist.

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Received for publication August 28, 2012; accepted after revision April 21, 2013.