FPIES Induced by Locust Bean Gum in an Infant

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Food protein–induced enterocolitis syndrome (FPIES) is a rare manifestation of food allergy that presents as persistent vomiting, diarrhea, lethargy, dehydration, hypotension, and hypothermia within 1-4 hours of exposure to an allergen, with no skin or respiratory symptoms.

An 11-week-old boy with chromosome 21 trisomy (23-year-old primipara, spontaneous vaginal delivery at 38 weeks' gestation, birthweight 3600 g, 9/9 Apgar score), and fed with cow's milk formula (CMF) was admitted to the emergency department due to persistent vomiting, watery diarrhea, nonresponsiveness, and drowsiness. On admission the child presented with lethargy, severe dehydration, hypotension (75/50 mmHg), anemia, high acute-phase reactant levels, metabolic acidosis, and electrolyte imbalance (Table). Fluids, electrolytes, treatment for acid-base disorders, and antibiotics were administered, and the clinical response was rapid.

While taking the history, we learned that the child had been in a residential child care community (RCCC) since birth; in the past he had been hospitalized 5 times in various centers, each time presenting symptoms similar to those described above. During the first hospitalization, he was diagnosed with sepsis and treated with antibiotic therapy and intravenous hydration. Microbiological and serological tests did not confirm bacterial or viral gastrointestinal infection. Similarly, no infectious factor was established during subsequent incidents, and metabolic acidosis, endocrine disorders, immunodeficiency, and IgE-dependent food allergy were excluded.

Based on the clinical picture, we suspected FPIES due to cow's milk protein (CMP). CMF was replaced by casein-based extensively hydrolyzed formula (EHF), which led to a fast improvement in the child's condition. Over the next 3 months the child was readmitted to our department 3 times. Owing to social circumstances, each hospitalization lasted 3 to 4 weeks; the patient returned to the hospital within 1-2 days after discharge with similar symptoms. In hospital, the child tolerated EHF well. Therefore, during the stable period, we performed an oral food challenge (OFC) with incremental amounts of CMF (up to 15 mL [0.3 g protein]). Vomiting and

Table. Laboratory Data

On first admission	Hemoglobin, 9.8 g/dL; WBC, 23 400/μL; neutrophils, 68%; CRP, 64.09 mg/L; procalcitonin, 15.58 ng/mL; pH, 7.243; base excess, 11.1; Na, 132 mmol/L; K, 3.4 mmol/L.
OFC with CMF	*Baseline*: WBC, 8 700/μL; neutrophils, 68%; CRP, 0.23 mg/L; hemoglobin, 12.1 g/dL *After OFC*: WBC, 21 200/μL; neutrophils, 68%; CRP, 52.33 mg/L; fecal calprotectin, 520 μg/g *2 weeks after OFC*: calprotectin, 90 μg/g
OFC with thickener	*Baseline*: WBC, 12 500/μL; neutrophils, 47%; CRP, 3.9 mg/L; calprotectin, 63 μg/g *After OFC*: WBC, 19 000/μL; neutrophils, 75%; CRP, 41.6 mg/L; calprotectin, 350 μg/g *2 weeks after OFC*: calprotectin, 60 μg/g

Abbreviations: CMF, cow's milk formula; CRP, C-reactive protein; OFC, oral food challenge; WBC, white blood cell.

lethargy were observed after 2 hours and diarrhea after 6 hours; laboratory tests revealed increased inflammatory marker values (Table). The child required intensive intravenous hydration. The diagnosis of CMP-induced FPIES was confirmed, and the repeated presentation aroused a suspicion of nonadherence to dietary recommendations outside the hospital. However, the RCCC team reported full adherence to medical guidance. Detailed questioning of the director and staff revealed that a thickener (locust bean gum [LBG], also known as carob gum) had been added to the EHF. Subsequently, an OFC was performed with the thickener, which was added to the EHF (0.5 g, increased to 1.0 g after 60 minutes). The patient presented with vomiting and lethargy after 100 minutes and diarrhea after 6 hours. The laboratory tests revealed elevated C-reactive protein, white blood cells, and fecal calprotectin (Table). In the follow-up, EHF was maintained, and, from the tenth month of life, the patient's diet was gradually expanded (with the first exposure to the new product in hospital settings). Rice cereals, carrot, potato, and turkey were introduced, with no pathological reaction. At the age of 3 years, the child was put up for international adoption.

Food allergy is an adverse reaction to food mediated by an immunologic mechanism, which may be IgE-mediated, non–IgE-mediated, or both IgE- and cell-mediated [1]. Negative specific IgE to the suspect food does not rule out allergy.

FPIES is a non–IgE-mediated form of food allergy. Most patients have undetectable food sIgE, although sIgE may be present at diagnosis or develop during follow-up in 2%-20% of patients. The pathophysiology of the disease has not been fully explained [2,3].

The most common allergens causing FPIES include cow's milk, soya, rice, and oats [2,3]. Katz et al [4] estimated the incidence of CMP-induced FPIES at 0.34% [4], while reports of allergic reactions caused by LBG are rare. To the authors' knowledge, the only case report of allergy to carob was published by Savino et al [5], who described a 5-month-old infant with acute IgE-mediated allergic reaction to LBG. A characteristic feature of FPIES is the absence of skin lesions and respiratory symptoms [2], as in the case we report, where the patient experienced manifestations typical of the acute form of the syndrome: recurring, persistent vomiting (1-4 hours after exposure), diarrhea, pallor, lethargy, hypotension, and laboratory abnormalities. The chronic form of FPIES entails periodic vomiting, chronic diarrhea, and failure to thrive [2,6].

Diagnosis of FPIES is based on detailed history taking and confirmed by resolution of symptoms after eliminating the trigger. Although the OFC remains the diagnostic gold standard for food allergy, in case of FPIES with clear clinical manifestations, the procedure may be avoided [2]. In the present case, owing to the inconsistency between the medical history and clinical presentation, as well as to a very rare possible trigger (thickener), we decided to perform the challenge.

The differential diagnosis of acute FPIES is complex, including anaphylactic shock, sepsis, gastroenteritis, necrotizing enterocolitis, pyloric stenosis, allergic colitis, IgE-dependent food allergy, and intussusception [2,3,7]. The present case appears to be the first description of FPIES triggered by LBG in an infant.

LBG (food additive code, E410) is used as a thickener in antireflux milk formulas [8]. It is also used as a stabilizer and emulsifier in the food industry. We report that LBG may cause a life-threatening reaction in the form of acute FPIES in children. In the present case, elevated fecal calprotectin concentrations and their normalization during remission were recorded during OFC. Calprotectin is a sensitive marker of gastrointestinal inflammation and is assessed mainly in inflammatory bowel disease [9,10]. We observed a considerable increase in the protein concentration after the OFC and subsequent normalization, thus indicating that calprotectin might be a useful objective marker of mucosal barrier damage in monitoring an OFC in FPIES.

The diagnostic dilemmas in the case we report were caused by inadvertent omission of symptoms and important information about the child's nutrition by caregivers, as well as the nonspecific clinical symptoms that were misinterpreted as sepsis. As in the case of every new clinical syndrome, FPIES included, making an accurate diagnosis requires an in-depth knowledge and understanding of the nature of the disease.

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Conflicts of Interest

The authors declare that they have no conflicts of interest.

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