

## Locust bean gum induced FPIES in infant

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**Palabras clave:** Síndrome de enterocolitis inducido por proteínas alimentarias, Alergia a leche de vaca, Goma garrofin, Provocación oral con alimentos, Calprotectina

Food protein induced enterocolitis syndrome (FPIES) is a rare manifestations of food allergy (FA) presenting with persistent vomiting, diarrhoea, lethargy, dehydration, hypotension and hypothermia occurring within 1-4 hours after exposure to the allergen, without any skin or respiratory symptoms.

An 11-week-old boy with chromosome 21 trisomy (primipara, 23 years old mother, spontaneous vaginal delivery at 38 week' gestation, birthweight 3600 g, 9/9 Apgar score), cow's milk formula (CMF) fed, was admitted to the emergency department due to persistent vomiting, watery diarrhoea, non-responsiveness, drowsiness. On admission the child presented with lethargy, severe dehydration, hypotension (BP 75/50 mmHg), anaemia, high acute-phase reactants, metabolic acidosis, electrolyte imbalance (Table). Fluids, electrolytes, acid-base disorders management and antibiotics were administrated with rapid clinical response.

Based on history-taking, it was established that the child had stayed in a residential child care community (RCCC) since birth; in the past he had been hospitalized five times in various centres, each time presenting symptoms similar to the above-described. During the first hospitalization he was diagnosed with sepsis; antibiotic therapy and intravenous hydration were applied; microbiological and serological tests did not confirm bacterial or viral gastrointestinal infection. During subsequent incidents no infectious factor was established either; metabolic acidosis, endocrine disorders, immunodeficiency and IgE-dependent FA were excluded.

Based on clinical picture, we put forward a suspicion of cow's milk protein (CMP) FPIES. CMF was replaced by casein-based extensively hydrolysed formula (EHF) with fast improvement in the child's condition. Over the next 3 months the child was readmitted to our department 3 times; due to social circumstances each hospitalization lasted 3 to 4 weeks, after every release the boy returned to the hospital within 1-2 days with similar clinical

presentation. In hospital the child tolerated EHF well. Therefore during the stable period we performed the oral food challenge (OFC) with incremental amounts of CMF (up to 15 ml = 0,3 g protein). After 2 hours vomiting, lethargy and after 6 hours diarrhoea were observed; laboratory tests revealed increased inflammatory markers (Table). The child required intensive intravenous hydration. The diagnosis of CMP-FPIES was confirmed and reproducible presentation aroused a suspicion of non-compliance with dietary recommendations outside the hospital. Meanwhile RCCC team unwaveringly declared full compliance with medical guidance and it was only a detailed interrogation of the director and staff that revealed administering a thickener (locust bean gum – LBG; carob gum) along with the EHF. Subsequently OFC with thickener which was added to the EHF (0,5 g, increased to 1,0 g after 60 minutes) was performed. After 100 minutes the boy presented with vomiting, lethargy and after 6 hours diarrhoea occurred. The laboratory tests revealed elevated CRP, WBC and faecal calprotectin (Table). In the follow-up EHF was maintained and subsequently, since the 10th month of boy's life, the 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 subjected to the international adoption.

FA is an adverse reaction to food mediated by an immunologic mechanism: IgE-mediated, non-IgE-mediated or both IgE- and cell-mediated mechanisms [1]. The negative specific IgE to the suspicious food do not rule out the allergy.

FPIES is a non-IgE-mediated form of FA. The majority of patients have undetectable food sIgE, however sIgE may be present at diagnosis or develop during the 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 Y. *et al.* estimates the incidence of CMP-FPIES at 0.34% [4], while reports of allergic reactions caused by LBG are rare. The only to the authors' knowledge description of a case of allergy to carob in an infant was published by Savino *et al.* [5] and regarded 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], such a course was observed in our patient demonstrating manifestations typical of the acute form of the syndrome: recurring, persistent vomiting (1-4 hours after exposure), diarrhoea, pallor,

lethargy, hypotension and laboratory abnormalities. The chronic form of FPIES entails periodic vomiting, chronic diarrhoea and failure to thrive [2,6].

FPIES diagnosis is based on detailed history-taking and confirmed by resolution of symptoms after eliminating the triggering factor. Although the OFC remains the gold diagnostic standard for FA, in case of FPIES with clear clinical manifestation the procedure may be avoided [2]. In our case, due to inconsistency between the medical history and clinical presentation, and additionally very rare possible trigger (thickener) we decided to perform the challenge.

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 case presented by us appears to be the first description of FPIES triggered by a locust bean gum intake in an infant.

LBG (code for food additives E410) is used as a thickener of anti-reflux milk formulas [8]. It is also utilized as a stabilizer and emulsifier in the food industry. The presented case indicates that LBG may cause life-threatening reaction in the form of acute FPIES in children. In our patient, elevated faecal calprotectin concentrations and their normalization in the remission were established during OFC. Calprotectin is a sensitive marker of gastrointestinal inflammation, applied mainly in IBD [9,10]. Our observations, demonstrating a considerable increase in the protein concentration after the OFC and subsequent normalization, indicate that calprotectin might be useful objective marker of mucosal barrier damage in monitoring a OFC in FPIES.

Diagnostic dilemmas in the described case were caused by inadvertent omitting of symptoms important information about the child's nutrition by caregivers and the unspecific 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 disease nature.

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### **Conflicts of Interest**

The authors declare that they have no conflicts of interest.

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Table Laboratory data of the patient.

On first admission	Hemoglobin - 9.8 g/dl; WBC - 23 400/ $\mu$ l; Neutrophils - 68%; CRP - 64.09 mg/l; PCT - 15.58 ng/ml; pH - 7.243; BE: -11.1; Na - 132 mmol/l; K - 3.4 mmol/l
OFC with CMF	<i>baseline</i> : WBC - 8 700/ $\mu$ l; Neutrophils - 68%; CRP - 0.23 mg/l; Haemoglobin 12,1 g/dl; <i>after OFC</i> : WBC - 21 200/ $\mu$ l; Neutrophils - 68%; CRP - 52.33 mg/l; fecal calprotectin - 520 $\mu$ g/g; <i>2 weeks after OFC</i> : Calprotectin - 90 $\mu$ g/g
OFC with thickener	<i>baseline</i> : WBC - 12 500/ $\mu$ l; Neutrophils - 47%; CRP - 3,9 mg/l; Calprotectin - 63 $\mu$ g/g <i>after OFC</i> : WBC - 19 000/ $\mu$ l; Neutrophils - 75%; CRP - 41,6 mg/l; Calprotectin - 350 $\mu$ g/g; <i>2 weeks after OFC</i> : Calprotectin - 60 $\mu$ g/g

Abbreviations: OFC Oral Food Challenge; CMF Cow's Milk Formula.