

Severely Altered-Consciousness Status and Profuse Vomiting in Infants

Food Protein–Induced Enterocolitis Syndrome (FPIES) a Challenging Diagnosis

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Abstract: In infants, the causes of acute repetitive vomiting and severely altered-consciousness status include a broad differential diagnosis, that is, primarily sepsis, infectious gastroenteritis, head injury, and intoxication, as well as neurologic, metabolic, and cardiologic condition diseases. In patients developing such symptoms, allergy as an etiological cause is often not considered by primary care physicians. With this case report, we aim to draw the attention of general pediatricians, emergency physicians, and intensivists to the fact that non-immunoglobulin E–mediated food allergic gastrointestinal disorders such as food protein–induced enterocolitis syndrome should be considered in patients with sepsis-like symptoms.

Key Words: food protein–induced enterocolitis syndrome, food allergy, children

(*Pediatr Emer Care* 2016;00: 00–00)

CASE

In infants, the causes of acute repetitive vomiting and severely altered-consciousness status include a broad differential diagnosis, that is, primarily sepsis, infectious gastroenteritis, head injury and intoxication, as well as neurologic, metabolic, and cardiologic condition diseases (Table 1).¹ In patients developing such symptoms, allergy as an etiological cause is often not considered by primary care physicians. We aim to draw the attention of general pediatricians, emergency physicians, and intensivists to the fact that non-immunoglobulin E (IgE)–mediated food allergic gastrointestinal disorders such as food protein–induced enterocolitis syndrome (FPIES) should be considered in patients with sepsis-like symptoms.

Because FPIES is a diagnosis of exclusion without confirmatory testing in the acute setting, clinicians should have a better understanding of the presentation and maintain a high level of suspicion to make this diagnosis.

We present a case of an infant with a final diagnosis of FPIES, who underwent many invasive investigations and intensive

care hospitalization. We aim to demonstrate the severity with which FPIES can present, the importance of a detailed history in reaching this diagnosis, and the negative consequences of delayed or missed diagnosis of FPIES.

A healthy 8-month-old boy without allergic history presented to the emergency department with acute onset of profuse emesis and asthenia. Symptoms began abruptly 1 hour after ingestion of a meal with chicken and milk. Parents denied recent illness, toxic exposures, or head injury. Physical examination was characterized by pallor and lethargy with a Glasgow Coma Scale between 9 and 10.

A very broad differential diagnosis was discussed by the emergency pediatricians and led to various investigations. The blood gas analysis highlighted a metabolic acidosis (pH 7.26; PCO₂ 6.9 kPa; HCO₃ –22.2 mEq/L; Base Excess (BE) –3.9), and the complete blood count showed leukocytosis (26.8 G/L) with left shift of the polymorphonuclear leukocytes (ie, nonsegmented neutrophils of 1.07 G/L) and thrombocytosis (663 G/L). An abdominal x-ray and ultrasonography did not reveal any significant anomaly. Cerebrospinal fluid analysis, including white blood cell count and protein, and head computed tomography were normal.

Our patient was rapidly treated with an intravenous bolus of normal saline solution (20 mL/kg) and was transferred to the intensive care unit because of fluctuating levels of consciousness. An hour after admission, the patient's clinical condition improved significantly, particularly his state of consciousness; thus, antibiotics were not given at that time. After a few hours, the boy developed abundant and odorous liquid stools. Occult blood testing was positive. At 48 hours, although the leukocytes were in the reference range (9.8 G/L), a normocytic normochromic anemia (hemoglobin of 90 g/L) was detected. Of note, stool bacterial culture and viral tests were negative.

After 5 days of extensive and unrevealing workup, food allergy was suspected on the basis of a more precise clinical history revealing a similar milder reaction after chicken ingestion, several weeks before. Indeed, our patient had 1 episode of intractable vomiting after ingestion of a meal containing chicken. He did not receive this food between those 2 episodes.

An allergic workup including skin prick test and specific IgE to cow's milk and chicken was negative. Because of a low index of suspicion (ie, no ingestion of milk during the first episode), a food challenge to cow's milk was performed and was negative. On the basis of clinical diagnostic criteria, FPIES to chicken was diagnosed.²

Food protein–induced enterocolitis syndrome is a relatively common severe non-IgE-mediated food allergy, with an estimated prevalence of 0.34% for milk-FPIES in a birth cohort from Israel.³ Its diagnosis is based on clinical criteria defined by Powell in 1978 and recently revised by several groups.² However, this disorder is clearly underdiagnosed, partly due to the lack of knowledge of pediatricians, but also due to the lack of diagnostic tests.⁴ Indeed, although elevated white cell with a left shift, thrombocytosis, and methemoglobinemia have been described in a subset of patients, these tests are not specific to diagnose

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Disclosure: The authors declare no conflict of interest.

All authors are responsible for the reported case report.

Judith Barasche wrote the first draft of the article. All authors have contributed significantly to the concept, drafting, and revising of the article.

All authors have read and accepted the article for submission.

No honorarium, grant, or other form of payment was given to anyone to produce the present article.

The authors declare having no conflicts of interest regarding this article. No sponsor has been implicated in this case report and at any stage (collection, analysis, and interpretation of data; writing of the manuscript; or decision to submit the article for publication).

This article or any of its data have not been published previously. The present article is not under consideration elsewhere and will not be submitted elsewhere while under consideration by the *Pediatric Emergency Care*.

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ISSN: 0749-5161

TABLE 1. Clinical Features of Acute FPIES and Its Differential Diagnosis¹

Clinical Features	Differential Diagnosis
Signs and symptoms Repetitive vomiting every 10 to 15 min, onset 1 to 3 h after ingestion (>90%) Diarrhea, onset about 5 h after ingestion (<50%) Lethargy (70%) Pallor (70%) Dehydration Hypotension (15%) Hypothermia (25%) Abdominal distension Laboratory findings Elevated neutrophil count Thrombocytosis Metabolic acidosis Methemoglobinemia Fecal leukocytes and eosinophils Frank or occult fecal blood Increased carbohydrate content in stool Elevated gastric juice leukocytes Negative IgE test to the trigger food in most cases Radiologic features Intramural gas Air fluid levels	Infections Viral gastroenteritis Sepsis Bacterial enteritis (<i>Salmonella</i> , <i>Shigella</i> , <i>Campylobacter</i> , <i>Yersinia</i>) Parasites Allergic disorders Other gastrointestinal non-IgE-mediated food allergy disorders (food protein-induced enteropathy and eosinophilic gastrointestinal disorders) Acute IgE-mediated allergy (anaphylaxis) Gastrointestinal disorders Gastroesophageal reflux disease Hirschsprung disease Intussusception Volvulus Pyloric stenosis Celiac disease Other Neurologic disorders (ie, seizure, encephalopathy, or bleeding) Heart defects (ie, congenital heart disease, cardiomyopathy, or arrhythmia) Necrotizing enterocolitis Congenital methemoglobinemia Intoxication Metabolic disorders (ie, hypoglycemia, MCAD deficit, biotinidase deficit, or anomalies of urea cycle)

MCAD, medium-chain-acyl-CoA-dehydrogenase.

FPIES. The general experience shows that 10% of children with FPIES had up to 4 episodes before the diagnosis is made.⁵ Although this was only the second episode in our patient, it took 5 days to reach the definitive diagnosis. In the absence of classical manifestations of the most commonly recognized type of IgE-mediated food allergy, that is, urticaria and anaphylaxis symptoms, an allergic cause was not considered initially.

The onset of emesis and lethargy within 1 to 3 hours of chicken ingestion, the rapid improvement after intravenous hydration, and the development of loose stool are typical for FPIES. The case also demonstrates the severity with which FPIES can present, as well as the potential harm and cost that can result from missed or delayed diagnosis of FPIES.

In addition, mis- and underdiagnosis are also due to typical involvement of foods that are usually considered hypoallergenic. Although most frequently incriminated foods in FPIES are milk and soy, other food such as grains, rice, meats, poultry, seafood, fruits, and vegetable have been shown to cause FPIES.⁶ In our case, none of the pediatricians in charge included a food allergy in the initial differential diagnosis, although the initial clinical history revealed a similar milder reaction (vomiting) after chicken ingestion few months before. A higher index of suspicion and a more precise clinical history would have diminished the number of painful diagnostic tests, exposition to radiation, length of hospitalization, and, consequently, medical costs. Moreover, risks related to misdiagnosis could be even more dangerous when patients are submitted to laparotomies if a surgical etiology is suspected. Of note, it is important to mention that initial aggressive treatment and diagnostic tests are necessary in undiagnosed FPIES patients to stabilize the patient and exclude other common causes such as sepsis.¹

The mainstay of management of FPIES is avoidance of the offending food. Our child was advised to avoid chicken and all

poultry meats due to the lack of data regarding the cross-reactivity between different poultries. During the acute phase of the reaction, classical therapy includes intravenous rehydration. Corticosteroids are also commonly used, although they have not been systematically studied.^{7,8} Recently, small case series provided promising results for the use of intravenous and intramuscular ondansetron during the acute phase.^{9,10} As most of these children outgrow their allergy, an oral provocation test is usually proposed 12 to 18 months after the initial reaction to assess tolerance acquisition.¹¹

In conclusion, this case illustrates that FPIES should be suspected in the presence of typical clinical symptoms such as profuse vomiting and altered status of consciousness, especially in patients with rapid improvement. A careful clinical history is mandatory to look for past similar episodes after ingestion of a specific food. This case report may help clinicians in the diagnosis of FPIES and reduce unnecessary and invasive investigations and costs associated with prolonged hospitalisations.

REFERENCES

1. Fiocchi A, Claps A, Dahdah L, et al. Differential diagnosis of food protein-induced enterocolitis syndrome. *Curr Opin Allergy Clin Immunol*. 2014;14:246–254. doi:10.1097/ACI.0000000000000057.
2. Serafini S, Bergmann MM, Nowak-Węgrzyn A, et al. A case of food protein-induced enterocolitis syndrome to mushrooms challenging currently used diagnostic criteria. *J Allergy Clin Immunol Pract*. 2015;3:c–137. doi:10.1016/j.jaip.2014.09.016.
3. Katz Y, Goldberg MR, Rajuan N, et al. The prevalence and natural course of food protein-induced enterocolitis syndrome to cow's milk: a large-scale, prospective population-based study. *J Allergy Clin Immunol*. 2011;127:647–53.e1–3. doi:10.1016/j.jaci.2010.12.1105.

4. Menon N, Feuille E, Huang F, et al. Knowledge of food protein–induced enterocolitis syndrome (FPIES) among general pediatricians. *J Allergy Clin Immunol*. 2013;131(Suppl. 2):AB177.
5. Miceli Sopo S, Greco M, Monaco S, et al. Food protein–induced enterocolitis syndrome, from practice to theory. *Expert Rev Clin Immunol*. 2013;9:707–715. doi:10.1586/1744666X.2013.814418.
6. Leonard SA, Nowak-Węgrzyn A. Food protein–induced enterocolitis syndrome. *Pediatr Clin North Am*. 2015;62:1463–1477. doi:10.1016/j.pcl.2015.07.011.
7. Leonard SA, Nowak-Węgrzyn A. Clinical diagnosis and management of food protein–induced enterocolitis syndrome. *Curr Opin Pediatr*. 2012;24:739–745. doi:10.1097/MOP.0b013e3283599ca1.
8. Burks AW, Jones SM, Boyce JA, et al. NIAID-sponsored 2010 guidelines for managing food allergy: applications in the pediatric population. *Pediatrics*. 2011;128:955–965. doi:10.1542/peds.2011-0539.
9. Holbrook T, Keet CA, Frischmeyer-Guerrero PA, et al. Use of ondansetron for food protein–induced enterocolitis syndrome. *J Allergy Clin Immunol*. 2013;132:1219–1220. doi:10.1016/j.jaci.2013.06.021.
10. Miceli Sopo S, Battista A, Greco M, et al. Ondansetron for food protein–induced enterocolitis syndrome. *Int Arch Allergy Immunol*. 2014;164:137–139. doi:10.1159/000363384.
11. Caubet JC, Ford LS, Sickles L, et al. Clinical features and resolution of food protein–induced enterocolitis syndrome: 10-year experience. *J Allergy Clin Immunol*. 2014;134:382–389. doi:10.1016/j.jaci.2014.04.008.