

CORRESPONDENCE

Food-induced immediate response of the esophagus: A first report in the pediatric age

Eosinophilic esophagitis is an emerging allergic disease characterized by symptoms of esophageal dysfunction and the eosinophilic infiltration of the esophagus.¹ Eosinophilic esophagitis symptoms generally vary with age. Young children and toddlers usually experience vomiting, regurgitation, abdominal pain, and feeding refusal. On the contrary, dysphagia and food impaction are predominant in adolescents and adults and are generally related to advanced tissue remodeling.² Recently, Biedermann et al. identified a group of symptoms referred to as “food-induced immediate response of the esophagus” (FIRE) in adults with EoE.³ FIRE is a novel syndrome characterized by an intense, unpleasant, or even painful retrosternal sensation,

occurring rapidly and reproducibly after esophageal contact with specific foods or liquids.^{3,4} These symptoms are distinguished and unrelated to dysphagia and gastroesophageal reflux disease (GERD).^{3,4} To date, FIRE has been described in adults, and no pediatric cases have been reported. This article reports the first pediatric case of FIRE. In January 2021, a 9-year-old Caucasian boy was referred to our Pediatric Allergy-Immunology Unit with a history of vomiting, solid food dysphagia, and feeding refusal that had worsened in the last month. The patient also reported a self-resolved episode of food impaction with meat. His history was negative for food and respiratory allergies, autoimmune diseases, or connective tissue disorders.

TABLE 1 Patient's feature

Age at diagnosis, years	9
Sex, M/F	M
History of allergy, yes/no	No
EoE symptoms duration, months	Not clearly reported by the family
Episodes of food impaction, yes/no	Yes
Total EREFS score at diagnosis, 0–8	4
Peak of eosinophil count at diagnosis, eos/HPH	62
Total PEESS score at diagnosis, 0–80	38
Total EREFS score at follow-up ^a , 0–8	6
Peak of eosinophil count at follow-up ^a , eos/HPH	61
Total PEESS score at follow-up ^a , 0–80	22
FIRE symptoms	Chest tightness, esophageal burn
Time to onset, min	10
Duration, min	10–20
Identified foods	Honey, pumpkin seed
SPT, mm	
Honey, mm	4
Pumpkin seed, mm	7
Total IgE, KU/L	72.3
Specific IgE, KU/L	
Honey, KU/L	0.38
Pumpkin seed, KU/L	0.43

Abbreviations: EoE, eosinophilic esophagitis; eos, eosinophils; EREFS, endoscopic reference score; FIRE, food-induced immediate response of the esophagus; HPH, high power field; IgE, immunoglobulin E; PEESS, pediatric eosinophilic esophagitis symptom score; SPT, skin prick test.
^aEight weeks after the beginning of PPI therapy.

A complete allergic evaluation was performed with no evidence of sensitization to common food and pollen antigens. The upper GI tract x-ray exam ruled out the leading causes of esophageal stenosis. Thus, the child underwent the esophagogastroduodenoscopy (EGD) that showed longitudinal furrows, mucosal edema, and white exudates (Table 1). The histology confirmed the eosinophil-predominant infiltration of the esophagus. A high-dosage proton pump inhibitor (PPI) therapy (40-mg daily) was started to improve his symptoms. After 1 month of PPI therapy, the child developed two episodes of chest tightness and esophageal burn after 10 min from the ingestion of pumpkin seeds mixed with yogurt and honey that he previously tolerated. The symptoms self-resolved after about 15 min and did not require any medication. The patient distinguished between these symptoms and the well-known swallowing difficulties and dysphagia that previously experienced. Skin prick tests with fresh foods and serum-specific IgEs were positive for honey and pumpkin seeds. The immunoCAP® assay was negative for inhalants and other food allergens. After 8 months of PPI therapy, the follow-up EGD with biopsies still showed signs of active disease (Table 1). Therapy was switched to swallowed corticosteroids (budesonide 1 mg daily). The child did not report other FIRE episodes and EoE symptoms since the swallowed budesonide was introduced.

We believe that this is a pediatric case of FIRE meeting several of FIRE patient characteristics recently reported.⁴ FIRE appeared distinct from the patient's reported EoE symptoms (solid food dysphagia, vomiting, and food refusal), GERD (symptoms improve with PPI therapy), and pollen food allergy syndrome (PFAS), where symptoms are generally limited to the oral mucosa and due to fresh fruits and vegetables. Moreover, no sensitization to inhalant allergens was found as generally described in patients with PFAS. Finally, FIRE symptoms may immediately occur after a culprit food comes into direct contact with the esophagus and is confined to this portion of the gastrointestinal tract. Although the pathogenesis of FIRE is still undetermined, a putative local immunologic factor causing the immediate mucosal response has been postulated.⁴ Furthermore, the inflamed esophageal epithelium may also play a part in the allergic sensitization as reported for the skin in atopic dermatitis.⁵ Cases of FIRE syndrome in children may be underestimated because symptoms could be attributed to EoE, and patients are too young to distinguish between typical EoE, PFAS, and FIRE symptoms. The differential diagnosis between FIRE and PFAS might be challenging to discriminate also for gastroenterologists and allergists. An accurate history of FIRE symptoms should be considered in the routine management of EoE children. Further research is needed to understand the epidemiology and the underlying pathogenetic mechanisms of FIRE in adults and children.

KEYWORDS

children, eosinophilic esophagitis, food-induced immediate response of the esophagus, pediatrics

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CONFLICT OF INTEREST

The authors declare that they have no conflicts of interest.

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REFERENCES

1. Dellon ES, Liacouras CA, Molina-Infante J, et al. Updated international consensus diagnostic criteria for eosinophilic esophagitis: proceedings of the AGREE conference. *Gastroenterology*. 2018;155(4):1022-1033.
2. Muir AB, Brown-Whitehorn T, Godwin B, Cianferoni A. Eosinophilic esophagitis: early diagnosis is the key. *Clin Exp Gastroenterol*. 2019;12:391-399.
3. Biedermann L, Holbreich M, Atkins D, et al. Food-induced immediate response of the esophagus-A newly identified syndrome in patients with eosinophilic esophagitis. *Allergy*. 2021;76:339-347.
4. Holbreich M, Straumann A. Features of food-induced immediate response in the esophagus (FIRE) in a series of adult patients with eosinophilic esophagitis. *Allergy*. 2021;76:2893-2895.
5. Wechsler JB, Bryce PJ. Allergic mechanisms in eosinophilic esophagitis. *Gastroenterol Clin North Am*. 2014;43:281-296.