Food Protein-Induced Enterocolitis Syndrome

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KEYWORDS

- Non-IgE–mediated food allergy
- Food protein-induced enterocolitis syndrome (FPIES) • Cow's milk • Soy
- Oral food challenge • Failure to thrive

KEY POINTS

- Awareness of food protein-induced enterocolitis syndrome is low.
- Food protein-induced enterocolitis syndrome (FPIES) can present as a medical emergency with symptoms including delayed persistent emesis with or without bloody diarrhea that can lead to severe dehydration and hemodynamic instability with abnormal laboratory markers.
- The mainstay of management is trigger avoidance.
- The natural history of the disease is spontaneous resolution over time.
- More studies are needed to better drive evidence-based practices for FPIES in clinical practice.

INTRODUCTION

Food protein-induced enterocolitis syndrome (FPIES) was first formally recognized by Powell in the 1970s.[1] FPIES is a non-immunoglobulin E (IgE)–mediated food allergy characterized by repetitive vomiting and frequent diarrhea that may lead to dehydration, lethargy, and pallor in the acute form. The chronic form is characterized by failure to thrive, emesis, and diarrhea. An atypical form, in which there is concomitant presence of specific IgE to the triggering food, has also been described.[2] Limited prevalence data exist, but this disorder is thought to be relatively rare.[3] The diagnosis is often missed likely because of the broad differential, delayed presentations, and limited awareness in the medical community.[4,5] Furthermore, the diagnosis is based solely on clinical criteria because no confirmatory test exists.[6] Implicated foods, onset

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of the disorder, and time to resolution vary by geographic area and regional dietary practices.[2,3,7,8] Treatment consists of education and avoidance of the offending foods. Many questions remain regarding this syndrome, and further research is needed.

EPIDEMIOLOGY

Food allergy prevalence has overall been increasing over the last 10 to 20 years.[9] FPIES, a non-IgE–mediated food allergy, has been reported as rare, although more than 1000 cases have been reported and cases reported per year have varied from 1 to 90.[10] There are few studies reviewing the prevalence of FPIES, and the true prevalence is unknown. The single population-based birth cohort study to date is by Katz and colleagues[3] in Israel, who prospectively studied 13,019 infants for development of FPIES related to cow's milk over 2 years. The study results showed a cumulative incidence for FPIES of 0.34% (44/13,019), with 8 of these patients subsequently developing IgE-mediated cow's milk allergy. In comparison, 0.5% (66/13,019) of the study population had IgE-mediated cow's milk protein allergy. All patients were diagnosed within the first 6 months of life in the study; however, the age of presentation can vary anywhere from 7 days of life to about 12 months of age.[2,3,8] Multiple studies report a male predominance similar to IgE-mediated food allergy.[3,8,11] There is an increased incidence of comorbid atopic disease in infants with FPIES, with about 30% of infants having atopic dermatitis, asthma, allergic rhinitis, or IgE-mediated food allergy.[8,11,12] Family history of atopy is common (40%–80%) in infants with FPIES; however, there are no cases of parents of infants with FPIES having had childhood or adult-onset FPIES, suggesting a lack of familial association.[10,12]

DIAGNOSIS

Symptoms

FPIES usually presents between 2 and 7 months of age as formulas and solid foods are introduced into the infant's diet. Milk and soy protein are the most common causes, although several studies also report reactions to other foods, including rice, oat, or other cereal grains, such as barley and wheat.[3,11,13] Children may have multiple food triggers. Cow's milk and soy FPIES often present at an earlier age than solid food-induced FPIES to grains, which is likely due to earlier introduction of cow's milk and soy. There are geographic variations of food triggers and age of diagnosis, likely based on differences in dietary implementation practices, with solid food-induced FPIES being more common in Europe and Australia than in North America (**Table 1**).[14] FPIES can present with both acute and chronic symptoms that are reflective of the non-IgE–mediated process and usually lack the typical expected IgE-mediated symptoms.

Acute symptoms

FPIES usually presents initially in infancy as severe emesis with or without diarrhea that may contain blood or mucous with exposure to the causative food (**Table 2**). The severe emesis is repetitive and may include up to 15 to 20 episodes of projectile repetitive vomiting within 1 to 4 hours of ingesting the suspected food.[4,9,14] The timing of onset of symptoms is important for the diagnosis. Secondary to these symptoms, children may have pallor, lethargy, metabolic acidosis, and hypothermia.[8,9,14] Laboratory abnormalities also include an increased neutrophil count, which peaks at 6 hours, and thrombocytosis (>500 $\times$ 10^9/L).[8] Often with this presentation, infants will undergo evaluation for sepsis, especially if marked laboratory abnormalities and hemodynamic