



Food Protein-Induced Proctocolitis: A Unique Subtype of Gastrointestinal Non-IgE-mediated Food Allergy

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Food allergy (FA) is an abnormal clinical reaction to proteins in which immunologically mediated mechanisms are implicated [1]. Certainly, FA is a major global health problem, and its geographic distribution may be linked to genetic, environmental, lifestyle, and dietary factors [2]. Pediatricians are the first specialists to be sought out by family members of children suspected of having FA. Therefore, they must be trained in the principles of diagnosis and carry out appropriate referrals when necessary [3-5]. Although more than 160 foods can cause allergic reactions, eight are considered significant allergens (cow's milk, soy, egg, wheat, fish and shellfish, peanuts, and tree nuts). These food allergens are responsible for 90% of allergic reactions [3], especially in the first year of children's lives.

FA presents a broad spectrum of clinical manifestations ranging from mild urticaria to severe anaphylaxis. The skin and gastrointestinal tract are the most commonly affected target organs. Patients with non-IgE-mediated food allergies often develop gastrointestinal symptoms (vomiting, diarrhea, abdominal pain). The FA-specific subtypes named Gastrointestinal Non-IgE-mediated (Non-IgE-GIFAs) are classified into three different clinical entities: Food Protein-Induced Enterocolitis Syndrome, Food Protein-Induced Enteropathy, and a unique and the most common subtype, the Food Protein-Induced Allergic Proctocolitis (FPIPC) [6-8].

In addition, while rectal bleeding is not a rare problem in healthy infants, FPIPC is broadly regarded as the most common type of colitis in infancy. The estimated prevalence ranges from 18% to 64% of infants with rectal bleeding [9-13]. Indeed, the relationship between bloody stools and food is not novel. Cases of infants with rectal bleeding and allergic proctocolitis in the first few months of life have been reported since the 1940s. Nevertheless, only in 1982 did Lake, et al. [14] first suggest cow's milk protein passed through breast milk as a possible cause of rectal bleeding in 6 infants who developed bloody diarrhea while exclusively breastfed in the first month of life. All six patients improved after switching to hydrolyzed milk or soy-based formula.

Many patients with FPIPC are breastfed and become sensitized due to maternally ingested proteins excreted in breast milk. Cow's milk and soy-based formulas are the primary causative foods. The risk factors for developing allergic colitis are an immature immune system, altered intestinal permeability, and other factors that activate the focal immune function, such as genetic susceptibility in combination with particularly sensitizing foods (milk, soy, egg, fish).

FPIPC is usually seen during the first six months of life, especially between 2 and 8 weeks (neonates and infants between 2 days and three months old). Most parents describe a gradual onset of symptoms that persist unless the offending food is removed. The

symptoms are always gastrointestinal and include small spots of blood mixed with the stools to abundant bleeding (rectorrhagia). Bloody stools can increase gradually, with the erratic appearance of blood for several days, followed by the presence of blood in most bowel movements. Some infants may be fussy or have increased bowel movements but not usually diarrhea. Almost all patients with FPIPC develop no systemic symptoms and seem to be well except for the bloody stool. They have no growth delay or poor weight gain, and the child's general condition is unaffected. The abdominal examination reveals no alterations, but careful attention should be made to exclude anal fissures.

On investigation, a few may develop discrete alterations such as mild microcytic anemia and peripheral blood eosinophilia on a complete blood count—also, a mildly elevated serum IgE and low serum albumin in isolated cases. Bacterial stool culture studies are recommended to assess for underlying infection. The Skin Prick tests and Serum-Specific IgE titers for foods are negative, as this is a non-IgE mediated pathogenetic mechanism. The diagnosis is founded on a detailed case history and patient response to eliminating suspect proteins from the diet. Suppose the patient is ill-appearing, not growing well, or develops additional symptoms. In that case, the diagnosis of FPIPC is probably incorrect, and other conditions should be considered, such as infectious diarrhea, anal fissure, coagulation defects, vitamin K deficiency, intussusception, necrotizing enterocolitis, pseudomembranous colitis, inflammatory bowel diseases, failure to gain weight, weight loss, Hirschsprung disease, and other surgical abdominal conditions [15,16].

The main characteristics of FPIPC are summarized in the Table.

1	Usually, it appears in the first six months of the infants, in both breastfed or formula-fed.
2	Appears in otherwise well-appearing infants and growing well
3	Cow's milk and soy protein are the most common causes.
4	The infants present with blood streaks in their stool.
5	Diagnosis is based on clinical history, skin prick tests, and serum food-IgE negatives.
6	Both the infant and mom (if nursing) must avoid offending food.
7	Treatment consists of eliminating the causal protein, with symptom resolution in 48-72 hours.
8	The prognosis is excellent, and tolerance of the allergen generally occurs at one year.

Table 1: Main characteristics of Food Protein-Induced Proctocolitis.

Next, an illustrative classic presentation of an infant with FPIPC.

A 3-month-old, full-term male infant who was exclusively breastfed was brought to his pediatrician for further evaluation of streaks of blood in his stools, which were otherwise normal in consistency and frequency (4-5 times a day). He was nursing well but appeared to some extent uncomfortable. He was growing along the 50th percentile for both height and weight. He was afebrile and had no ill contacts. Physical examination was normal, including no evidence of an anal fissure. The Skin Prick Tests to commercial milk, soy extract, and Serum Milk- and Soy-IgE measurement revealed negative results. The stool bacterial culture was negative. Although the diagnosis is almost always reached on clinical grounds, recto sigmoidoscopy biopsies were performed, and histopathology is exposed in the Figure. So, based on clinical features and laboratory investigation, the diagnosis of FPIPC was confirmed. Cow's milk formula was removed from the mother's diet, with some improvement in blood in stools, without complete resolution, within five days after maternal dietary modification. On review, the mother had increased soy consumption. At this point, the pediatric gastroenterologist, with a nutritionist's help, recommended stopping soy in the maternal diet, which resolved the symptoms and permitted the continuation of breastfeeding. At six months, the patient tolerated the gradual introduction of solid foods (chicken meat, rice cereal, fruits, and vegetables prepared with corn oil). By 12 months old, the mother was advised to gradually introduce soy and cow's milk products into her diet. He tolerated his diet without any adverse reactions. So, breastfeeding was discontinued, and cow's milk was subsequently given.

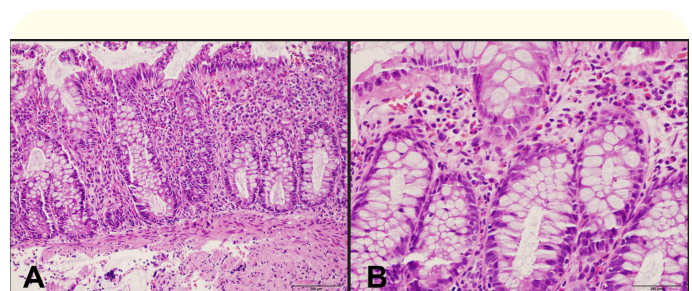


Figure 1: Eosinophil infiltration (>20/field) in the lamina propria of the colonic mucosa (H&E, 40x).

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