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ORIGINAL ARTICLE

Tolerance development in food protein-induced allergic proctocolitis: Single centre experience

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KEYWORDS
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Abstract
Background: Food protein-induced allergic proctocolitis (FPIAP) is characterised by inflammation of the distal colon in response to one or more food proteins. It is a benign condition of bloody stools in a well-appearing infant, with usual onset between one and four weeks of age.
Objective: Our objective was to examine the clinical properties of patients with FPIAP, tolerance development time as well as the risk factors that affect tolerance development.
Methods: The clinical symptoms, offending factors, laboratory findings, methods used in the diagnosis and tolerance development for 77 patients followed in the Paediatric Allergy and Gastroenterology Clinics with the diagnosis of FPIAP during January 2010–January 2015 were examined in our retrospective cross-sectional study.
Results: The starting age of the symptoms was 3.3 ± 4.7 months (0–36). Milk was found as the offending substance for 78% of the patients, milk and egg for 13% and egg for 5%. Mean tolerance development time of the patients was 14.7 ± 11.9 months (3–66 months). Tolerance developed before the age of one year in 40% of the patients. Tolerance developed between the age of 1–2 years in 27%, between the age of 2–3 years in 9% and after the age of 3 years in 5% of the patients.
Conclusions: Smaller onset age and onset of symptoms during breastfeeding were found associated with early tolerance development. In the majority of the patients, FPIAP resolves before the age of one year, however in some of the patients this duration may be much longer.

Abbreviations: APT, atopy patch test; EAACI, European Academy of Allergy and Clinical Immunology; eHF, extensively hydrolysed formula; FPIAP, food protein-induced allergic proctocolitis; LNH, lymphoid nodular hyperplasia; OFC, oral food challenge; SPT, skin prick tests.

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Introduction

The prevalence of food allergy has increased in recent decades, especially in the paediatric population.[1,2] According to the World Allergy Organisation guidance, food allergy can be IgE-mediated or non-IgE-mediated.[3] Even though the mechanism and pathogenesis of IgE-mediated food allergy are understood much better, the mechanism and pathogenesis of non-IgE-mediated gastrointestinal food allergies are still unclear. Food protein-induced allergic proctocolitis (FPIAP) is one of these.[2] FPIAP starts usually during the first months of life in otherwise healthy infants. FPIAP is characterised by mucus, blood and foam in the stool. The patients do not have growth retardation; however, weight gain may be slow. Mild anaemia and hypoalbuminaemia are rarely observed. FPIAP was first defined in 1982 by Lake et al. in six breastfed infants.[1,2,4] The most common offending food that has been reported until now is cow's milk.[2,4] Approximately 60% of cases occur in breastfed infants. It is postulated that ingestion of allergen food proteins from human breast milk causes inflammatory response in rectum and distal sigmoid colon.[2,4]

There is no specific diagnosis test for FPIAP. The diagnosis is made based on improvement in gross bleeding with the elimination of the offending food in 72–96 h and the recurrence of the symptoms following food challenge.[2,4,6] Infants with proctocolitis become tolerant to the offending food by one to three years of age and the majority of the patients achieve clinical tolerance by one year. Up to 20% of breastfed infants have spontaneous resolution of bleeding without changes in the maternal diet.[7] The long-term prognosis is excellent, there are no reports of inflammatory bowel disease development in infants with FPIAP followed for more than 10 years.[4]

Data about prevalence, diagnosis, treatment and prognosis of FPIAP is limited and factors that affect prognosis are not exactly known. Our objective was to examine the clinical properties of FPIAP patients, tolerance development time and the risk factors that have effects on tolerance development.

Methods and materials

FPIAP definition

In the study, the diagnosis of allergic proctocolitis is defined according to the criteria suggested in the European Academy of Allergy and Clinical Immunology (EAACI) food allergy and anaphylaxis guidelines and the expert panel report (Guidelines for the Diagnosis and Management of Food Allergy in the United States). These guidelines suggest the use of: ''history, improvement of symptoms by eliminating the offending food, recurrence of symptoms following oral food challenge (OFC)''.[8]

Data collection

This crosssectional retrospective study was performed in BehcetUz Children's Hospital Department of Paediatric Allergy and Gastroenterology, between January 2010 and January 2015. The clinical properties, laboratory data, diagnostic procedures and data about tolerance development of 77 patients with the diagnosis of FPIAP were evaluated. Patients with missing data in their files, patients for whom FPIAP diagnosis could not be verified via challenge following elimination, patients with infections leading to bloody diarrhoea, patients with anal fissure, perianal dermatit/excoriations, invagination, coagulation defects, necrotising enterocolitis, inflammatory bowel diseases, vitamin K deficiency and immunodeficiency were excluded.

Skin prick tests (SPT), specific IgE

In patients with additional atopic findings such as atopic dermatitis, recurrent wheezing, anaphylaxis, both food specific IgE test and SPT were performed. SPT was applied via prick microlancet (stallerpoint) method for the most common allergens (ALK-Abellò (Madrid, Spain); cow and goat's milk, soy, egg, wheat, fish, pistachio, sesame) to all patients and for the foods that the family of the patient was suspicious about to specific patients. Histamine (10 mg/mL) and physiological saline (ALK-Abellò (Madrid, Spain)) were used as positive and negative references, respectively. Skin reactions were evaluated 20 min after the skin test. A positive reaction was characterised as wheal diameter $\geq$3 mm. Specific IgE levels were measured using the immuno-CAP system (Phadia, Uppsala, Sweden). 0.35 kUa/L was taken as the cut-off value.

Atopy patch test (APT)

Fresh food was applied to the back of the patient via finn-chamber (aluminium disc). The tested region was evaluated 48 and 72 h later.[9] Isotonic saline was applied as negative control. APT reactions were graded as per the European Task Force for Atopic Dermatitis consensus report.[10]

Oral food challenge (OFC) and age of resolution

Milk and milk products were eliminated from the diet of the mothers for breastfed infants. Primarily extensively hydrolysed formulas (eHF) were used. In patients unresponsive to eHF or in patients considered to be with multiple food allergy, aminoacid based formulas were preferred. The formula was replaced with extensively hydrolysed formula (eHF) or aminoacid-based formula for formula-fed infants. In infants, for whom clinical improvement was observed within 72–96 h (complete resolution in the stool sample can take one week if there is significant blood), the offending food was restarted in the third week. The patient was diagnosed with FPIAP if the offending food caused rectal bleeding, diarrhoea and mucus again in the provocation period. If there was no response with the first step diet with eHF or aminoacid based formula, egg and wheat products were eliminated from the diet of the mother of the infant to be started again three weeks after for provocation. Elementary diet was preferred in case there was no response to milk, egg and wheat products in patients with multiple food allergies. Foods were started one by one after all the symptoms were resolved with the elimination diet and in this manner,

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