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【 CASE REPORT 】

Diagnosing Pollen-food Allergy Syndrome Allergologically in a Patient with Suspected Eosinophilic Gastroenteritis

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Abstract:
Pollen-food allergy syndrome (PFAS) consists of type I allergy to pollen and multiple food items that are cross-reactive to the pollen. PFAS typically occurs in the oral cavity and can co-occur with eosinophilic esophagitis. However, it is infrequently reported to present with symptoms of eosinophilic gastroenteritis (EGE), such as abdominal pain and eosinophilic infiltration of the gastrointestinal tract. We herein report a patient with a condition initially suspected of being EGE based on symptoms and pathological findings that was later diagnosed as PFAS associated with birch pollen. PFAS should be considered as a differential diagnosis in patients with EGE-like symptoms.

Key words: pollen-food allergy syndrome, eosinophilic esophagitis, eosinophilic gastroenteritis

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Introduction

Pollen-food allergy syndrome (PFAS) is an IgE-dependent type I allergy caused by prior sensitization to pollen and sensitivity to various kinds of fruit and vegetable with cross-reactivity to the pollen. It is also known as oral allergy syndrome (OAS), as it causes symptoms mainly in the oral mucosa due to antigen instability (1). PFAS also has affinities with eosinophil-associated gastrointestinal disorders (EGID), which involve eosinophilic infiltration of gastrointestinal tissue. Twenty-six percent of cases of eosinophilic esophagitis (EoE), a form of EGID causing dysphagia and heartburn, are reportedly associated with PFAS (2). However, PFAS is not known to cause gastrointestinal symptoms, such as abdominal pain, peripheral blood eosinophilia, intestinal edema or eosinophilic infiltration of the gastrointestinal tract, as in eosinophilic gastroenteritis (EGE), another type of EGID. Thus, an allergological approach is useful for distinguishing between EGID and food allergy, such as PFAS.

In the present case, EGE was suspected owing to the presence of abdominal pain and eosinophilic infiltration of the duodenal mucosa. Close observation during hospitalization revealed that the symptoms had an onset within 30 minutes after meals, suggesting that the patient might have had IgE-dependent type I food allergy. However, the absence of a single, causative allergen suggested the possibility of PFAS. All of the suspected dietary triggers were found to be cross-reactive to birch pollen. The symptoms stopped recurring after the allergens with suspected cross-reactivity were eliminated. Based on these findings, along with the patient's history of seasonal pollinosis in spring and positivity for birch on multiple antigen simultaneous test (MAST), PFAS associated with birch pollen was finally diagnosed.

Case Report

A 34-year-old man was admitted for abdominal pain that had worsened over the preceding 3 months. He had a history of allergic rhinitis, coughing, pollinosis, and asthma and was receiving epinastine. On admission, a physical examination demonstrated a blood pressure 134/87 mmHg, heart rate 65 beats per minute, temperature 36.5 °C, and oxygen saturation 95% on room air. Severe abdominal tenderness was

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Table 1. Laboratory Data on Admission.

Peripheral blood		Total bilirubin	0.9 mg/dL
White blood cells	10,500 /μg	Aspartate aminotransferase	18 IU/L
Neutrophils	34.8 %	Alanine aminotransferase	24 IU/L
Eosinophils	33.3 %	Gamma-glutamyl transpeptidase	21 IU/L
Monocytes	4.4 %	Alkaline phosphatase	153 IU/L
Lymphocytes	27.1 %	Lactate dehydrogenase	207 IU/L
Red blood cells	479×10^4 /μg	Creatine kinase	90 IU/L
Hemoglobin	14.8 g/dL		
Platelets	20.6×10^4 /μL	**Immunological**	
		IgG	1,246 mg/dL
Biochemistry		IgA	159.7 mg/dL
Sodium	140 mEq/L	IgM	96.8 mg/dL
Potassium	3.7 mEq/L	IgE	82.7 mg/dL
Chloride	104 mEq/L	Soluble interleukin-2 receptor	435 IU/mL
Blood urea nitrogen	16.9 mg/dL	Anti-nuclear antibody	Negative
Serum creatinine	0.99 mg/dL	Myeloperoxidase anti-neutrophil cytoplasmic antibody	Negative
Estimated glomerular filtration rate	71.3 mL/min/1.73 m^2	Proteinase 3 anti-neutrophil cytoplasmic antibody	Negative
Total protein	7.6 g/dL	Tuberculosis interferon-gamma release assay	Negative
Albumin	4.7 g/dL	Parasite test of stool and blood	Negative

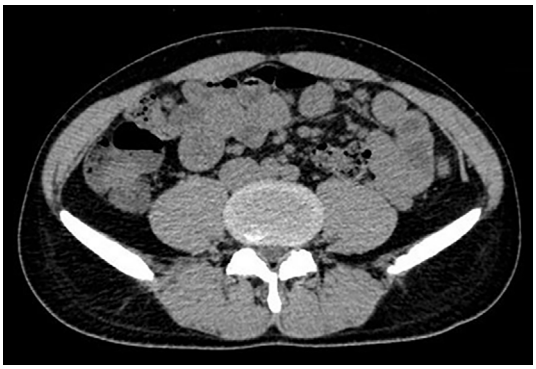

Figure 1. Computed tomography of the abdomen without contrast. Fluid retention and edematous wall thickening were observed in the small intestine.

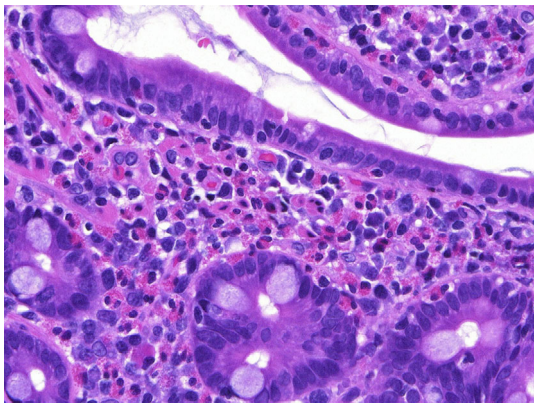

Figure 2. Histopathological finding of the descending duodenum. Thirty eosinophils/HPF were observed (Hematoxylin and Eosin staining, magnification ×400).

noted. A blood test revealed peripheral blood eosinophilia (3,496 /μL) and normal IgE (82.7 IU/mL) (Table 1). Computed tomography (CT) of the abdomen showed fluid retention and edematous wall thickening in the small intestine (Fig. 1).

Based on these findings, EGE was suspected. Upper gastrointestinal endoscopy revealed no gross abnormalities. A biopsy was performed in accordance with the recommendation of a previous study, as eosinophilic infiltration can be seen in EGE even in the absence of gross abnormalities (3). A pathological analysis of the biopsy specimen from the descending duodenum and duodenal bulb revealed eosinophilic infiltration at 30 /high-power field (HPF) and 20 /HPF, respectively (Fig. 2). The differential diagnoses for gastrointestinal symptoms associated with peripheral eosinophilia, such as intestinal parasites, leukemia, lymphoma, and vasculitis, were considered unlikely. EGE was further suspected based on the presence of pathological eosinophilic infiltration of the duodenal mucosa.

Corticosteroid therapy was planned. However, fasting improved the symptoms and restored the peripheral blood eosinophil count to the normal range (322/μL) after four days. After improvement of the intestinal edema was confirmed on CT, the plan to administer corticosteroid therapy was cancelled. However, upon resuming a normal food intake, the abdominal pain recurred several times. Symptoms occurred sporadically and apparently depended on the ingredients of the meal; when they occurred, they typically did so 30 minutes after eating and resolved spontaneously within a few hours.

Initially, the patient complained of persistent pain, but a detailed observation during hospitalization revealed intermittent pain after meals, strongly suggesting IgE-dependent type I food allergy. Careful history-taking again revealed oral symptoms occurring concomitantly with the abdominal pain. MAST was positive for a variety of antigens (Table 2). However, it was not possible to identify a single antigen

Table 2. Results of a Multiple Antigen Simultaneous Test.

Allergen	Class
Soybean	2
Kiwi	1
Japanese cedar	2
Birch	2
Ragweed	2
Orchard glass	2
House dust	3

common to all of the possible dietary triggers. Therefore, an elemental diet regimen, in which the amount of non-allergenic foods was gradually increased, was prescribed.

During this regimen, potential antigens were identified, and a scratch test was performed for boiled soybean, carrot, and orange pulp, but the results were negative. An oral loading test (10 g → 40 g → 50 g every 30 minutes) with tofu (soybean) produced irritation of the oral cavity, bloating in the epigastric region, and wheals on the left cheek about 20 minutes after ingesting 50 g. Thus, soybean was identified as an allergen. However, as the symptoms still recurred after soybean was eliminated, other items in the diet were reviewed, and kiwi, mango, and orange were also found to cause irritation in the oral cavity and slight abdominal pain.

PFAS associated with birch pollen was finally diagnosed based on several considerations: the patient's history of seasonal pollinosis in spring, his MAST positivity for birch, the unlikelihood of simultaneous sensitization to multiple allergens, and the cross-reactivity of soybean, kiwi, mango, and orange to birch pollen. Indeed, after eliminating these suspected allergens, the patient's symptoms stopped recurring. Only the avoidance of specifically allergenic foods was able to prevent symptom recurrence and minimize the negative effects on the patient's quality of life.

Discussion

Initially, EGE was suspected as the cause of the abdominal pain and eosinophilia in the present case. EGE, like EoE, is a form of EGID and produces abdominal symptoms, including abdominal pain, peripheral eosinophilia, intestinal edema, and eosinophilic infiltration of the intestines (3). Furthermore, EGE is a non-IgE-dependent allergic disease, and treatment often consists of long-term steroid therapy and the avoidance of various foods, but there is still no consensus concerning the optimal treatment. In the present case as well, abdominal pain occurred, and eosinophilic infiltration >30/HPF was observed in the descending duodenal leg, leading to a strong suspicion of EGE. However, excluding other eosinophilic diseases is also necessary to diagnose EGE definitively (3). Soybean, kiwi, mango, and orange, all of which caused symptoms in this case, have allergens that are cross-reactive with birch pollen (1, 2, 4). The patient was sensitized to birch pollen and had symptoms of pollinosis. Recurrence of the symptoms was prevented by avoiding the allergens suspected of triggering their onset. Based on these findings, we concluded that the symptoms in the present case were due to PFAS associated with birch pollen on the grounds that the patient presented with both oral and gastrointestinal manifestations, depending on the stability of the allergens.

In the present case, the instability of the fruit allergens may have been related to the oral symptoms, known as OAS. PFAS is reportedly associated with EoE in 26% of cases (2) and is thought to cause symptoms localized to the esophagus, as with the oral symptoms of OAS, because of the instability of the allergens. However, soybean allergens reportedly have a greater tendency than other allergens to cause systemic symptoms in PFAS owing to their stability (5). Because Gly m 4, the main soybean allergen, is heat-stable (6), it may act as a highly stable allergen in PFAS. In the present case, soybean is thought to have induced the intestinal eosinophilic infiltration and peripheral eosinophilia like those seen in other, common food allergies (7-9).

The allergological approach was key to diagnosing the present case for two reasons. First, close observation during hospitalization revealed a course typical of IgE-dependent type I allergy, suggesting that the patient had some sort of food allergy. The patient initially complained of persistent abdominal pain, but during hospitalization, the pain occurred 30 minutes after meals and resolved spontaneously and quickly with fasting. Second, the absence of a single causative allergen in the context of suspected IgE-dependent type I food allergy suggested the possibility of PFAS, which stems from cross-reactivity between pollen and multiple, apparently unrelated food allergens which may initially not be recognized as such because the symptoms are not traceable to any single allergen.

PFAS is associated with a family of proteins (e.g. PR-10 and profirin) that occur in pollen and class II food allergens. Class I food allergens cause allergic symptoms via gastrointestinal sensitization, whereas Class II food allergens, including pollen, usually cause allergic symptoms via airway sensitization (1). Therefore, multiple foods may become allergenic via cross-reactivity to pollen in individuals sensitized to pollen. Whenever PFAS is suspected, the patient should be tested for sensitization to pollen and carefully examined for potential cross-reactivity.

If the pathogenesis of PFAS had not been identified in the present case, long-term glucocorticoid therapy would have been prescribed on the supposition that the diagnosis was EGE. Correctly diagnosing PFAS can help avoid unnecessary steroid administration and food avoidance.

In conclusion, PFAS can cause EGE-like symptoms, such as abdominal pain, peripheral eosinophilia, intestinal edema, and intestinal eosinophilic infiltration. The allergological approach is key to assessing EGE-like symptoms. If no single causative allergen can be identified in the presence of acute, EGE-like symptoms, PFAS should be suspected, and the pa-

tient should be tested for multiple potential allergens.

Informed consent was obtained from the patient.

The authors state that they have no Conflict of Interest (COI).

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