

Eosinophilic esophagitis linked to pollen food syndrome



Hannah Hunter, BSc^{a,b}, Terence Wong, MA, MD, FRCP^c,
Alison Winstanley, MBBS, BSc, MRCPATH^d, and
Stephen J. Till, PhD, FRCP^b

Clinical Implications

- Cross-reactive foods, particularly between tree pollen and pathogenesis-related class 10 proteins, should be considered as targets for exclusion diets in eosinophilic esophagitis.
- Investigation of pollen-food cross-reactive antigen sensitization may have a role in the context of a suggestive clinical history.

TO THE EDITOR:

Dietary intervention has been shown to be effective for the management of eosinophilic esophagitis (EoE).¹ However, even an elemental diet devoid of food antigen only achieves remission rates on average of 91%,¹ suggesting that eosinophilia may not always be food driven. Seasonal exacerbations demonstrated in some pollen-sensitized children with EoE² imply a role for outdoor aeroallergens such as tree and grass pollen in the etiology or pathophysiology of the condition although this is not yet fully understood.

A high incidence of pollen food syndrome (PFS, or oral allergy syndrome) has been reported in EoE.³ In pediatrics, a case of eosinophilic gastrointestinal disease appeared to be linked to pollen cross-reactive foods.⁴ Cases of EoE induced by pollen sublingual immunotherapy (SLIT) have also been described.^{5,6}

We report a case of EoE in an adult with PFS where histological remission was achieved with removal of birch-pollen cross-reactive foods.

A 38-year-old man presented with a 10-year history of mid to low chest dysphagia. He described food bolus obstruction occurring approximately once every 3 years including 1 endoscopic removal of an impacted food bolus. His medical history included springtime seasonal allergic rhinitis, childhood asthma, and eczema.

On esophagogastroduodenoscopy pseudo-trachealization and linear furrows were seen; 12 esophageal plus 2 gastric and 4 duodenal biopsies were taken. Basal cell hyperplasia and eosinophilia were found at 3 levels of the esophagus (Figure 1). Gastric and duodenal biopsies were normal and his full blood count was unremarkable. A 24-hour pH impedance study showed no evidence of acid or nonacid reflux. High-resolution manometry showed ineffective motility and esophageal outflow obstruction. All features were consistent with EoE.

Skin prick tests to common foods such as wheat, milk, oat, egg, fish, corn, sesame, peanut, tree nuts, and soya were negative and positive to silver birch tree pollen (7 mm) and grass pollen (4 mm). Specific IgE levels were negative to all foods except hazelnut (1.87 kUA/L). ImmunoCAP ISAC multiplex testing

revealed sensitization to pathogenesis-related class 10 (PR-10) proteins from birch, alder, hazel pollen, hazelnut, apple, and peanut.

He reported oral itching after consuming raw cherries and perceived dysphagia to be triggered by omelets and baked beans. For the past 10 years, he had consumed daily fresh fruit smoothies containing raw fruit including apples, correlating approximately with the onset of dysphagia. Based on the sensitization to pollens and the reactions to cherries, a diagnosis of PFS was made. He was advised to avoid fruit smoothies and raw fruit but cooked or tinned versions were permitted. No other dietary elimination was recommended. At repeat endoscopy 3 months later, 12 esophageal biopsies were taken that revealed a full histological response (Figure 2). The diagnostic biopsy was taken in the winter, whereas the second was performed during the birch pollen season.

Despite the resolution of eosinophilia, his dysphagia persisted. A low esophageal stricture had been observed at endoscopy, and he therefore subsequently underwent esophageal dilatation to 15 mm, which resulted in symptom relief. He has since reintroduced citrus fruits without recurrence in symptoms.

Given that EoE is an allergic disorder with a high coincidence of atopic sensitization, it is logical that a high prevalence of other atopic disorders including PFS is to be expected. Indeed, a recent study found the incidence of PFS in pollen-sensitized individuals to be 5 times higher in EoE than in allergic rhinitis.³ Component-resolved diagnostics in a Dutch cohort have shown the dominant pattern of food sensitization in EoE to be those cross-reactive to birch pollen (primarily PR-10 proteins),⁷ consistent with the predominant pattern of sensitization for PFS in Northern Europe.⁸ These investigators speculated that sensitization to pollens leads to sensitization to cross-reactive foods, exposure to which induces or maintains esophageal inflammation.^{3,7} PR-10 proteins are generally rapidly degraded by low pH or pepsin in the stomach,⁸ which may account for the localization of allergic inflammation in the esophagus.

The onset of symptoms in this patient coincided with the addition of raw fruit smoothies to his diet and histological remission of EoE was achieved on removal of PR-10 proteins from the diet, suggesting a causative effect. Cases of EoE that presented during SLIT—which involves repeated gastrointestinal tract exposure to allergen—have been reported in tree⁵ and grass.⁶ Both cases resolved after cessation of treatment, also suggestive of a causative effect due to exposure to allergen in the esophagus.

The vehicle for allergen delivery is likely relevant, because severe reactions have been reported in PFS after consumption of fresh juice or smoothies as opposed to intact fruit. Anaphylaxis has been described in a PR-10-sensitized individual after consuming apple juice during exercise,⁹ presumably unpasteurized. The authors postulate that large quantities of allergen can be ingested in liquid form without the oral symptoms that would normally develop consuming solid foods. Individuals with PFS are generally advised to exercise caution with fresh (unpasteurized) juices and smoothies. We suspect that blending raw fruit into smoothies without heat treatment may release allergens from the fruit matrix thus increasing the effective allergen dose. The

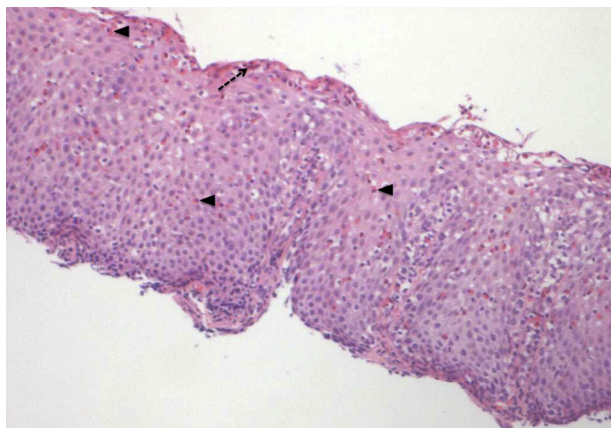


FIGURE 1. Lower esophageal biopsy specimen at diagnosis, showing basal cell hyperplasia, edema, intraepithelial eosinophils (arrowheads), and eosinophilic microabscesses (dotted arrow). Biopsies at different levels showed up to 30 eosinophils per high power field (hpf) (upper) 73/hpf (mid), 65/hpf (lower).

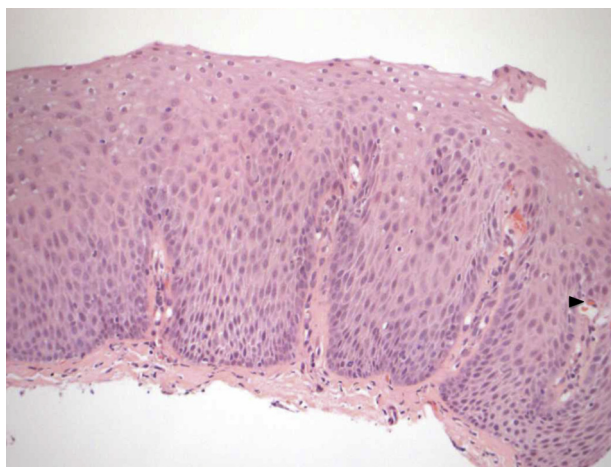


FIGURE 2. Lower esophageal biopsy specimen after intervention showing mild basal cell hyperplasia and scattered eosinophils (arrowhead) with maximum 2 eosinophils per high power field.

viscosity of blended fruit is also likely to coat the esophagus for longer than a liquid or food bolus.

Immunotherapy has been proposed as a potential treatment option for EoE; however, current evidence is limited to case studies.⁴ This was not considered for our case as his seasonal allergic rhinitis was mild and he did not meet the criteria for immunotherapy. In addition, his EoE completely resolved with exclusion of 1 food group.

This case highlights the possible importance of considering pollen cross-reactive foods as therapeutic targets for dietary

exclusion in EoE. A detailed allergy-focused diet history should include exposure to relevant allergens, particularly in blended or liquid foods, in which the effective esophageal allergen exposure may be greater than with intact foods. Although the role of testing for food-specific IgE responses in EoE remains controversial, investigation of pollen-food cross-reactive antigen sensitization may have a role in the context of a suggestive clinical history.

^aDepartment of Nutrition and Dietetics, Guy's and St Thomas' NHS Foundation Trust, London, UK

^bDivision of Asthma, Allergy and Lung Biology, King's College London, London, UK

^cDepartment of Gastroenterology, Guy's and St Thomas' NHS Foundation Trust, London, UK

^dDepartment of Cellular Pathology, University College London Hospital, London, UK

No funding was received for this work.

Conflicts of interest: H. Hunter has received travel support from Nutricia. S. J. Till has received consultancy fees from ALK Abello and Aimmune; and has received research support from ASIT Biotech and AstraZeneca. The rest of the authors declare that they have no relevant conflicts of interest.

Received for publication May 3, 2017; revised June 22, 2017; accepted for publication June 23, 2017.

Available online September 6, 2017.

Corresponding author: Stephen J. Till, PhD, FRCP, Division of Asthma, Allergy and Lung Biology, 5th Floor Bermondsey Wing, Guy's Hospital, London, SE1 9RT, UK. E-mail: stephen.till@kcl.ac.uk.

2213-2198

© 2017 American Academy of Allergy, Asthma & Immunology

<http://dx.doi.org/10.1016/j.jaip.2017.06.040>

REFERENCES

1. Arias A, Gonzalez-Cervera J, Tenias JM, Lucendo AJ. Efficacy of dietary interventions for inducing histologic remission in patients with eosinophilic esophagitis: a systematic review and meta-analysis. *Gastroenterology* 2014;146:1639-48.
2. Ram G, Lee J, Ott M, BrownWhitehorn TF, Cianferoni A, Shuker M, et al. Seasonal exacerbation of esophageal eosinophilia in children with eosinophilic esophagitis and allergic rhinitis. *Ann Allergy Asthma Immunol* 2015;115:224-8.
3. Mahdavinia M, Bishehsari F, Hayat W, Elhassan A, Tobin MC, Ditto AM. Association of eosinophilic esophagitis and food pollen allergy syndrome. *Ann Allergy Asthma Immunol* 2017;118:116-7.
4. De Swert L, Veereman G, Bublin M, Breiteneder H, Dilissen E, Bosmans E, et al. Eosinophilic gastrointestinal disease suggestive of pathogenesis-related class 10 (PR-10) protein allergy resolved after immunotherapy. *J Allergy Clin Immunol* 2013;131:600-602.e3.
5. Miehke S, Alban O, Schroder S, Straumann A. Induction of eosinophilic esophagitis by sublingual pollen immunotherapy. *Case Rep Gastroenterol* 2013;7:363-8.
6. Antico A, Fante R. Esophageal hypereosinophilia induced by grass sublingual immunotherapy. *J Allergy Clin Immunol* 2014;133:1482-4.
7. Van Rhijn BD, Van Ree R, Versteeg SA, VliegBoerstra BJ, Sprickelman AB, Terreehorst I, et al. Birch pollen sensitization with cross-reactivity to food allergens predominates in adults with eosinophilic esophagitis. *Allergy* 2013;68:1475-81.
8. Andersen MB, Hall S, Dragsted LO. Identification of European allergy patterns to the allergen families PR-10, LTP, and profilin from Rosaceae fruits. *Clin Rev Allergy Immunol* 2011;41:4-19.
9. Roseler S, Balakirski G, Plange J, Wurpts G, Baron JM, Megahed M, et al. Anaphylaxis to PR-10 proteins (Bet v1 homologues). *Hautarzt* 2013;64:890-2.

Reproduced with permission of copyright owner. Further reproduction prohibited without permission.