

Natalia Ukleja-Sokołowska, MD*
 Ewa Gawrońska-Ukleja, PhD, MD*
 Magdalena Żbikowska-Gotz, PhD*
 Ewa Socha, MSc*
 Kinga Lis, PhD*
 Łukasz Sokołowski, MD†
 Zbigniew Bartuzi, PhD, MD, Prof*
 *Department and Clinic of Allergology
 Clinical Immunology and Internal Diseases
 L. Rydygier Collegium Medicum
 Bydgoszcz, Poland
 †Division of Ergonomics and Exercise Physiology
 Department of Hygiene, Epidemiology, and Ergonomics
 L. Rydygier Collegium Medicum
 Bydgoszcz, Poland
 ukleja@10g.pl

References

- [1] Portnoy J, Kennedy K, Sublett J, et al. Environmental assessment and exposure control: a practice parameter—furry animals. *Ann Allergy Asthma Immunol*. 2012;108. 223.e1–223.e15.
- [2] Ukleja-Sokołowska N, Gawrońska-Ukleja E, Żbikowska-Gotz M, et al. Analysis of feline and canine allergen components in patients sensitized to pets. *Allergy Asthma Clin Immunol*. 2016;12:61.
- [3] Uriarte S, Sastre J. Clinical relevance of molecular diagnosis in pet allergy. *Allergy*. 2016;71:1066–1068.
- [4] Asero R, Arena A, Cecchi L, et al. Are IgE levels to foods other than Rosaceae predictive of allergy in lipid transfer protein-hypersensitive patients? *Int Arch Allergy Immunol*. 2011;155:149–154.
- [5] Konradsen JR, Nordlund B, Onell A, Borres MP, Grönlund H, Hedlin G. Severe childhood asthma and allergy to furry animals: refined assessment using molecular-based allergy diagnostics. *Pediatr Allergy Immunol*. 2014;25:187–192.
- [6] Bjerg A, Winberg A, Berthold M, Mattsson L, Borres MP, Rönmark E. A population-based study of animal component sensitization, asthma, and rhinitis in schoolchildren. *Pediatr Allergy Immunol*. 2015;26:557–563.
- [7] Wisniewski JA, Agrawal R, Minniccozzi S, et al. Sensitization to food and inhalant allergens in relation to age and wheeze among children with atopic dermatitis. *Clin Exp Allergy*. 2013;43:1160–1170.

Eosinophilic esophagitis induced by aeroallergen sublingual immunotherapy in an enteral feeding tube–dependent pediatric patient



Eosinophilic esophagitis (EoE) is an increasingly recognized eosinophilic gastrointestinal disorder that affects children and adults, with a prevalence of 5 per 10,000 inhabitants in Europe and the United States.¹ Food antigens trigger more than 90% of cases; however, data suggest that aeroallergens may also play a pathogenic role.^{2,3} In addition, sublingual immunotherapy (SLIT) is being increasingly used for the treatment of allergic rhinitis and allergic asthma. In this report, we describe a 9-year-old enteral feeding tube–dependent boy who developed increased esophageal eosinophilia, suggesting EoE after initiating aeroallergen SLIT.

The patient was diagnosed with autism and severe feeding disturbance as a toddler. As he aged, he took minimal food (occasional licking and small bites of mashed potatoes, pancakes, and avocado) by mouth, and in July 2011, initial endoscopic biopsies were performed during surgical gastrostomy tube placement for his persistent oral aversion. At the time, he was receiving proton pump inhibitor (PPI) therapy; histologic findings of the biopsies revealed mild proximal esophagitis with no eosinophils and distal acute erosive esophagitis consistent with gastroesophageal reflux disease (GERD).

In June 2013, the patient experienced worsening feeding refusal and became completely dependent on enteral elemental gastrostomy tube feeds (Elecare Junior) and PPI treatment. Additional endoscopic biopsies were performed in June 2013 because of the patient's increased feeding refusal. These biopsies revealed mild esophagitis without eosinophils in the proximal and middle esophagus and marked esophagitis with 57 eosinophils per high-power field (HPF) in the distal esophagus, which was concerning for EoE. In June 2014, while continuing to receive treatment with elemental diet, PPI therapy, and nonadherence of the prescribed slurry formulation of budesonide (0.5 mg/2 mL twice per day), his eosinophilia persisted and was more diffuse, with 32, 46, and 47 eosinophils per HPF in the distal, middle, and proximal esophagus, respectively. Because of the persistent eosinophilia, he was referred to a multidisciplinary eosinophilic gastrointestinal disease clinic.

In October 2014, the patient had his first visit to the eosinophilic gastrointestinal disease clinic, where he met with an allergist/immunologist and a gastroenterologist. It was discovered that an outside otolaryngologist had started aeroallergen SLIT in May

2013 for this patient. This therapy consisted of drops of grass (Bermuda and rye) pollen, tree (eastern cottonwood, mesquite, orange, and olive) pollen, and dust mite extracts (*Dermatophagoides farinae*). The patient was taking 1.6 mL of the antigens (0.2 mL of each antigen) mixed with 3.4 mL of 50% glycerin for a total of 5 mL, and he received 5 drops of SLIT once weekly for his perennial allergic rhinoconjunctivitis. At this time, it was recommended that SLIT and topical corticosteroid treatment be discontinued. Percutaneous allergy testing was performed, and the patient was found to be allergic to tree, grass, and weed pollen. In June 2015, while following his unchanged elemental diet and taking an increased dose of PPI, the patient's surveillance endoscopy revealed resolution of the eosinophilia with only mild esophagitis at the gastroesophageal junction (5 eosinophils per HPF), consistent with GERD. Clinically, he returned to his baseline and was willing once again to bite and lick his favorite foods. Table 1 provides a summary of the patient's endoscopic biopsy results from 2011 to 2015.

In this case report, the patient was found to have increased feeding disturbance and endoscopic biopsy results consistent with EoE just a month after starting SLIT. At this time, no other changes in the child's environment, diet, or new medications could be found. Although there was an increase in his PPI dose during this time (Table 1), this increase was to better control his reflux symptoms, and it is very unlikely that such a small dosage increase could be the cause of his marked pathologic and symptomatic changes. The child's increased esophageal eosinophilia, suggesting EoE, and clinical symptoms resolved shortly after discontinuing SLIT. The patient continued with an elemental diet and PPI therapy throughout, implicating aeroallergen SLIT as the trigger. Although reexposing the patient to SLIT and confirming a relapse could provide unequivocal proof, we did not perform this therapy because of ethical considerations.

In the literature, multiple cases of EoE during oral immunotherapy for food allergens have been reported.⁴ There have also been 2 previous case reports that described the development of EoE after receiving SLIT with aeroallergens (one in an adult and one in a child).^{5,6} Both of these resolved after discontinuation of SLIT. However, neither of these case reports described baseline endoscopic biopsy results or individuals following an elemental diet

Table 1
Summary of Patient's Endoscopic Biopsies (2011–2015)^a

Variable	Date of biopsy (age of child)			
	July 26, 2011 (5 years 11 months)	June 5, 2013 (7 years 9 months)	June 11, 2014 (8 years 9 months)	June 1, 2015 (9 years 9 months)
Reason for biopsy	Feeding disturbance	Increased feeding refusal	Surveillance of EoE	Surveillance of EoE vs GERD
Esophageal pathologic finding by location				
Proximal esophagus	Mild esophagitis; no eosinophils	Mild esophagitis; no eosinophils	47 eosinophils per HPF	No pathologic diagnosis
Middle esophagus		Mild esophagitis; no eosinophils	46 eosinophils per HPF	
Distal esophagus	Acute erosive esophagitis with necrosis; 6 eosinophils per HPF	Marked esophagitis; 57 eosinophils per HPF	32 eosinophils per HPF	Gastroesophageal junction with mild esophagitis; 5 eosinophils per HPF
Gross description of esophageal pathologic finding by location				
Basal cell hyperplasia				
Proximal	–	–	+	–
Distal	+	+	+	+
Papillae elongation (rete pegs)				
Proximal	–	–	+	–
Distal	+	+	+	–
Eosinophil degranulation				
Proximal	–	–	+	–
Distal	–	+	+	–
Proton pump inhibitor dose	Lansoprazole, 15 mg (0.5 mg/kg)	Lansoprazole, 30 mg (1 mg/kg)	Lansoprazole, 30 mg (1 mg/kg)	Lansoprazole, 60 mg (2 mg/kg)
Budesonide therapy	No	No	Poor adherence	No
SLIT	No	Yes	Yes	No
Diet	Elemental (Elecare Junior) tastes of foods	Elemental (Elecare Junior)	Elemental (Elecare Junior)	Elemental (Elecare Junior) tastes of foods
Diagnosis	GERD	EoE from SLIT	EoE from SLIT	Normal

Abbreviations: EoE, eosinophilic esophagitis; GERD, gastroesophageal reflux disease; HPF, high-power field; SLIT, sublingual immunotherapy.

^aMinus signs indicate negative; plus signs, positive.

throughout, as in this case. Thus far, this case portrays the most definitive correlation between EoE and aeroallergen SLIT. Although the cases describing EoE induced by aeroallergen SLIT are limited, they are not surprising. A previous study found a seasonal variation in the prevalence of EoE that correlated with aeroallergen levels, suggesting that they likely play a role in EoE.^{7,8} There are also several cases of de novo EoE after high-volume exposure of aeroallergens.⁹ With the increased use of SLIT for allergic rhinitis and asthma, it may become important to monitor for gastrointestinal symptoms, including dysphagia, reflux, and abdominal pain.

This case reveals that aeroallergen SLIT is capable of increasing esophageal eosinophilia in a pediatric patient. Physicians prescribing SLIT need to be aware of this adverse effect from SLIT and should monitor for gastrointestinal symptoms during treatment.

Michaela Rokosz, MD*

Cindy Bauer, MD†

Shauna Schroeder, MD‡

*Creighton University School of Medicine
Omaha, Nebraska†Department of Allergy and Immunology
Phoenix Children's Hospital
Phoenix, Arizona‡Department of Gastroenterology
Phoenix Children's HospitalPhoenix, Arizona
michaelatvrdik@gmail.com

References

- [1] Hruz P. Epidemiology of eosinophilic esophagitis. *Dig Dis*. 2014;32:40–47.
- [2] Liacouras CA, Furuta GT, Hirano I, et al. Eosinophilic esophagitis: updated consensus recommendations for children and adults. *J Allergy Clin Immunol*. 2011;128:3–20.e6.
- [3] Olson AA, Evans MD, Johansson MW, et al. Role of food and aeroallergen sensitization in eosinophilic esophagitis in adults. *Ann Allergy Asthma Immunol*. 2016;117:387–393.
- [4] Lucendo AJ, Arias A, Tenias JM. Relation between eosinophilic esophagitis and oral immunotherapy for food allergy: a systematic review with meta-analysis. *Ann Allergy Asthma Immunol*. 2014;113:624–629.
- [5] Miehke S, Alpan O, Schröder S, Straumann A. Induction of eosinophilic esophagitis by sublingual pollen immunotherapy. *Case Rep Gastroenterol*. 2013;7:363–368.
- [6] Béné J, Ley D, Roboubi R, Gottrand F, Gautier S. Eosinophilic esophagitis after desensitization to dust mites with sublingual immunotherapy. *Ann Allergy Asthma Immunol*. 2016;116:583–584.
- [7] Moawad FJ, Veerappan GR, Lake JM, et al. Correlation between eosinophilic esophagitis and aeroallergens. *Aliment Pharmacol Ther*. 2013;31:509–515.
- [8] Ram G, Lee J, Ott M, et al. Seasonal exacerbation of esophageal eosinophilia in children with eosinophilic esophagitis and allergic rhinitis. *Ann Allergy Asthma Immunol*. 2015;115:224–228.
- [9] Wolf WA, Jerath MR, Dellon ES. De-novo onset of eosinophilic esophagitis after large volume allergen exposures. *J Gastrointest Liver Dis*. 2013;22:205–208.

Drug eruption caused by memantine

The treatment of Alzheimer disease has continued to develop during the past decade. Although an acetylcholine esterase (AChE) inhibitor has been widely used for the treatment of cognitive function in patients with Alzheimer disease through an enhancement of cholinergic function, an open-channel blockade agent

targeted for N-methyl-D-aspartate (NMDA) has recently been established as a novel treatment of Alzheimer disease, namely, memantine. Memantine reduced clinical deterioration in moderate-to-severe Alzheimer disease. We report the first case, to our knowledge, of drug eruption caused by memantine in the English-language literature.

