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## Eosinophilic Esophagitis During Latex Desensitization

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Nucera E<sup>1,\*</sup>, Urbani S<sup>1,\*</sup>, Buonomo A<sup>1</sup>, Andriollo G<sup>1,\*</sup>, Aruanno A<sup>1,\*</sup>

<sup>1</sup>Allergy Unit, Fondazione Policlinico Universitario A. Gemelli IRCCS, Rome, Italy

\*These authors contributed equally to this work.

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Latex allergy is a relevant clinical problem observed mainly among health care workers, spina bifida patients, and individuals who have undergone multiple surgical procedures.

Type I hypersensitivity latex reactions are more frequent than type IV reactions (latex allergic contact dermatitis) and consist of skin involvement (urticaria and/or angioedema), respiratory symptoms (asthma/rhinitis), and even systemic anaphylaxis. The reactions are elicited by direct contact with natural rubber latex items (ie, medical devices) or by inhalation of airborne latex proteins.

After diagnosis, prevention is the standard and best measure, although strict avoidance is often impossible. Therefore, in selected cases, sublingual immunotherapy (SLIT) may modify the long-term natural history of latex allergy [1].

Immediate adverse reactions have been reported during SLIT [2], although long-term complications are less common.

We report a case of eosinophilic esophagitis (EoE) occurring after 3 years of latex maintenance SLIT.

The patient was a 38-year-old woman who experienced anaphylactic shock during cesarean delivery.

We carried out a complete allergological evaluation including a skin prick test with latex (SPT, Alk-Abelló), a specific IgE assay with latex and chlorhexidine (UniCAP-Phadia, Thermo Fisher), and SPTs and intradermal tests for all the drugs involved in the event (ketorolac, ampicillin, and bupivacaine) [3]. The only positive SPT result was to latex, with a mean wheal diameter of 10 mm. This finding was confirmed by the result of specific IgE to latex (15.5 kU<sub>A</sub>/L). Therefore, the patient underwent provocation challenges (glove wearing and mucous-oral, nasal, conjunctival, and sublingual tests). The cutaneous provocation test was performed by asking the patient to wear a latex glove (Triflex Allegiance Health Care Co.) for 1 hour. The mucous-oral challenges were carried out by asking the patient to hold a latex-gloved test tube in the mouth until symptoms appeared or for up to 1 hour. The conjunctival and nasal challenges were performed by instilling latex into the inferior fornix of each eye or by inhaling latex solutions of the commercial extract, starting with a concentration of  $500 \times 10^{-8}$  µg/mL and

increasing to 50 µg/mL. A positive result in the conjunctival challenge (conjunctival hyperemia) and mucous-oral challenge (erythematous papular lesions throughout the oral mucous membrane) confirmed the diagnosis of latex allergy [1,4].

Therefore, the patient began SLIT for latex allergy (Alk-Abelló, 500 µg/mL of latex) with a rush induction phase (4 days) [1]. No adverse events were recorded.

After 3 years of maintenance treatment (200 µg of latex 3 times a week), she developed solid food dysphagia, heartburn, and dyspepsia. Since these symptoms did not recede with 2 months of proton pump inhibitor therapy, we suspected EoE and performed a complete blood cell count and esophageal endoscopy. The complete blood count revealed eosinophilia ( $0.82 \times 10^9/L$ ); this had been normal at a check-up 1 year previously. Esophageal endoscopy revealed circular rings, linear furrows, and white mucosal exudates, with 25 eosinophils per high-power field (HPF) in mucosal biopsies from the upper, middle, and lower esophagus.

Although a mild increase in latex-specific IgG4 (UniCAP System, Thermo Fisher Scientific) was observed during the years of immunotherapy (0.64 mgA/L after 2 years of immunotherapy and 0.82 mgA/L after 3 years), SLIT was interrupted, with progressive clinical, endoscopic, and histopathological improvement after 3 months. After SLIT was discontinued, endoscopy showed 10 eosinophils per HPF, and peripheral eosinophilia was reduced to  $0.19 \times 10^9/L$ .

EoE is an inflammatory immune-mediated disease characterized by upper gastrointestinal dysfunction and dense eosinophilic infiltration of the esophageal mucosa (at least 15 eosinophils per HPF) and exclusion of secondary causes of EoE [6].

The incidence of EoE has increased significantly during the last few decades, thus indicating a role for environmental factors in pathogenesis. In fact, food allergens and aeroallergens have been associated with EoE.

In recent years, EoE has been recognized as a long-term complication of oral immunotherapy (OIT) and SLIT [6]. In fact, onset of EoE during OIT or SLIT has already been reported in patients with allergy to food [6], pollen [7], and dust mite [8]. However, recurrence of EoE following SLIT with latex had not yet been reported in the literature.

It is still unclear whether EoE is caused specifically by the allergen, becomes unmasked during treatment, or is coincidental to treatment. The diagnosis of esophagitis requires a biopsy that cannot be performed routinely before starting immunotherapy; therefore, the prevalence of EoE due to immunotherapy becomes very difficult to estimate. A recent meta-analysis indicated a 2.7% risk of EoE in patients undergoing OIT [6].

A role for OIT in pathogenesis was suggested by Sanchez et al [9], who reported 3 cases of EoE induced by milk OIT; baseline endoscopy did not reveal eosinophilic infiltration in 1 case. Moreover, as in the case we report, EoE frequently resolves simultaneously with discontinuation of immunotherapy.

We observed a mild increase in the latex sIgG4 value during SLIT, although we did not determine total IgG4 over

time. Serum IgG4 may have a pathogenic role in the onset of EoE, as demonstrated by recent studies [10].

We report the first case of a possible relationship between SLIT with latex and EoE.

Latex exposure may be a potential trigger for de novo EoE or could aggravate an unknown pre-existing disease. In the present case, we assumed that EoE developed during treatment, because the patient presented symptoms after only 3 years of SLIT. This hypothesis is supported by the decrease in eosinophil count and resolution of the histological features of EoE after interruption of treatment, although endoscopy was not performed prior to SLIT.

In conclusion, we recommend strict and prolonged follow-up of patients undergoing immunotherapy for latex allergy in order to detect adverse events.

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#### Conflicts of Interest

The authors declare that they have no conflicts of interest.

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**Arianna Aruanno**

Allergy Unit, Fondazione Policlinico Universitario A. Gemelli IRCCS  
Largo F. Vito, 1 – 00168 Rome, Italy  
E-mail: arianna.aruanno@policlinicogemelli.it  
aarianna@hotmail.it