Eosinophilic esophagitis during latex desensitization

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Latex allergy is a relevant clinical problem observed especially among health-care workers, spina bifida patients and individuals who had multiple surgical procedures.

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

After diagnosis, prevention is the standard and best measure, but the strict avoidance is often impossible. Therefore in selected cases, the sublingual immunotherapy (SLIT) may be a therapeutic approach able to influence the long-term natural history of latex allergy [1].

During SLIT, immediate adverse reactions have often been reported [2], but long-term complication are less described.

We showed the case of an eosinophilic esophagitis (EoE) occurring after 3 years of latex maintenance SLIT.

We present the case of a 38-years old woman, who experienced anaphylactic shock during cesarean section birth.

We carried out a complete allergological evaluation including latex skin prick test (SPT, Alk-Abellò, Milan, Italy), latex and chlorhexidine specific IgE assay (UniCAP-Phadia, Thermofisher, Uppsala, Sweden) and the SPT and intradermal tests for all the drugs involved (ketorolac, ampicillin and bupivacaine) in the event [3]. We found only a positive latex SPT with a mean wheal diameter of 10 mm. This data was confirmed by the result of specific latex-IgE value of 15.5kUA/l. So the patient underwent provocation challenges (glove-wearing, mucous-oral, nasal,
conjunctival and sublingual test). The cutaneous provocation test was performed by making the patient wear a latex glove (Triflex Allegiance Health Care Co., McGaw Park, IL, USA) on the hand for 60 minutes. 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 up to 1 h. The conjunctival and nasal challenges were performed by instilling latex into the inferior fornix of alternate eyes or by inhaling latex solutions of the commercial extract, starting with the concentration of $500 \times 10^{-8} \mu g/ml$ up to $50 \mu g/ml$. The positivity of conjunctival (conjunctival hyperemia) and mucous-oral (erythematous-papularlesions scattered throughout the oral mucous membrane) challenges confirmed latex allergy diagnosis [1, 4].

Therefore, the patient began latex SLIT (Alk-abellò, Milan, Italy- 500 µg/ml of latex) with a rush-induction phase performed in 4 days without side effects [1].

After 3 years of maintenance phase (200 µg of latex three times a week), she developed solid food dysphagia, heartburn and dyspepsia. Since these symptoms did not recede with two months long pump-protonic inhibitors therapy, suspecting an EoE, we performed a complete blood cell count (CDC) and an esophageal endoscopy.

The CDC revealed eosinophilia (0.82 x 10^9/l), while in her previous determination of one year before the eosinophils count was normal. The esophageal endoscopy showed circular rings, linear furrows and white mucosal exudates with 25 eosinophils per HPF in mucosal biopsies from the upper, middle and lower esophagus.

Although the patient presented a mild increase of latex specific IgG4 (UniCAPSystem, Thermo-fisher) during the years of immunotherapy (their value was 0.64 mgA/l after two year of immunotherapy and 0.82 mgA/l after three years), the SLIT was interrupted with a progressive clinical, endoscopic and histopathological improvement after three months. After SLIT discontinuation, the endoscopy performed showed 10 eosinaphils X HPF and also the peripheral eosinophilia was reduced to 0.19 x10^9/l.
Eosinophilic esophagitis is an inflammatory immune-mediated disease characterized by upper gastrointestinal symptoms dysfunction and dense eosinophilic infiltration of the esophageal mucosa (at least 15 eosinophils per HPF) excluding of secondary causes of esophageal eosinophilia [6].

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

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

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

A decisive causal role of OIT in its pathogenesis is suggested by Sanchez et al.[9], that reported 3 EoE cases induced by milk OIT, one of which having a baseline endoscopy without eosinophilic infiltration. Moreover, frequently, as in our case, EoE resolves simultaneously with discontinuation of immunotherapy.

In our case we observed a mild increase of latex sIgG4 value during the SLIT but we have not determinate total IgG4 value over time. Serum IgG4 could have a possible pathogenetic role in the onset of EoE as demonstrated by recent studies[10].

We show the first case report suggesting a possible relationship between latex SLIT and EoE.
Latex exposure may be a potential trigger for de-novo EoE or could get worse an unknown pre-existing disease. We can assume that EoE is developed during the treatment because the patient presented symptoms only after 3 years of SLIT. Eosinophilia decrease and resolution of EoE histological features after treatment interruption support this hypothesis, although endoscopy was not performed prior to SLIT.

In conclusion, we recommend a strict and prolonged follow-up of the patients undergoing latex immunotherapy to detect the adverse events.
Conflict of interests

The authors declare that they have no conflict of interest.

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