Right to privacy and informed consent. The authors have obtained the informed consent of the patients and/or subjects mentioned in the article. The author for correspondence is in possession of this document.

Protection of human subjects and animals in research. The authors declare that no experiments were performed on humans or animals for this investigation.

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Severe repeated anaphylactic reactions to sublingual immunotherapy

To the Editor,

Sublingual immunotherapy (SLIT) for allergic rhinitis is a well-established and effective therapy, currently considered to be safer and almost equally effective alternative to classical subcutaneous immunotherapy (SCIT).

Regarding the safety of SLIT, recent meta-analyses and systematic reviews suggest a remarkably safe profile without any severe systemic reactions, anaphylaxis or use of adrenaline in 49 studies, reviewed by Radulovic et al.[1] So far, only 11 cases of anaphylaxis to SLIT have been published.[2–7]

We present a case of a 35-year-old female suffering from persistent, perennial rhinoconjunctivitis and well-controlled asthma with seasonal aggravation. Symptoms appeared 15 years ago, and were becoming more severe each year, while symptomatic relief medications had been partly effective during the pollen season.

Sensitivity to *Olea europaea* pollen, *Dermatophagoides pteronyssinus* and *Dermatophagoides farinae* were identified by SPTs and serum s-IgE measurement. SLIT was carried out during the pollen season (in September) with standardised extracts of Sublivac (HAL, Netherlands) (10,000 allergy units/ml, 500 AU/drop) *Olea europaea* and Sublivac *D. pteronyssinus* 50%, *D. farinae* 50%.

Induction of immunotherapy was initiated on two consecutive weeks. During the first week SLIT with HDM extract was advanced without any side-effect and the following week we proceeded to SLIT with *Olea*. The patient was administered the first drop of *Olea* extract and was attended in our department according to current guidelines. Within 10 min, she developed an anaphylactic reaction (flushing, hoarseness, dyspnoea, dizziness and mild hypotension) and was treated with epinephrine, antihistamines and corticosteroids. In every attempt to increase the dose according to ordinary regiment she suffered a severe anaphylactic reaction (in all five reactions). Therefore, we adopted a modified build-up protocol (Table 1) and educated our patient to use autoinjectable adrenaline (no reaction occurred at home, where the dose remained unchanged).

The step-up process with SLIT to olive was quite difficult to advance because she could not tolerate more than three drops of extract per day. On the contrary, SLIT to House Dust Mites advanced with no reaction, and the maintenance dose was reached in five days.

Although our patient did not have to withdraw from SLIT, she eventually remained on a lower maintenance dose (3 drops/day), because she had got tired and refused to consent to any subsequent dose increase. That maintenance dose proved to be effective, as she reported a 50% decline on symptom-medication score during the next pollen season.

Despite the fact that the safety of SLIT is well-established, adverse reactions may occur, mainly during the build-up phase. Furthermore all previously published reports of anaphylaxis during SLIT, were characterised either by a deviation from international guidelines,[1,3] or by previous frequent reactions during SCIT.[4,6]

Table 1 Anaphylactic reactions to SLIT – modification of ordinary regiment.

Time	*Olea* regiment administration	Outcome	Therapy	Following administration at home	Premedication
Day 1	1 drop of ordinary regiment	Anaphylaxis (flushing, hoarseness, dyspnoea, dizziness and mild hypotension)	Adr sc, H1-AH, H2-AH, C/S iv	–	–
Day 7	Drop dilutions: 1/5, 2/5, 3/5, 5/5	No reaction	None necessary	1 drop/day	H1-antihistamine p.o.
Day 14	2 drops of ordinary regiment	Anaphylaxis (flushing, hoarseness, dyspnoea, dizziness and mild hypotension)	Adr sc, H1-AH, H2-AH, C/S iv	1 drop/day	H1-antihistamine p.o.
Day 21	Drop dilutions: 1 + 1/3, 1 + 2/3, 2	No reaction	None necessary	2 drop/day	H1-antihistamine p.o.
Day 28	3 drops of ordinary regiment	Anaphylaxis (flushing, hoarseness, dyspnoea, dizziness and mild hypotension)	Adr sc, H1-AH, H2-AH, C/S iv	2 drop/day	H1-antihistamine p.o.
Day 35	Drop dilutions: 2 + 1/3, 2 + 2/3, 3	No reaction	None necessary	3 drop/day	H1-antihistamine p.o.
Day 42	4 drops of ordinary regiment	Anaphylaxis (flushing, hoarseness, dyspnoea, dizziness and mild hypotension)	Adr sc, H1-AH, H2-AH, C/S iv	3 drop/day	H1-antihistamine p.o.

In-hospital attempts to increase dose during build-up phase, outcomes and self-administered doses at home the subsequent days. Dilutions of ordinary regiment were prepared using saline and administered in 30 min intervals.
AH, antihistamines.

In our case, anaphylactic episodes occurred in-hospital following the first dose and also after any subsequent dose increase, in a young female asthmatic patient lacking any history of anaphylaxis. During the build-up phase, asthma was well controlled and no predicting factor for a subsequent anaphylaxis was present. Despite these reactions, we managed to increase the tolerated dose, by administering premedication (antihistamine p.o.) during the build-up phase, increasing gradually the dose only in-hospital and maintaining the same dose for seven consecutive days at home (Table 1).

The remarkable safety profile of SLIT allowed the recent modification of SLIT schedules, omitting the up-dosing phase and starting with the maintenance dose. However, it seems that there is a subgroup of sensitive patients who need a more conservative build-up schedule in order to avoid a severe anaphylactic reaction.

Although SLIT seems to have an excellent safety profile this does not rule out the possibility of an anaphylactic reaction even if current guidelines have been followed precisely. It is imperative to administer the first dose under medical supervision and be vigilant to immediately recognise any possible systemic reaction. Our case indicates that SLIT schedules with a large dose of allergens, omitting up-dosing phase, may not be safe enough for a minority of high sensitive patients to whom a more gradual dose increase could be necessary. So far, the majority of studies focus mainly on effectiveness of SLIT and, to a lesser extent, on side-effects (usually considered as secondary outcomes). Therefore, more studies primarily focused on adverse reactions to SLIT are needed.[1]

Conflict of interest

The authors have no conflict of interest to declare.

Ethical disclosures

Patients' data protection. Confidentiality of data. The authors declare that they have followed the protocols of their work centre on the publication of patient data and that all the patients included in the study have received sufficient information and have given their informed consent in writing to participate in that study.

Right to privacy and informed consent. Right to privacy and informed consent. The authors declare that no patient data appears in this article.

Protection of human subjects and animals in research. Protection of human and animal subjects. The authors declare that no experiments were performed on humans or animals for this investigation.

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Coexistence of allergic bronchopulmonary aspergillosis and atopic dermatitis: Is total IgE level useful to identify relapses of allergic bronchopulmonary aspergillosis?☆

To the Editor,

Allergic bronchopulmonary aspergillosis is a hypersensitivity reaction to *Aspergillus fumigatus* colonisation of the tracheabronchial tree.[1] Atopic dermatitis is a chronic skin disease presenting with relapses and characterised by a disturbance of the epidermal barrier function, which culminates in dry skin, as well as by IgE mediated sensitisation to environmental allergens.[2] ABPA and AD are rare conditions in which an increment in total IgE is a hallmark.[3–5] So far, no case reporting the coexistence of AD and ABPA has been reported. Herein, we report a case of AD coexistence with ABPA in which a conflict occurred about the role of total serum IgE in the follow-up of treatment for ABPA.

A 49-year-old woman who had suffered from AD for 20 years and asthma for four years was admitted to our outpatient clinic because of uncontrolled asthma. The patient had applied to the emergency room for asthma several times in the last year despite regular use of inhaled beclomethasone/formoterol 200/12 mcg/day and montelukast 10 mg/day. She needed topical steroids and emollients for AD, occasionally with a favourable response.

Physical examination of the chest revealed decreased breathing sounds and diffuse expiratory rhonchi in the bilateral lung zones. On her skin, eczematisation, lichenification and xerosis were noticed mainly on the neck and volar surfaces of the forearms. The patient was examined by a dermatologist. The diagnosis of atopic dermatitis was confirmed according to the criteria of Hanifin and Rajka (5). Contact dermatitis and polymorphic light eruption were excluded by the dermatologist. Laboratory evaluation revealed a white blood cell count of 6800/mm^3 (eosinophil 13.2%) and a total immunoglobulin (Ig)E level of 2527 kU/L. Serum specific IgE against *Aspergillus fumigatus* was 1.6 kUA/L (<0.35 kUA/L normal range) (Pharmacia, Uppsala, Sweden). Skin-prick tests with *Aspergillus fumigatus* antigen showed a positive reaction for type I hypersensitivity (Histamine: 7×7 mm, aspergillus mix: 3×3 mm) (Allergopharma, Reinbek, Germany). Intradermal tests with *Aspergillus fumigatus* antigen showed a positive reaction (histamine 7×7, aspergillus mix: 15×15). Spirometry showed airway obstruction (FEV1: 69%, FEV1/FVC: 67) with significant bronchodilator reversibility (360 ml [% change 20%]). High Resolution Computed Tomography (HRCT) demonstrated ground glass and nodular infiltrations in different segmental areas. Regarding the differential diagnosis of increased total IgE levels, the patient had asthma and allergic rhinitis. However allergic rhinitis and asthma might not include diseases presenting very high total IgE levels.[11] Parasitic infections which are associated with high elevated total IgE levels were also excluded by documentation of negative stool examination for three occasions. She also had no clinical evidence of other diseases which cause elevated total IgE levels such as gastroenteritis, hyper IgE syndrome, lympho-reticular malignancies, netherton syndrome, HIV infection.[11] CSS syndrome was ruled out due to absence of CSS prodromal period, absence of both extra pulmonary symptoms such as peripheral neuropathy, and a progressive lack of eosinophilia. Based on the clinical and laboratory findings, the patient was diagnosed as ABPA.[6] Oral methylprednisolone (0.5 mg/kg/day) and itraconazole (200 mg/day) were introduced. Two weeks later, the daily doses of methylprednisolone were switched to alternate days for an additional eight weeks. The dose of methylprednisolone was tapered down over the following eight months until a dose of 4 mg/day was reached. The patient was maintained on methylprednisolone for a total of 14 months. Antifungal therapy was continued for 12 months. Clinical improvement was evident with a significant reduction in respiratory symptoms accompanied by a reduction in total IgE (145 kU/L), blood eosinophil count and an improvement in spirometry (Table 1). Recovery was also noticeable on the HRCT taken 14 months after diagnosis. Four months after discontinuation of methylprednisolone, the patient had no asthma symptoms. However, her total IgE level had risen to 1440 kU/L (Table 1). On skin exam-

☆ We assure the Editorial Board that this work as seen and approved by all co-authors has not been published previously and is not currently under consideration for publication elsewhere. The authors declare they have no conflict of interest.