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Severe adverse drug reaction due to Cypress Sublingual Immunotherapy

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To the Editor:

Literature data indicate sublingual immunotherapy (SLIT) as an effective and safe therapy,¹⁻³ and up to date, few reports are present on systemic reactions to subcutaneous immunotherapy (SCIT), as well as on SLIT.⁴

A 66-year-old Caucasian male patient referred to our Department with a 5-year history of allergic rhino-congiuntivitis and asthma with an exacerbation in the period December-April. This has resulted in a substantial reduction in his quality of life (QoL). The disease was unresponsive to conventional systemic antihistaminic therapy administered from 2010 until 2015. Personal medical history was positive for allergy to cypress and for an ischemic myocardial infarction.

According to EAACI guidelines^{3,5}, we performed routine laboratory chemical investigations and allergological analyses. Skin prick tests and RAST showed that he was becoming increasingly sensitive to *Dermatophagoides mix* and cypress. Prist was 610 (normal value ≤ 100), cypress ratio allergen sorbent test resulted to be ≥ 100 (being normal values 0.10-100).

According to these results and to EAACI guidelines, we started the SLITone^{ULTRA®} (ALK-Abelló A/S · Bøge Allé 6-8, DK-2970 Hørsholm · Denmark) in April 2016. SLIToneULTRA® is a biologically standardized allergenic extract presented in a single-dose container of 50 standardized reactivity units (SRU), 150 SRU, and 300 SRU. The treatment was divided in three phases: an initiation phase characterized by 50 SRU/day for five consecutive days followed by 150 SRU/day for five additional consecutive days, while the maintenance phase was characterized by 300 SRU/day (once a day), for at least 3 months.(Fig.1)

At the beginning of the induction phase (about 20 minutes after the first administration of SLIT, during the day 1), the patient developed a generalized urticarioid rash with extreme itch in association with a severe respiratory involvement (asthma, rhinorrhea, sneezing), tachycardia and hypotension. The patient was taken to the emergency room (ER) where an intravenous 4mg dose of betamethasone was administered along with an intramuscular dose of adrenaline (0.5 mL of 1:1000). This produced an immediate improvement of the symptoms. A diagnosis of severe adverse reaction to SLIT was made and the Authority was properly advised about this case.

SLIT is considered an effective and safe therapy. According to the literature^{4,6} and to our experience, in SLIT therapy we noticed only oral itching in about 13% of cases, with an early spontaneous resolution, after the induction period. However, we have never observed a severe general reaction to SLIT.

Rodriguez – Calderon et al. reported recently that only 1.53% of pediatric patients under allergen immunotherapy (AIT) experienced a systemic reaction.⁴ The authors reported also 3 cases of anaphylaxis to AIT, but they did not observe cases of SLIT-related anaphylaxis.⁴ Accordingly, our case remains the first case of a SLIT-related anaphylaxis.

In general, polysensitization (>3), grass pollen extracts and the use of natural extracts (vs. allergoids), seem to be the main risk factor to develop an anaphylactic reaction to AIT.⁴ However our patient did not meet all these features.

SLIT remains a safe therapeutic option and it is associated with a low incidence of generally non-severe systemic reactions. However, our report highlights that sometimes severe systemic reactions can be present also in SLIT patients. In this regard, a careful monitoring of the patients during the initial phase of a SLIT therapy should always be performed, in order to intervene as soon as possible and avoid even fatal consequences.

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Figure legends

Figure 1 Standardized reactivity units (SRU) according to days.

