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Occupational allergy to Spagulax[®] (*Plantago ovata* seed)

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KEY WORDS

Plantago ovata; psyllium; nasal challenge test; rhinoconjunctivitis; occupational allergy

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Summary

We report the case of a 36-year-old male pharmaceutical laboratory worker. On handling Spagulax[®] sachets whose content is a laxative called *Plantago ovata*, he immediately presented rhinoconjunctivitis. **Methods.** Specific allergy study included SDS-PAGE with Western Blot and specific nasal challenge to *Plantago ovata* extract. **Results.** Prick by prick for Spagulax[®] was negative. Total IgE: 126.5 U/mL. Western Blot recognized two proteins of 15 and 20 kDa in the extract of *Plantago ovata* and three proteins of 15, 18 and 50 kDa in the extract of *Plantago lanceolata*. **Conclusions.** We present a case of occupational allergy due to inhalation of and/or contact with *Plantago ovata* seeds.

Introduction

Plantago ovata is a herb whose small brown seeds look like fleas, hence its name in Greek, *psyllium*. The shells are pulverized and the resulting powder is known as *ispaghula*. This dust disperses very easily through the air when handled, and is a powerful occupational allergen (1). *Psyllium* seeds contain a large amount of mucilage, that expands when it comes into contact with water and becomes very gelatinous, which is why they are used as a volume laxative (2). Since Ascher (3) described the first case of *Plantago ovata* seed allergy in 1941, multiple occupational allergic reactions (rhinitis and asthma), and anaphylaxis have been reported (1,4). In workers in the pharmaceutical industry, the prevalence of asthma is around 3.6% and sensitization to *Plantago ovata* seeds is 27.9%, based on prick tests and determination of specific IgE (5). In most individuals, sensitization occurred due to inhalation of the powder of *Plantago ovata* seeds in the workplace (5).

Sensitization may be asymptomatic or may trigger reactions ranging from rhinitis or asthma to anaphylaxis (6).

Plantago lanceolata is a known aeroallergen in our country that usually produces seasonal rhinoconjunctivitis mediated by IgE (7). Despite the phylogenetic relationship between *Plantago ovata* and *Plantago lanceolata*, most studies suggest a lack of cross-reactivity between them (8,9).

Case report

We report the case of a 36-year-old male pharmaceutical laboratory worker since 2013, who was responsible for handling Spagulax[®] sachets, whose content is a laxative called *Plantago ovata* to market in France. On march 2016, he referred rhinoconjunctivitis that started thirty minutes later on sealing those sachets of Spagulax[®], and improved after administration of a 20 mg oral ebastine tablet. He performed this task for hours only

three or four times a year. Personal history of atopy: allergic to nuts, corn and peach in the form of acute urticaria. He did not refer rhinoconjunctivitis out of his place of work.

Materials and methods

Prick tests were performed based on the predominant aeroallergen batteries in our area and on foods with commercial extracts (Bial Aristegui company, Bilbao, Spain). Total IgE and IgE specific to positive allergens in the skin test were determined by ImmunoCAP (Thermo Fisher Scientific, Phadia, USA). Hydrochloride histamine 10 mg/mL and 0.9% saline were used as positive and negative controls, respectively.

Prick by prick was performed using the Spagulax[®] sachet provided by the patient.

Allergenic extracts

Proteins were obtained from *Plantago ovata* and *Plantago lanceolata* as follows. *Plantago ovata* seeds (Natupur, Spain) and *Plantago lanceolata* pollen (Pharmalerga, Czech Republic) were weighed, crushed and suspended at 0.25 g/mL in phosphate buffered saline (PBS) [1.37 mM NaCl, 14.7 mM KH₂PO₄, 78.1 mM Na₂HPO₄, 26.8 mM KCl], pH 7.4. The homogenate was magnetically stirred for 30 min at 5 ± 3°C. The sample was sieved to remove the residues of seeds and the extract was centrifuged at 10,000 g for 15 min at 5 ± 3°C. The extract was obtained by filtering the soluble fraction through an AP type 20 glass fibre filter (Merck-Millipore[™], Darmstadt, Germany), comprising a glass fibre profiler and a 0.8 mm membrane (AP membrane 2009000, Merck-Millipore[™], Darmstadt, Germany), and dialyzed against de-ionized water with membranes with a molecular cut-off of 3500 Da (Visking, Iberlabo) for 16 h at 5 ± 3°C and then stabilized by freeze drying.

SDS PAGE/IgE Western blot

Proteins from *Plantago ovata* and *Plantago lanceolata* were analysed by sodium dodecyl sulfate polyacrylamide gel electrophoresis (SDS-PAGE), according to Laemmli (10) in 15% polyacrylamide gels under reducing conditions. Proteins were visualised by Coomassie Brilliant Blue R-250 staining and electrophoretically transferred to polyvinylidene difluoride (PVDF, Trans-blot turbo[™], BIORAD, Hercules, CA, USA). Binding of IgE antibody to allergens was analysed by Western Blot using the patient's serum and anti-human IgE peroxidase conjugate (Southern Biotech, Birmingham, USA). Chemiluminescence detection reagents (Western Lightning[®] Plus-ECL, Perkin Elmer, Waltham, MA, USA) were added following the manufacturer's instructions. IgE binding bands were identified using the BioRad Diversity database program.

Specific nasal challenge

Specific nasal challenge was performed with *Plantago ovata* extract controlled by an acoustic rhinometer (Rhinometrics SRE 2000) following Rhinoconjunctivitis Committee of the Spanish Society of Allergy and Clinical Immunology recommendation (11). The extract was supplied by Diater laboratories and prepared at two concentrations: 0.107 mg/mL and 1.07 mg/mL. The test was completed by observing a positive response: reduction of nasal volume of between 2 and 6 from the nasal orifice ≥ 20%.

Results

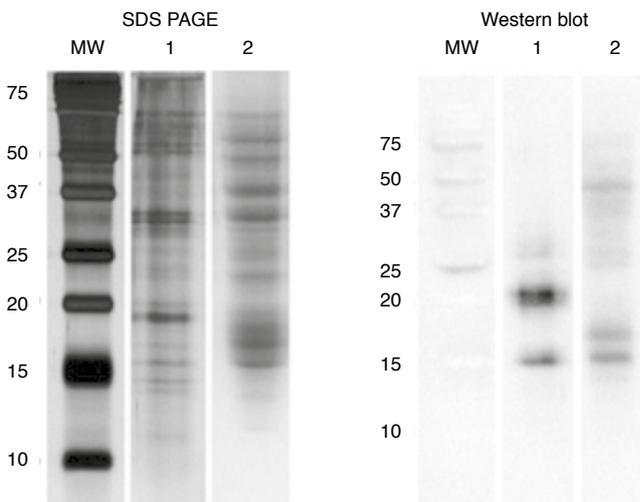
Inhalant skin tests were only positive for house dust mites. Skin test and specific IgE with *Plantago lanceolata* pollen were negative. Food battery tests were positive for nuts (hazelnut, almond and peanut), peach and cereal (rice and corn). Panallergens such as LTP, profilin or polcalcin were negative. Prick by prick to Spagulax[®] was negative.

Total IgE was 126.5 U/mL and specific IgE to corn: 0.86; rice: 0.23; almond: 0.77; hazelnut: 0.22; peanut: 0.33 and peach: 5.31 kU/L.

Western Blot showed two proteins of 15 and 20 kDa in the *Plantago ovata* extract and three proteins of 15, 18 and 50 kDa in the *Plantago lanceolata* extract, one of which was compatible in molecular weight with Pla 1 (18 kDa), corresponding to the major allergen (**figure 1**).

Nasal challenge with the *Plantago ovata* extract was positive with a minimum cross area (MCA) and nasal cavity volume 2 cm

Figure 1 - SDS PAGE and Western blot for specific immunoglobulin E of an extract from a laxative containing *Plantago ovata* seed and *Plantago lanceolata*.



to 6 cm from the nostril = -49% being observed 30 minutes after the last concentration administered (1.07 mg/mL). The symptom score (11) was ≤ 3 points in all tested categories (rhinorrhea, nasal obstruction, nasal itch and sneezing).

Discussion

Plantago ovata is a herb whose seeds are called *psyllium*. The shells are pulverized and the resulting powder is known as *ispaghula*. This dust disperses very easily upon handling and is known to be a potent occupational allergen, that can produce immediate hypersensitivity in exposed workers, especially healthcare workers who dispense it to patients, and workers in the pharmaceutical industries that process the seeds (5,12). Inhalation appears to be the most frequent route of sensitization, but there are also reported cases of anaphylaxis after oral consumption of the laxative or some cereals containing it (2). Our patient developed IgE-mediated rhinoconjunctivitis by inhaling and/or manipulating *Plantago ovata* while packaging it for sale. The frequency of sensitization is high in exposed individuals: 32% of pharmaceutical industry workers have skin tests and/or specific IgE positive for *psyllium* (5). However, the prevalence of occupational asthma in exposed workers is around 3.6-4%, indicating that not all exposed individuals develop the disease; therefore, specific challenge tests are necessary to confirm the diagnosis (5,13).

In our patient, skin tests were negative but the specific nasal challenge was positive, and therefore we confirmed the initial suspicion of occupational rhinoconjunctivitis due to *Plantago ovata*.

Analysis of *Plantago ovata* by immunoblotting showed bands of 15 and 20 kDa, values similar to those reported in previous studies (allergenic proteins oscillate between 10 and 66 kDa) (2,14). To date, no specific immunoblot pattern associated with respiratory or systemic symptoms has been found (15).

Most reports indicate no cross reactivity between *Plantago ovata* and *Plantago lanceolata*, although Bernedo et al. reported the opposite (15). In our case, the patient did not present rhinoconjunctivitis symptoms outside the work place and tests did not demonstrate cross reactivity with *Plantago lanceolata*. Therefore, further studies are warranted.

Conclusions

In conclusion, we report a case of occupational allergy due to inhalation of Spagulax® powder formulated with *Plantago ovata* seeds. Western Blot recognized two proteins with molecular weights of 15 and 20 kDa for *Plantago ovata* and three proteins of 15, 18 and 50 kDa for *Plantago lanceolata*.

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