

SHORT REPORT

Occupational asthma due to IgE mediated allergy to the flower *Molucella laevis* (Bells of Ireland)

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Background: About 25% of greenhouse flower and/or ornamental plant growers sensitised to workplace flowers or moulds have occupational asthma, a disease that is suffered by 8% of the growers who cultivate these crops.

Aim: To document a case of occupational asthma due to IgE mediated allergy to the flower *Molucella laevis*.

Methods and Results: There was a history of work related seasonal asthmatic and rhinoconjunctivitis symptoms in a *Molucella laevis* grower. Bronchial obstruction following exposure to *Molucella laevis* was documented by a fall in FEV₁ from 89% to 73% of predicted during seasonal exposure to *Molucella laevis*. Daily PEF measurements showed a fall from 500 to 250 l/min during this period following withdrawal of inhaled steroids. Bronchial reactivity to inhaled methacholine was increased (PC₂₀ 1.45 mg/ml). Confirmation of sensitisation to *Molucella laevis* flower pollen extract was done using an SPT and by demonstration of *Molucella laevis* specific serum IgE (18 IU/ml; class 4). Specific inhalation challenge with *Molucella laevis* extract provoked an early and late asthmatic reaction (EAR and LAR) with a fall in FEV₁ compared with control day of 40% and 53% respectively, with associated 5.1-fold increase in absolute sputum eosinophil cell counts and 2.9-fold increase in neutrophil cell counts.



Figure 1 *Molucella laevis* (Bells of Ireland) is a lightly scented plant that grows 36 inches tall. The 2-inch, white-veined green bells that cling closely to stems are not really flowers but enlarged calyxes. The true flowers, tiny, fragrant, and white, are deep within the bells. The popular name alluding to Ireland has been applied to this plant only because of the green colour of the bells; it is native to the eastern Mediterranean region, primarily Syria.

Workplace exposure to specific inhaled allergens is an important cause of new-onset asthma and exacerbation of pre-existing asthma. The term occupational asthma (OA) usually refers to new-onset asthma caused by workplace exposure; 5–15% of new-onset asthma is reported to be occupational in origin.¹

About 25% of greenhouse flower and/or ornamental plant growers sensitised to workplace flowers or moulds have OA; 8% of greenhouse flower growers have OA.²

We describe the first case of OA due to IgE mediated allergy to the decorative flower *Molucella laevis* (fig 1).

METHODS

The patient was a 60 year old male *Molucella laevis* grower presenting with progressive seasonal respiratory symptoms, consisting of productive coughing, wheezing, and chest tightness, occurring primarily during two hours of work with *Molucella laevis* in his greenhouse in the early morning and evening, and eventually persisting at night.

Symptoms were confined to the period of pollination of *Molucella laevis* (June until October) and started in the first year that he was growing this flower. He had experienced two symptomatic growth seasons on presentation to our outpatient clinic.

The greenhouse contained 14 000 flourishing *Molucella laevis* plants in an area of 250 m² (10% of the total greenhouse). The greenhouse has a yearly production and sale of 90 300 stalks

per year, representing one third of the production marketed in Aalsmeer (one of five flower whole sale auction centres in the Netherlands). It is estimated that 100 greenhouses grow *Molucella laevis* throughout the Netherlands. The patient was personally involved in planting, harvesting, trimming, and transporting the *Molucella laevis* plants.

A protector, colloquially referred to as “dust mask” or “gas mask” was used by the patient.³ An air supplying positive pressure, self contained breathing apparatus was used after onset of symptoms and seemed effective in preventing them. However, in the warm climate of the greenhouse (temperature 38°C), perspiration and condensation of the goggle was not tolerated, and caused malfunctioning of the protector. The patient therefore decided not to use it, despite symptoms.

Symptoms decreased after one day of avoiding the greenhouse. Salbutamol inhalation therapy gave immediate relief of symptoms. Rhinoconjunctivitis was associated with the above mentioned respiratory symptoms. His wife (the only other exposed worker in the patient’s greenhouse) and one neighbouring colleague who both grew *Molucella laevis* had no allergic or irritant symptoms while working in the greenhouse. The patient had no prior history of symptoms of allergic diseases. Physical examination revealed expiratory wheezing. Chest radiography and routine laboratory investigations showed no abnormalities.

Abbreviations: EAR, early asthmatic response; FEV₁, forced expiratory volume in 1 second; HEP, histamine equivalent prick test; LAR, late asthmatic response; OA, occupational asthma; PEF, peak expiratory flow; SPT, skin prick test

Skin prick tests (SPTs) were performed with common inhalant allergens including grass, trees, weeds, house dust mites, animal danders, fungi, food, and latex (ALK, Denmark), as well as with extracts of *Molucella laevis* flowers (including pollen), and extracts of branches and leaves. Final protein extract concentrations of 0.1 mg/ml, 1 mg/ml, and 10 mg/ml were prepared in our laboratory.

Preparation of allergenic extracts from *Molucella laevis* plants was as follows. Flowers (including pollen) were suspended in a 0.01 M NH_4HCO_3 buffer (pH 7.8) and homogenised in a Vortex blender for 10 minutes in an ice bath. After centrifugation, the supernatant was successively dialysed, filtered, and freeze dried.

Allergens in freeze dried *Molucella laevis* extracts were biotinylated and immobilised to streptavidin coated Caps of the Unicap system (Pharmacia, Sweden).

Specific IgE binding to the different immobilised extracts and common inhalant allergens including grass, trees, weeds, house dust mites, animal danders, fungi, food, and latex were measured (Pharmacia).

Spirometry was performed for measurement of FEV₁ (forced expiratory volume in 1 second) with an electronic pneumotachograph (Jaeger, Germany).

Serial measurements of peak expiratory flow (PEF) were recorded by using a Mini-Wright peak flow meter.

The PC₂₀ to metacholine (provocative concentration of metacholine producing a 20% fall in FEV₁) was measured according to the method described by Cockcroft and colleagues.⁴

Specific inhalation challenge with *Molucella laevis* pollen extract was performed using a DeVilbiss nebuliser, as described previously.⁵

Inhaled corticosteroids and β adrenergic drugs were discontinued, four weeks and one week, respectively before the *Molucella laevis* inhalation challenge. Work exposure to *Molucella laevis* was stopped one week before a four day admission in our hospital for *Molucella laevis* inhalation challenge testing.

Metacholine challenge followed by sputum induction and processing⁶ was performed two days before (one day before control day) and one day after the specific inhalation challenge.

RESULTS

SPT with *Molucella laevis* pollen extract was positive at a concentration of approximately 10 mg/ml (histamine equivalent prick test (HEP) = 1.0 SPT, with the same extract being negative in patient his exposed wife and five healthy non-exposed controls). No other tests were performed with either his wife or controls.

SPTs with the other abovementioned allergens yielded negative results (HEP 0.0). IgE specific for the flower (pollen) extract of *Molucella laevis* was 18 IU/ml (class 4). The IgE test for *Molucella laevis* branches and the common inhalant allergens were negative (<0.35 IU/ml). Total IgE content was 122 IU/ml.

Sequential spirometry during the *Molucella laevis* season revealed a declining FEV₁ from 3.3 (89% predicted) to 2.7 litres (73% predicted).

Visual inspection of a serial daily peak flow plot showed a decrease in morning peak flow values from 500 to 250 l/min within a week after cessation of therapy with inhaled steroids during continued exposure to *Molucella laevis*. Morning peak flow values returned to 500 l/min after one week of completely avoiding exposure to *Molucella laevis* in the greenhouse.

Bronchial inhalation challenge with *Molucella laevis* pollen with the final pollen extract concentration of 10 mg/ml induced a dual asthmatic response (early and late asthmatic response (EAR and LAR): a fall in FEV₁ of 40% and 53% compared with control day, respectively).

Sputum examination revealed a 5.1-fold increase in absolute eosinophil and a 2.9-fold increase in neutrophil numbers after exposure to *Molucella laevis* during the inhalation challenge (44.2% eosinophils and 23.3% neutrophils of TCC = $21.94 \times 10^6/\text{ml}$) compared with baseline numbers. Concomitantly, there was a 3.4-fold increase of PC₂₀ to metacholine from baseline to 24 hours after provocation value (PC₂₀ 0.43 and 1.45 mg/ml respectively).

After four months of avoidance of *Molucella laevis* and the institution of therapy with inhaled steroids our patient was free of asthmatic symptoms. Concomitantly, a decrease in sputum eosinophil number (3.3% eosinophils and 66.3% neutrophils of TCC = $5.09 \times 10^6/\text{ml}$) and an increase of PC₂₀ to metacholine (PC₂₀ 9.7 mg/ml) was found.

DISCUSSION

Decorative flower allergy and IgE mediated occupational asthma caused by these flowers has been previously reported for freesias, chrysanthemums, Easter lily, and tulips^{7,8} (floral shop workers), *Passiflora alata* and *Rhamnus purshiana*⁹ (pharmacy worker), sunflower¹⁰ (harvest worker), *Dianthus caryophyllus*¹¹, and *Stephanotis floribunda*¹² (greenhouse workers).

In the case presented here, *Molucella laevis*, a Lamiaceae species, was the only plant present in the greenhouse, and was thus suspected to be the cause of the new-onset asthma in this greenhouse worker with OA. The temporal relation between exposure in the pollination season and asthmatic and other allergic complaints was also suggestive.

We present a complete picture of an allergic asthmatic reaction to a new inhaled allergen, *Molucella laevis*. We found specific IgE and positive SPT to *Molucella laevis* (pollen) extract, as well as an EAR and LAR to pollen inhalation with the expected rise in airways eosinophilia and neutrophilia.

Ideally, the inhalation challenge test with *Molucella laevis* should also have been performed in non-sensitised asthmatic control subjects to exclude the possibility of a non-specific bronchial irritant response. However, in our opinion absence of irritant symptoms in the sentinel subject, a negative SPT result in controls, and the use of an allergen extract preparation method that eliminates low molecular weight chemicals made this possibility unlikely. Furthermore, no cases of OA were found among non-sensitised greenhouse growers in previous studies.²

Continued exposure to *Molucella laevis* may theoretically lead to the development of long lasting poorly reversible bronchial responsiveness and persistent asthma.

We advised our subject to avoid all future exposure to *Molucella laevis*. Initially, he preferred to continue growing this plant, reducing the intensity of OA by inhaling corticosteroids and β adrenergic drugs before exposure to the allergen and by using a protector and improved ventilation in the workplace. But eventually, because of persisting symptoms despite these protective measures, he had to stop growing *Molucella laevis*.

The cultivation of greenhouse flowers, exposure to specific flower crops, and work inside a greenhouse are risk factors for sensitisation to workplace allergens and bronchial asthma.² It has been estimated that 15% of flower growers abandon the occupation because of unbearable symptoms.²

For decades, many people have used respirators on the job to protect airways. However, reducing inhalation of pollen allergens in the greenhouse by using a respirator should be relied on only as a secondary means of protection. No respirator is fully protective, although an air supplying positive pressure, self contained breathing apparatus offers a high degree of protection.³ This high degree of protection comes at a cost. This protector is heavy and its use is limited to less than 30 minutes. The extra weight of the tank, high temperatures, high workload, required maintenance level, and interference with eyeglasses can exact a heavy toll on the wearer's endurance.

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