

Case report

Occupational asthma induced by aniseed

Fraj J, Lezaun A, Colás C, Duce F, Domínguez MA, Alonso MD.
Occupational asthma induced by aniseed.
Allergy 1996; 51: 337–339. © Munksgaard 1996.

This report deals with clinical and immunologic studies in a butcher with work-related asthma. Both the positive methacholine inhalation test and the significant changes observed in PEFr measurements supported the diagnosis of asthma. The significant fall observed in PEFr measurements when the patient handled aniseed supported the diagnosis of occupational asthma. Skin prick tests carried out with 13 spices showed positive reactions only to aniseed extract. The patient had high levels of specific anti-aniseed IgE antibodies. The bronchial challenge test with an aniseed extract showed an immediate response without a late response. These findings suggest that the respiratory symptoms in our patient were induced by the inhalation of aniseed dust through an IgE-mediated immunologic mechanism of immediate hypersensitivity. This study established the diagnosis of occupational asthma from aniseed dust sensitization.

**J. Fraj, A. Lezaun, C. Colás,
F. Duce, M. A. Domínguez,
M. D. Alonso**

Servicio de Alergología, Hospital Clínico
Universitario Lozano Blesa, Zaragoza, Spain

Key words: allergy; bronchial asthma; bronchial
provocation test; occupational asthma

Dr Juan Fraj
Servicio de Alergología
Hospital Clínico Universitario Lozano Blesa
C. San Juan Bosco 15
50009 Zaragoza
Spain

Accepted for publication 8 December 1995

It has long been known that exposure to grain and seed products may cause respiratory symptoms of rhinitis and asthma. Organic dust derived from grain and seed in the workplace is commonly identified as the cause of occupational asthma. This includes dust from cereal grains, buckwheat flour (1), *Lathyrus sativus* flour (2), and soybean (3) and other legumes (4).

Anise (*Pimpinella anisum* L.) is a vegetable belonging to the Umbelliferae family. Its powdered seeds are an important additive in some foods (e.g., sausage, salami, pork, ham) and liqueurs. We report an unusual case of IgE-mediated bronchial asthma due to aniseed dust inhalation.

Case report

A 24-year-old man, a nonsmoker, with no family or personal history of atopy, was studied in our department. For the last 4 years, he had been working in the meat industry, where he handled spices and other additives. Fine dusts of these substances were released during the work. Three years after he had started this job, the patient began to notice dyspnea, wheezing, unproductive cough, and chest tightness a few minutes after handling these substances. When he avoided exposure to additives and spices, his respiratory symptoms decreased markedly until he

was asymptomatic. A therapeutic trial with betamimetics and inhaled corticosteroids was effective in preventing asthma attacks.

Clinical examination of the patient was normal. The white blood cell count was 9000/ml with 450 eosinophils/ml. Total IgE was 347 U/ml. Spirometry revealed an FEV₁ of 98% and FVC of 113% of predicted.

Material and methods

Extracts for in vivo tests

We prepared extracts of 13 spices and garnishes: red pepper, cinnamon, garlic, cumin, cayenne, pepper, nutmeg, clove, black pepper, white pepper, aniseed, mustard, and parsley. Two grams of the spice was dissolved in 20 ml of phosphate-buffered saline (PBS, pH 7.3) at laboratory temperature. After stirring for 60 min and passing it through filter paper, the solution was dialyzed (10 kDa) in PBS for 24 h and then passed through a 0.22-µm Millipore filter (Millipore, Bedford, MA, USA) for sterilization to a final concentration of 1:10 w/v. Twofold dilutions were made for the study.

Skin prick tests

Skin prick tests were performed with spice extracts (1:10 w/v) as well as with a battery of commercially

available allergens, including pollen of grass (*Phleum pratense*, *Cynodon dactylon*, and *Phragmites communis*), trees (*Olea europaea*, and *Platanus acerifolia*), and weeds (*Artemisia vulgaris*, *Salsola kali*, and *Parietaria judaica*); fungi; dust mites; and mammal danders (Abelló SA, Madrid, Spain). Histamine phosphate 10 mg/ml and 0.9% normal saline were used as positive and negative skin test controls, respectively.

Skin prick tests were performed with the allergy pricker lancet (Dome-Hollister-Stier), as described elsewhere (5). Responses were examined after 15 min by measuring the two perpendicular diameters of the wheal. A reaction was considered positive if the wheal size was at least 3 mm in diameter larger than the negative control. The same tests were performed on 10 atopic and 10 normal nonexposed people who served as controls.

Specific IgE determination

Specific IgE concentrations to aniseed were determined by the RAST FEIA CAP System (Pharmacia Diagnostics AB, Uppsala, Sweden), according to the manufacturer's instructions.

Ambulatory monitoring of peak expiratory flow rate (PEFR)

PEFR was monitored every 2 h during the day, both at work and away from work, for 2 weeks with a Mini Wright peak flow meter (Clement Clarke International, London, UK). The best of three reproducible (± 20 l/min) values was kept for analysis. Daily changes $\geq 20\%$ were considered significant.

Bronchial provocation test (BPT)

Nonspecific BPT with methacholine inhalation was performed according to the method of Cockcroft et al. (6) with some modifications (7). The aerosolized particles were generated by a continuous pressurized Hudson nebulizer, model 1720, with a fixed input of 7.5 l/min and an output of 0.276 ml/min.

Specific BPT was done with aniseed extract. Inhaled β_2 -adrenergic agents were stopped 8 h before the challenge. The inhaled anti-inflammatory preparation was stopped on the morning of the test. It consisted of daily inhalation of the aerosolized allergen in progressively increasing concentrations (1:320, 1:160, 1:80, 1:40, 1:20, and 1:10 w/v) for 2 min at tidal volume until a reaction occurred. The different concentrations of extract were given on different days. A control challenge with PBS was performed before antigen challenge. Baseline measurements of FEV₁ and FVC were performed and

repeated at 5, 10, 15, 20, 30, and 60 min after each challenge. A positive immediate response was defined as a 20% fall from basal FEV₁. Hourly PEFR measurements were performed during a 24-h period, excluding sleeping periods, after each challenge to evaluate the late response.

Two asthmatic patients with similar, nonspecific bronchial reactivity were also challenged with 1:10 w/v aniseed extract.

Results

The nonspecific bronchial provocation test (BPT) with methacholine was done during symptomatic periods and revealed a PC₂₀ of 0.6 mg/ml. Monitoring of PEFR showed significant drops ($> 50\%$) from baseline values on the days the patient worked with aniseed. Skin prick tests (SPT) with the aniseed extract were strongly positive. The patient exhibited a 9×8 mm wheal and erythema response. SPT with the battery of common inhalants and spices were all negative. SPT with aniseed extract were negative in control subjects. IgE antibodies specific to aniseed extract were found in the patient's serum. The RAST FEIA value was 22 kU/l. IgE antibodies specific to aniseed were not measured in control subjects.

Specific BPT with the aniseed extract (1:160 w/v) elicited an isolated immediate response with a fall in FEV₁ of 29% from basal values (Fig. 1). It was done during asymptomatic periods. No late reaction was observed. This test was negative in the control subjects.

Discussion

Various vegetable proteins, such as those of wheat, rye, or soybean flour (8, 9), may cause occupational asthma, while other potential contaminants of flour and grain which are inhaled cause baker's asthma

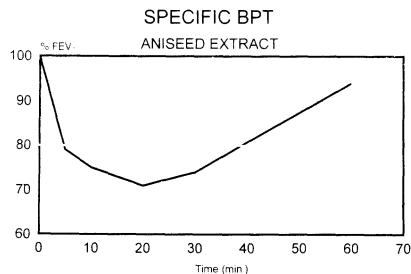


Fig. 1. Bronchial provocation test (BPT) with aniseed extract.

(10). In addition, workers involved in the processing of coffee beans, castor beans, tea, and tobacco may suffer from occupationally associated asthma due to proteins from those plant products (11). Finally, those exposed to pollen or other plant components in their work (e.g., florists) may become sensitized to those components as well (12).

The patient in our study experienced episodes of asthma due to inhalation of airborne dust particles of powdered aniseed. It was demonstrated by BPT that aniseed caused the respiratory symptoms that he presented at work when exposed to this allergen. Type I hypersensitivity is strongly suggested by the positivity of SPT and by the demonstration of specific IgE antibodies to aniseed by the RAST FEIA CAP System in the patient's serum. Although immunologic cross-reactivity among the Umbelliferae family has been demonstrated (13), the clinically relevant cross-reactivity among aniseed, cumin, and parsley was not found in our patient. To the best of our knowledge, this is the first report of bronchial asthma due to dust aniseed inhalation. Neither an irritant nor a toxic effect was suspected, as no response was observed in control subjects. No late reaction occurred after BPT. The quantity of antigen administered may be responsible for the production of certain late-phase reactions (14); this has been demonstrated by various investigators who could convert early allergen response to dual response just by administering a large dose of allergen with, e.g., a short-acting β_2 -agonist. Some studies of occupational exposure showed that increased airway responsiveness may occur after an early response alone, and that the late-phase response is not necessary (15).

The significant changes in PEFR records when the patient was working support the diagnosis of occupational asthma. The high degree of nonspecific bronchial hyperresponsiveness observed may have been due to continuous exposure to aniseed.

We have not yet characterized the allergens in aniseed extract. However, the results of the *in vivo* and *in vitro* tests suggest that the aniseed extract antigens are nondialyzable (molecular mass greater than 10 kDa). The patient's absence of symptoms

upon ingestion of aniseed contained in some food suggests that nonimmunologic factors (e.g., gastric acid and pepsin, pancreatic enzymes, and intestinal enzymes) may destroy antigens from aniseed.

References

1. Valdivieso R, Moneo I, Pola J, et al. Occupational asthma and contact urticaria caused by buckwheat flour. *Ann Allergy* 1988;63:149-52.
2. Valdivieso R, Quirce S, Sainz T. Bronchial asthma caused by *Lathyrus sativus* flour. *Allergy* 1988;43:536-9.
3. Bush RK, Schoeckenstein D, Meier-Davis S, Balmes J, Rempel D. Soybean flour asthma: detection of allergens by immunoblotting. *J Allergy Clin Immunol* 1988;82:251-5.
4. Martin JA, Compaired JA, De la Hoz B, et al. Bronchial asthma induced by chickpea and lentil. *Allergy* 1992;47:185-7.
5. Malling H-J, Andersen CE, Boas MB, Hogersen F, Munch EP, de Weed B. The allergy prickler. *Allergy* 1982;37:563-7.
6. Cockcroft D, Killian DN, Mellon JA, Hargreave FE. Bronchial reactivity to inhaled histamine: a method and clinical survey. *Clin Allergy* 1977;7:235-43.
7. Pola J. Asma bronquial por sensibilización a antígenos de cucaracha: aspectos clínicos, inmunológicos y patrones de respuesta bronquial. *Rev Esp Alergol Inmunol Clin* 1989;4:111-22.
8. Rodrigo MJ, Morell F, Helm RM, et al. Identification and partial characterization of the soybean-dust allergens involved in the Barcelona asthma epidemic. *J Allergy Clin Immunol* 1990;85:778-84.
9. Fraj J, Quirce S. Asma ocupacional por inhalación de harina de soja en ganaderos. *Rev Esp Alergol Inmunol Clin* 1994;9:47-52.
10. Sutton R, Skerritt JH, Baldo BA, et al. The diversity of allergens involved in baker's asthma. *Clin Allergy* 1984;14:93-107.
11. O'Hollaren MT. Occupational asthma due to high molecular weight allergens. *Immunol Allergy Clin North Am* 1992;12:795-817.
12. Quirce S, Garcia-Figueroa B, Olaguibel JM, Muro MD, Tabar AI. Occupational asthma and contact urticaria from dried flowers of *Limonium tataricum*. *Allergy* 1993;48:285-90.
13. Helbling A, López M, Schwartz HJ, Lehrer SB. Reactivity of carrot specific IgE antibodies with celery, apiaceous species and birch pollen. *Ann Allergy* 1993;70:495-9.
14. Hargreave FE, Dolovich J, Robertson DG, Kerigan AT. The late asthmatic responses. *Can Med Assoc J* 1974;110:415-24.
15. Machado L. Increased bronchial hypersensitivity after early and late bronchial reactions provoked by allergen inhalation. *Allergy* 1985;40:580-5.

This document is a scanned copy of a printed document. No warranty is given about the accuracy of the copy. Users should refer to the original published version of the material.