

Seasonal occupational asthma in an agricultural products merchant – a case report

Merget R, Heger M, Wahl R, Cromwell O, Rasche K, Schultze-Werninghaus G. Seasonal occupational asthma in an agricultural products merchant – a case report. Allergy 1994; 49: 897–901. © Munksgaard 1994.

A 52-year-old agricultural products merchant reported mild occupational asthma and rhinitis throughout the year, with severe asthma from February to May. He had been exposed to various substances, particularly grain, insecticides, fungicides, and fertilizers over 35 years. We identified a castor-bean-containing fertilizer as the cause of the disease by skin prick test and bronchial provocation test. Specific IgE against castor bean was detected by enzyme allergosorbent test, and proteins with mol. mass of less than 14.4 kDa and masses of 15.5, 29.5, and 30.5 kDa were identified as allergens by Western blot analysis. The seasonal character of symptoms could be explained by a more frequent use of the fertilizer during spring. Six months after avoidance of the allergen, the patient reported chronic bronchitis without asthma. Occupational allergy to castor bean should be considered in subjects with seasonal asthma and exposure to “natural” fertilizers.

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Key words: allergy; castor bean; occupational asthma; seasonal asthma.

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Accepted for publication 25 May 1994

Predominantly seasonal occupational asthma in an agricultural products merchant is reported. The history of this patient strongly suggested a potent seasonal allergen, but seasonal asthma has not been previously described in this profession. In French farmers, a seasonal pattern of asthma caused by sensitization to castor bean has been reported, the seasonal pattern being associated with a more frequent use of fertilizers containing castor bean during spring and late summer (5).

Asthma caused by castor bean was first reported in 1914 (1). The disease was described in laboratory workers, but it has also been recognized in industrial workers of oil-processing mills, fertilizer retailers, dockers, draymen, upholstery workers, farmers, and workers in contact with castor-bean-contaminated bags (5). Epidemics of asthma among citizens of towns with oil mills provide evidence of the high sensitizing potency of castor bean (4, 5).

Case report

A 52-year-old agricultural products merchant was admitted to our department for assessment of

occupation-related asthma and rhinitis. He had been occupationally exposed to various substances, particularly grain, seeds, insecticides, fungicides, other pesticides, and fertilizers, over 35 years. Since the age of 37 years, he had worked usually in the warehouse office, but had rarely handled the products. He reported increasing sale of a “natural” fertilizer since the age of 47 years. About 2 tons of the fertilizer per year were bought in January and sold in the late spring. One year before the investigation, the fertilizer had been stored throughout the year for the first time.

He had been healthy until 3 years before the investigation, when he experienced work-related mild asthma and rhinitis throughout the year, with severe asthma from February to May. During weekends and holidays, he was symptom-free. Recurrent episodes of asthma had been observed in the workplace with increasing frequency and intensity during the last year before admission. He could not relate his symptoms to a certain product or cause. There was no history of allergy or asthma in his family. He had suffered from diabetes mellitus for several years, and this was controlled by diet only. At the time of ex-

amination, his asthma was stable without medication.

Physical examination did not reveal any signs of asthma and was otherwise normal. The differential blood count showed 4% eosinophils, total serum IgE was 364 U/ml, and blood glucose was 221 mg/dl. Further laboratory findings were normal. Radiographs of the chest were normal, as were lung function tests, with an FEV₁ of 90% predicted.

Material and methods

In vivo tests

Skin prick tests (SPT). SPT were done with a battery of environmental allergens including house-dust mites, storage mites, cat, mouse, rat, arthropods, pollen, soybean, and molds (Allergopharma, Reinbek and Bencard, Neuss, Germany), as described by Pepys (6). SPT were also done with a 100 mg/ml aqueous extract of dust from the patient's office, and a 100 mg/ml solution of a castor bean fertilizer ("Rizinus Schrot", Overlack, Moenchengladbach, Germany). SPT with occupational substances were done in duplicate, and the mean wheal diameters were recorded.

Bronchial provocation tests. Methacholine (Aldrich, Steinheim, Germany) was inhaled with a jet nebulizer (Heyer, Bad Ems, Germany) in doubling doses. The output of the nebulizer was 0.23 ml/min. Specific airway resistance was recorded with a volume-constant body plethysmograph (Jäger, Würzburg, Germany) without an intervention (base line), after 10 inhalations of isotonic saline (placebo) or methacholine. The amount of aerosol released from the nebulizer was estimated by weighing the aerosol reservoir. PD₅₀ was calculated from the line between the last two data points of the (log)dose-response curve by interpolation with a Hewlett Packard 41C calculator. The cutoff point for bronchial hyperresponsiveness in our laboratory is a PD₅₀ of ≤ 1 mg. With a cutoff point for a PD₅₀ of ≤ 125 μ g, our method has a specificity of 85% and a sensitivity of 26% for wheeze during the last year as a standard (unpublished data). Tenfold dilutions of the 100 mg/ml extracts of the fertilizer or office dust were used for bronchial provocation tests with allergen. Inhalations started with 10 pg/ml of the fertilizer and 100 μ g/ml of the office dust. Inhalation of both the extracts and recording of the bronchial reaction were done as with methacholine. Time-response studies were done by measuring specific airway resistance at 0, 10, 20, 30, 60, and 120 min after the inhalation of the highest concentration. Peak-flow measurements were recorded for at least 8 h with a Mini-Wright peak-flow meter (Airmed, London, UK).

In vitro tests

Enzyme allergosorbent test (EAST). *In vitro* tests were done with castor bean and grass pollen extracts (Allergopharma). Ten CNBr-activated cellulose paper disks were incubated in 1 ml of the 10 μ g/ml castor bean extract for 16 h at 20°C. The conjugated disks were stored in incubation buffer (0.05 mol/l phosphate-buffered saline, pH 7.4, 0.05% NaN₃, 0.9% NaCl, and 0.3% human serum albumin) for up to 2 weeks at 4°C. Cellulose paper disks conjugated with grass pollen, as well as the EAST reagents, were provided by Allergopharma. Further analysis was done according to the manufacturer's directions. A pool serum from subjects with seasonal asthma and sensitization to grass pollen, with a total IgE of 202 U/ml, and RAST class III with grass pollen was used as a control. We did inhibition experiments with the serum of the castor-bean-allergic subject and with the pool serum from grass-pollen-allergic patients. Grass pollen and castor bean coupled to paper disks were used as solid phase. The same allergens were used as inhibitors; 50 μ l of a 1 + 9 dilution of serum was incubated for 1 h at 20°C with 50 μ l of diluted allergen. Threefold dilutions of allergens were used. EAST was done as described above except that the serum samples preincubated with inhibitor were added to the tubes instead of serum alone.

Immunoblot. The mol. mass of the proteins was determined by sodium dodecyl sulfate polyacrylamide gel electrophoresis (SDS-PAGE) (Kabi Pharmacia, Freiburg, Germany). Fifty-microgram aliquots of protein were applied to the gel. For visualization of the proteins, one part of the gel was stained with Coomassie brilliant blue (Merck, Darmstadt, Germany). The SDS-PAGE was done under reducing conditions. Electrophoretic transfer of the proteins to nitrocellulose was done, as described by Burnette (2), from that portion of the SDS-PAGE which was not stained. The nitrocellulose blot was then incubated with a fivefold dilution of the patient's serum, and after washing incubated with ¹²⁵I-labeled-anti-IgE (100 000 cpm/ml, Allergopharma). Specific IgE binding to allergens was detected by autoradiography with Kodak X-Omat AR film. Autoradiographs were evaluated after 14 days.

Results

SPT with the 100 mg/ml aqueous extract of dust from the patient's office gave a 9-mm diameter wheal. The extract of dust from the warehouse gave a 5-mm wheal, and the 100 mg/ml solution of the fertilizer a 16-mm wheal reaction (Fig. 1). A control group of 20 subjects without exposure to castor bean (14 atop-

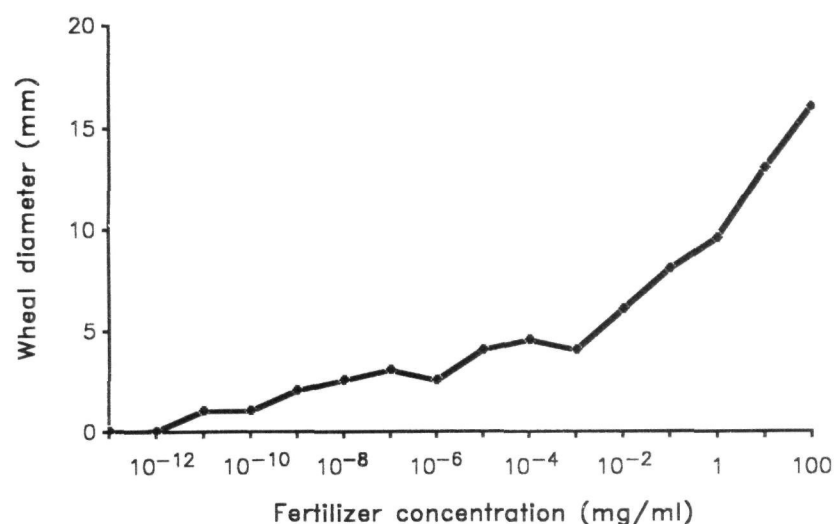


Fig. 1. Concentration-response relationship of skin prick test with fertilizer.

ics, six nonatopics) did not show wheal reactions of 2 mm or more with these extracts, with the exception of one nonatopic subject with a 4-mm wheal. Skin tests with environmental allergens were negative in the patient. Specific airway resistance rose from 0.6 kPa·s after isotonic saline to 2.4 kPa·s after inhalation of the 0.5 mg/ml methacholine solution (PD_{50} 70 μ g). This was considered to be severe bronchial hyperresponsiveness. Inhalation of a 1 μ g/ml solution of the fertilizer extract (PD_{50} 0.3 μ g), as well as inhalation of the 1 mg/ml extract of dust from the patient's office (PD_{50} 90 μ g), induced a clearly asthmatic reaction (Fig. 2). The time course was that of an immediate-type reaction with slow recovery in each case, and there was a weak late reaction with dust from the office about 8 h after the challenge (Fig. 3).

High titers of specific IgE against castor bean (44% binding, RAST class IV) were detected in the patient's serum, but not in the control pool serum (2% binding, RAST class 0). EAST inhibition analysis revealed an inhibitory effect of the castor bean extract in the homologous system without inhibition in the grass pollen system (Fig. 4).

Western blot analysis showed a high radiostaining intensity with the patient's serum at mol. mass less than 14.4 kDa, and moderate radiostaining intensities at 15.5, 29.5, and 30.5 kDa. A pool serum of eight healthy controls showed no allergen bandings (Fig. 5).

Discussion

This patient had occupational exposure mainly to grain, seeds, insecticides, fungicides, other pesticides, and fertilizers. One "natural" fertilizer contained castor bean, and sensitization to this allergen could be shown by a positive skin test. Bronchial provocation tests with extracts of the fertilizer and dust from the patient's office gave an immediate-type

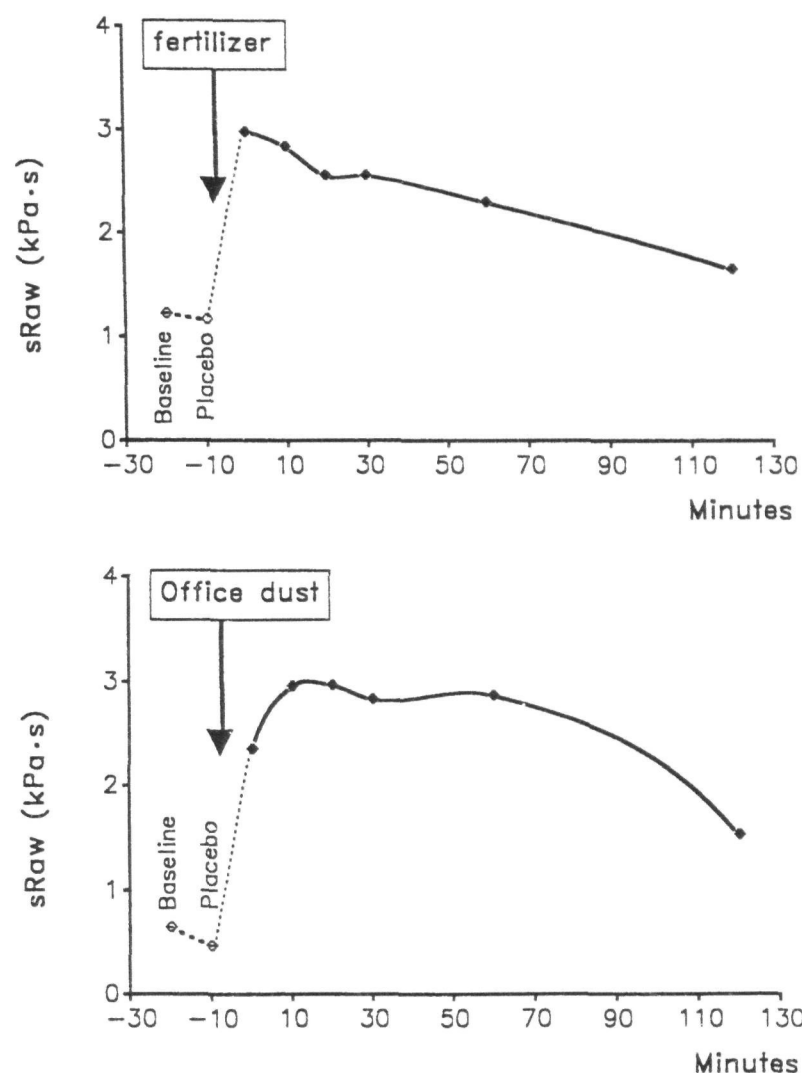


Fig. 2. Time-response relationship after inhalation of fertilizer extract (above) or extract of dust from patient's office (below).

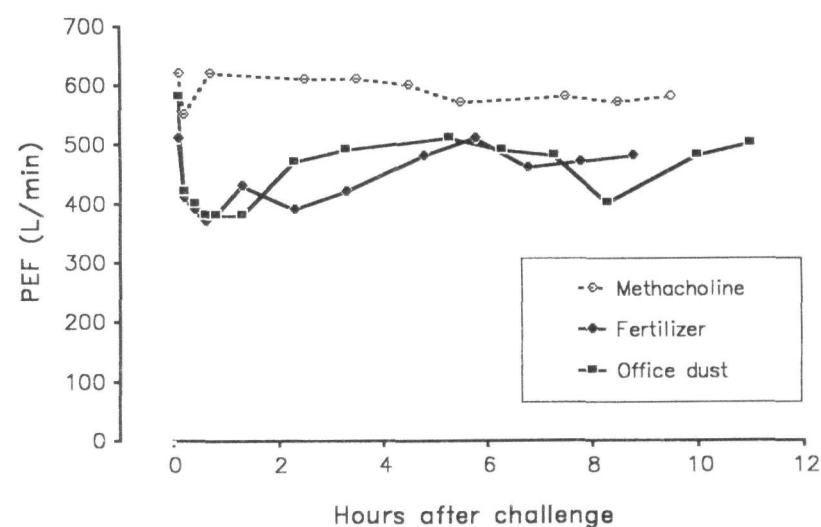


Fig. 3. Peak-flow measurements on days of methacholine challenge, as well as challenge with fertilizer and dust from office.

asthmatic reaction with a weak late reaction with the office dust. Bronchial provocation tests with castor bean have rarely been done. Isolated late reactions have been described in two out of three subjects considered to be allergic to castor bean (3). Others reported immediate-type asthmatic reactions, but late reactions were not assessed (5).

Specific IgE against castor bean was detected in the patient's serum by EAST, and the specificity of the reaction was confirmed by EAST inhibition

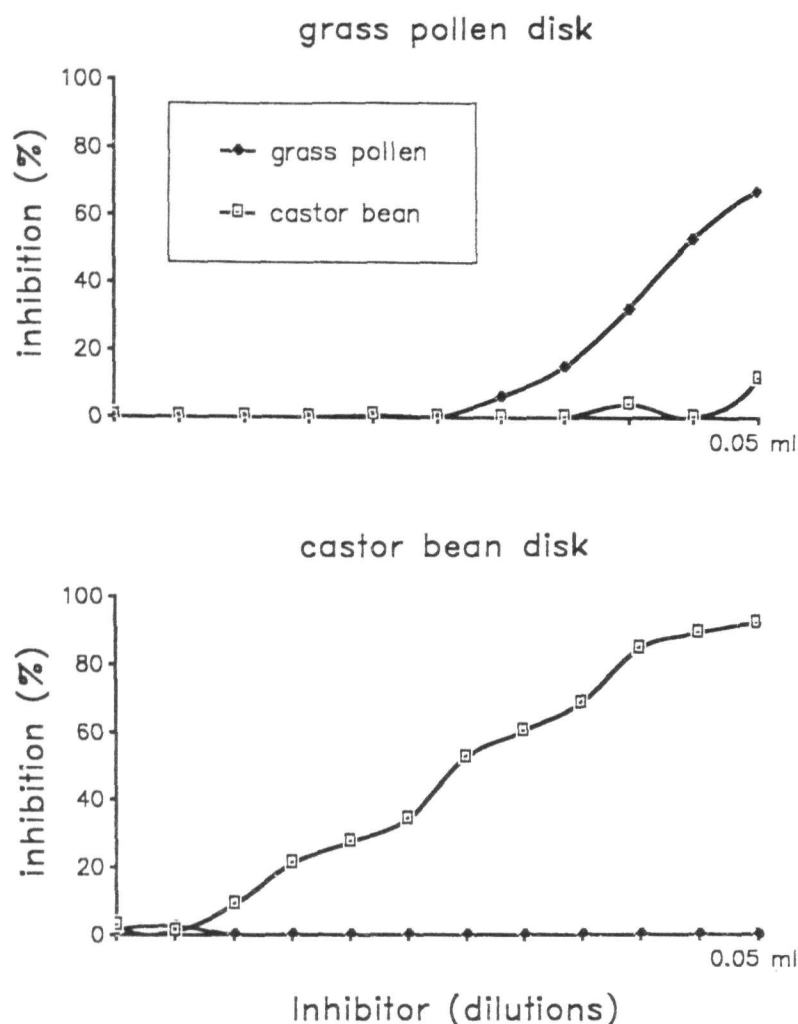


Fig. 4. EAST inhibition analysis. Tests were done with grass pollen (above) and castor bean (below) coupled to solid phase. Serum from patient was used for castor bean disks, and pool serum of grass-pollen-allergic subjects for grass pollen disks. Inhibitors are given in boxes. Threefold dilutions of inhibitors were used.

analysis. Specific IgE antibodies against castor bean, as assessed by RAST, have been found in many studies, and the sensitivity of RAST was 91% in skin-test-positive subjects (7).

As shown by immunoblot analysis, not all proteins of the castor bean were recognized as allergens by our patient. Strong radiostaining was shown with a protein at below 14.4 kDa, which has been shown to be a major allergen of the castor bean (8). Bandings in this region have been shown to represent the 2S storage albumin which is present in the storage bodies of the castor bean seeds. The patient showed further bandings in the 30-kDa region. These bandings have been identified as crystalloid proteins (8).

The seasonal character of the symptoms in this patient were associated with seasonal storage of the fertilizer. Sensitization to seasonal environmental allergens could be excluded. The increasing frequency and intensity of symptoms during the year before admission can be explained by the recent storage of the fertilizer throughout the year. Thus, exposure to castor bean was closely related to symptoms. After identification of the causal allergen, castor-bean-containing fertilizers were discarded immediately.

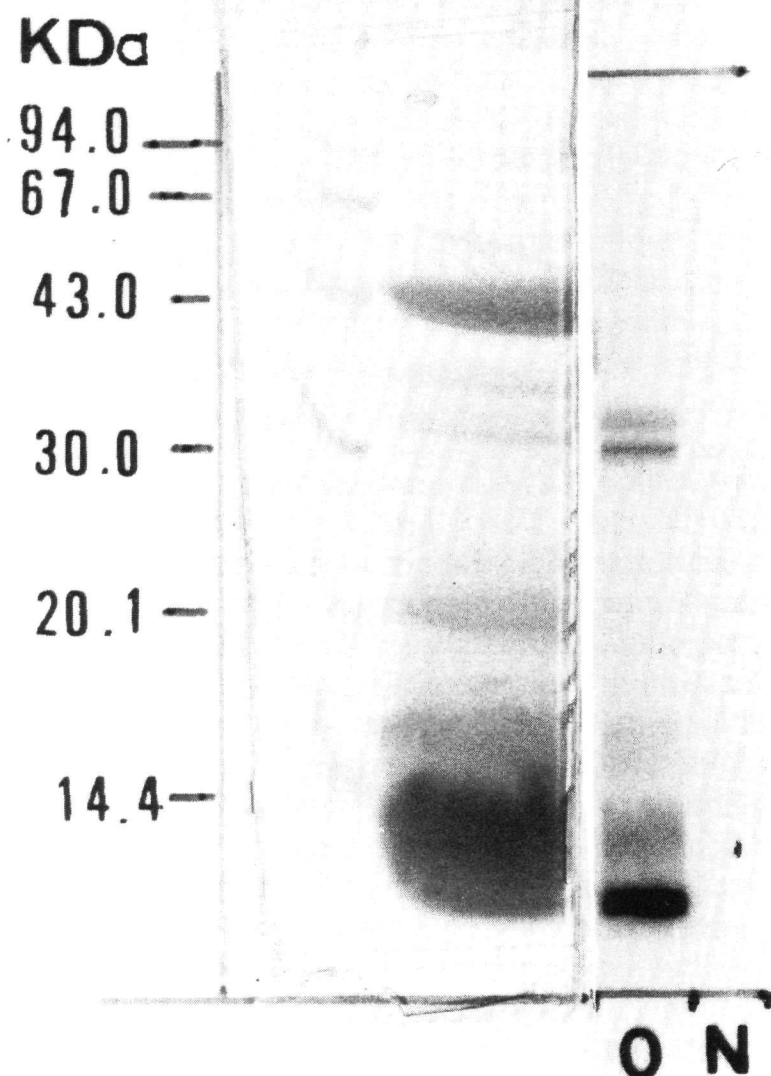


Fig. 5. SDS-PAGE (left) and Western blot (right) with castor bean. O: serum of patient. N: pool serum of eight healthy controls. Marker proteins from 14.4 to 94 kDa.

Six months after diagnosis, the patient reported mild chronic bronchitis without asthma.

To our knowledge, this is the first report of predominantly seasonal occupational asthma caused by castor bean in an agricultural products merchant.

Acknowledgments

We acknowledge the technical assistance of Mrs Eva-Maria Bergmann and Mrs Birgit Schärting.

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