

Case report

Occupational asthma and rhinoconjunctivitis caused by senna

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Occupational sensitization to senna is seldom reported. We describe a 21-year-old male atopic factory worker who developed IgE-mediated asthma and rhinoconjunctivitis 5 months after exposure to senna while he was working for a company manufacturing hair dyes. In the bronchial challenge test with senna, he exhibited a strong reaction. The skin prick test gave a 12-mm wheal reaction. The radioallergosorbent test (RAST) with senna was highly positive (33.6 PRU/ml, class 4), and could not be inhibited with pollens or foods. In protein staining with SDS-PAGE, two heavy bands were detected in senna at about 14 and 25 kDa, and two faint bands were visible at 19 and 21 kDa. In IgE immunoblotting with the patient's serum, one heavy band was detected at about 16 and four faint bands at 23, 25, 28, and 38 kDa. The patient became symptom free after he had changed his job within the same company.

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Senna, an old drug, consists of the dried leaves or pods of Indian senna (*Cassia angustifolia*) or traditional African senna (*C. acutifolia*, *C. senna*) (1). Senna contains glycosides (sennosides) widely used as a treatment for constipation (2). Sensitization to senna has been described among workers exposed to the dust in the process of manufacturing bulk laxatives (3). Exposure to senna mainly caused upper respiratory, eye, and skin symptoms, whereas occupational asthma was rare. Senna is used not only as a medical substance for laxatives but also as a coloring agent in hair dyes, often mixed with henna. We present a case of IgE-mediated occupational asthma and rhinoconjunctivitis caused by senna in an employee working in a factory producing hair dyes and shampoos.

Case report

A 21-year-old Caucasian man had been working in a technochemical factory for 5 years. He had a history of allergic rhinoconjunctivitis without any asthma symptoms. Otherwise he was in good health and had never smoked. Seasonal allergic symptoms were treated with nasal corticosteroid sprays and sodium cromoglycate eye-drops. He had no history of food allergy.

After 4 years, he was moved to hair-dye production. Five months later, he began to suffer from progressive rhinitis, itchy eyes, and dyspnea every time he mixed the dry powders of henna and senna used in hair dyes (Orient Henna®). He had no symptoms at home or when working elsewhere in mass production.

He tried using a protective mask, which somewhat relieved the symptoms. The patient himself suspected henna or senna to be the cause of his symptoms.

The physical examination and radiographs of chest and sinuses were normal. In laboratory tests, the concentration of serum eosinophil cationic protein (s-ECP) was increased to 25.4 µg/l (normal range 1.8–18 µg/l) (Pharmacia Diagnostics, Uppsala, Sweden). His flow-volume spirometry was normal (FVC 104% and FEV₁ 100% of predicted values).

A skin prick test was performed with a standard panel of common inhalant allergens (birch, timothy, meadow fescue, mugwort, *Cladosporium*, cat, dog, horse, cow, and latex) and foods (milk, egg, soy, fish, wheat, and shrimp) (Soluprick, ALK, Horsholm, Denmark). Fresh fruits, vegetables, and spices were tested with the skin prick-prick test.

For the prick-prick test with senna, dry powder

supplied by the patient was mixed with aqua (10 mg/ml). For all skin tests, histamine dihydrochloride (10 mg/ml) and saline solution were used as positive and negative controls, respectively. The largest wheal diameter was measured, and the reaction was considered positive if the wheal size was ≥ 3 mm over the negative control. All skin tests were read at 15 min. Five nonatopics and 10 atopics with allergy to pollens, foods, or animals served as controls.

The histamine challenge test was used to evaluate bronchial hyperresponsiveness. The specific bronchial challenge test was performed with senna in an inhalation chamber. Senna powder was puffed to the breathing zone with pressured air intermittently once a minute for 1 s. The whole challenge time was 5 min. A control challenge with placebo was not carried out. Lung volumes, FEV₁, and FVC were measured just before challenge and at 0, 10, 20, 30, and 60 min after challenge. Readings were continued at 2-h intervals for 8 h with the Micro Plus Spirometer (Micro Medical Ltd, Rochester, UK). A positive response was defined as $\geq 20\%$ fall in FEV₁ from baseline.

Serum total and specific IgE to pollens and foods was measured with the CAP system (Pharmacia Diagnostics, Uppsala, Sweden).

An extract was prepared from senna by overnight incubation of the dried powder in a ratio of 1:100 weight per volume (w/v) potassium phosphate buffer, 0.1 mol/l, pH 7.4. The total protein concentration was measured by the Bradford (Bio-Rad Laboratories, Richmond, CA, USA) method with bovine immunoglobulin as the standard.

RAST disks were prepared and RAST was performed as described by Ceska et al. (4), 48 µg of senna proteins being coupled per disk. Phadebas RAST reagents (Pharmacia Diagnostics) were used for the quantification of specific IgE. Values higher than 0.35 Pharmacia RAST unit/ml (PRU/ml) were considered positive. Sera from five nonatopic and 13 atopic patients with a high RAST value (at least class 3) to pollens, foods, or animals were used as controls.

The specificity of senna RAST was evaluated in RAST inhibition studies (5). Senna RAST was inhibited by dilutions (1:1 to 1:100 v/v) of commercial skin test extracts of pollens (birch, timothy, and mugwort), and foods (wheat and hazelnut) (Soluprick, ALK, Hørsholm, Denmark). As controls, pollen RAST (birch, timothy, and mugwort) in the patient's serum and three pollen-allergic controls were inhibited using dilutions of senna (10 mg/ml). An inhibition higher than 20% was considered significant.

For immunoblotting, a reduced extract (150 µg protein in 150 µl of sample buffer) and molecular

weight markers (Electrophoresis Low Molecular Weight Calibration Kit, Pharmacia Biotechnology, Uppsala, Sweden) were separated by SDS-PAGE in a 15% gel with a 4% stacking gel, according to Laemmli (6), and transferred to Immobilon-P sheet (Millipore 0.45 µm, Millipore Co, Bedford, MA, USA) for protein staining with Coomassie brilliant blue and to nitrocellulose sheets (Bio-Rad 0.22 µm) in Novablot apparatus (Pharmacia), according to Towbin et al. (7). The IgE antibodies bound from the serum (diluted 1:4) to allergens on the nitrocellulose were detected with radiolabeled anti-IgE (Pharmacia Diagnostics), as described previously (8). Sera from one nonatopic and one atopic patient with a high timothy RAST (> 52.5 PRU/ml) were used as controls.

The skin test was positive for birch (wheal diameter 5 mm), timothy (10 mm), meadow fescue (14 mm), cat (3 mm), wheat (4 mm), and hazelnut (10 mm). The skin prick test with senna caused a wheal of 12 mm. The histamine control was 6 mm and the saline control negative. Senna did not produce any reaction in nonatopic controls, whereas one atopic control showed a wheal of 3 mm (histamine control 5 mm). The other atopics remained negative.

The histamine challenge test showed mild bronchial hyperresponsiveness (provocative dose, PD₁₅ 1.0 mg). In the specific bronchial challenge test, the initial value for FEV₁ was 4.52 l, which was within normal limits. Immediately after the challenge with senna, FEV₁ was 3.47 l (23% reduction). At 20 min, FEV₁ had fallen by 33% (1.5 l), the patient had dyspnea, and wheezing was heard in auscultation. At the same time, eye symptoms with severe chemosis were noted. Inhalation of salbutamol (200 µg) and prednisolone (30 mg) taken orally revealed the symptoms gradually. A late asthmatic reaction was also observed.

Serum total IgE was 220 kU/l (normal < 110 kU/l). Specific IgE was positive to timothy (46.6 kU/l), meadow fescue (33.6 kU/l), meadow grass (13.7 kU/l), and birch (1.8 kU/l).

The patient's IgE test was highly positive for senna (33.6 PRU/ml, class 4). All nonatopic controls remained negative, whereas two atopic controls were slightly positive (0.38 and 0.44 PRU/ml, class 1).

In RAST inhibition, the pollens and foods tested did not cause any significant inhibition of senna RAST (all under 20%). The autoinhibition with senna was 76%. In addition, none of the pollen RASTs could be inhibited with senna in the patient's or the controls' sera. Inhibition of senna RAST by timothy along with the inhibition of timothy RAST by senna and the autoinhibition of senna in the patient's serum are depicted in Fig. 1.

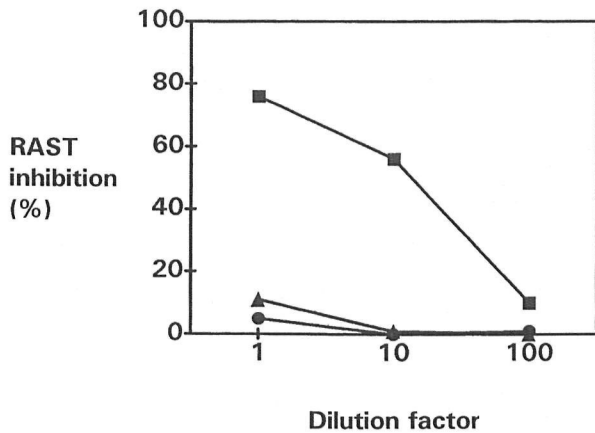


Fig. 1. Inhibition of RAST in serum from senna-allergic, pollen-sensitive patient. Inhibition of senna RAST by timothy (—●—) and timothy RAST by senna (—▲—). Inhibition was significant only in homologous system (senna-senna) (—■—).

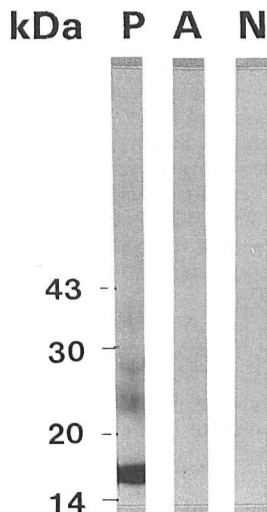


Fig. 2. Immunoblot analysis of binding of IgE antibodies from patient's serum (P), from atopic control serum (A), and from nonatopic control serum (N) to extract of senna leaves. IgE binding from patient's serum was demonstrated to 16-, 23-, 25-, 28-, and 38-kDa bands, but not from control sera. Molecular weight markers (kDa) on left.

In protein staining of senna after SDS-PAGE, two heavy bands were detected at about 14 and 25 kDa, and two other faint bands at 19 and 21 kDa. In IgE immunoblotting, one heavy band of about 16 kDa and four other bands at 23, 25, 28, and 38 kDa were detected for senna (Fig. 2). No bands were shown with the control sera.

Our patient had had occupational airborne exposure to senna when mixing hair dyes. After a 5-month exposure, he developed specific allergic symptoms of the upper and lower respiratory tract with a dramatic reduction in FEV₁ in the bronchial challenge test.

More than 500 species of *Cassia* are found in tropical and warm temperate regions, excluding

Europe (9). Senna is a medical herb which derives from *Cassia* species – small bushes cultivated mainly in southern India. They contain anthraquinones which may be irritant. However, skin prick tests were negative among nonatopics and, except for one, also among atopic controls. Senna belongs to the same plant family, Leguminosae, as pea, peanut, soybean, and white bean, and cross-reactions could be possible. However, our patient had no symptoms of food allergy, and his skin test and RAST response to pea, peanut, and soybean was negative.

In accordance with his atopic background, the patient showed positive RAST to pollens and cat dander. However, the IgE response to senna (33.6 kU/l) was distinct as compared with controls. All nonatopic controls were negative and only two atopics had a slightly positive RAST to senna (class 1). The specificity of IgE antibodies to senna was confirmed by cross-wise inhibitions in the patient's serum. The only significant inhibition was demonstrated in the homologous system (senna-senna) (Fig. 1). Pollens and foods giving a positive response in skin testing or RAST did not cause any significant inhibition of senna RAST. Neither did senna inhibit pollen RAST in the patient's or the controls' sera.

SDS-PAGE revealed protein bands in senna at about 14, 19, 21, and 25 kDa, all of which may be potential allergens. Even though the 16-kDa band demonstrated in IgE immunoblotting might represent various plant profilins known to be highly cross-reacting in several pollens, fruits, and vegetables (10), four other allergen bands (at 23, 25, 28, and 38 kDa) were also demonstrated with the patient's serum (Fig. 2). The IgE binding was specific, since no binding was demonstrated with the control serum from a highly pollen-allergic subject. Furthermore, results from RAST inhibition do not support allergen cross-reactivity.

The patient himself suspected henna as another possible cause of his symptoms. Therefore, henna was also evaluated (results not shown). However, our results were controversial, and specific allergy to henna could not be confirmed. Nevertheless, henna may have contributed to the patient's symptoms. The patient's skin response to henna was positive, as was the IgE binding in immunoblotting. However, the results were considered nonspecific since some of the atopic controls also showed similar or even more distinct positivity, probably due to a nonspecific reaction or possible cross-reactivity between grasses and henna. In contrast, henna RAST was negative in the patient's and the controls' sera. The bronchial challenge test was not performed with henna, because of the strong asthmatic reaction with senna. Occupational asthma (11), wheezing and generalized urticaria (12), and

contact dermatitis (13) from henna have previously been reported in hairdressers, occasionally with positive skin test and specific IgE test results.

Senna contains low molecular-weight glycosides (sennosides A and B) which are used in some laxatives. However, no IgE binding was demonstrated from the patient's serum to a purified sennoside-containing laxative (Sennapur[®], Leiras, Turku, Finland) in an immunospot assay (8) (not shown). Instead, a slightly positive RAST (0.41 PRU/ml, class 1) was demonstrated to a psyllium-containing laxative (Agiolax[®], Madaus, GmbH, Germany), which contains 14% unpurified senna pods. No IgE was demonstrated to pure psyllium. Instead, the patient had developed specific IgEs to proteins in the crude senna (4.8% protein in dry powder), as demonstrated by skin testing, RAST, and IgE immunoblotting.

We could find only one report of occupational allergy to senna (3). The study suggested that exposure to levels of senna dust sufficient to cause a positive skin test leads to symptoms, but is not commonly associated with asthma. The skin prick test was positive in 15.3% of 125 pharmaceutical workers, but specific IgE to senna has not been measured (3). Our patient was clearly sensitized to senna in his work. He developed symptoms after exposure to senna, and became symptom-free after changing his job within the factory.

In conclusion, our patient had occupational asthma and rhinoconjunctivitis caused by senna. The bronchial provocation test, skin prick test, and specific-IgE test were all positive. The specificity of IgE antibodies was confirmed in RAST inhibition studies. In IgE immunoblotting, the patient's serum revealed one heavy band at about 16 kDa and four other less distinct bands in an extract of senna.

Senna should be regarded as a potent allergen capable of causing occupational asthma and rhinoconjunctivitis.

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