

Case report

Occupational asthma and rhinoconjunctivitis from inhalation of dried cow's milk caused by sensitization to α -lactalbumin

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G. Bernaola¹, S. Echechipía², I. Urrutia², E. Fernández², M. Audicana¹, L. Fernández de Corres²

¹ Allergy Section, Galdakao Hospital, Galdácano (Vizcaya), and ² Allergy Department, Santiago Apostol Hospital, Vitoria-Gasteiz, Spain

A chocolate candy worker was diagnosed as having occupational asthma and rhinoconjunctivitis on the basis of clinical record and methacholine challenge. Positive conjunctival and bronchial challenge tests with lactalbumin showed that this protein was the pathogenetic agent. Type I hypersensitivity mechanism is demonstrated by means of skin prick test and RAST.

Key words: allergy; asthma; conjunctivitis; food hypersensitivity; α -lactalbumin; milk proteins; occupational disease; rhinitis.

Gonzalo Bernaola Hortigüela
Sección de Alergología (Servicio de Medicina Interna)
Hospital de Galdakao
Barrio Labeaga S/N
48960 Galdácano (Vizcaya)
Spain

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Ramazzini first described occupational asthma in 1773. Most of the pathogenetic agents of this disease have been reported since 1911 when asthma caused by platinum salts was demonstrated among graphic arts workers (8). To date, more than 200 substances causing occupational asthma have been identified (5).

Sensitization to cow's milk is an important cause of food allergy, and the responsible proteins are well known. Asthma caused by inhalation of foods (except wheat flour) is uncommon. We here present a case of occupational asthma caused by inhalation of dried milk, proving that α -lactalbumin is the protein responsible. To the best of our knowledge, no similar cases have been previously published.

Case report

A 27-year-old woman had been working in a chocolate candy factory for 13 years. She had a history of hepatitis and an appendectomy. During the last 5

years, she had experienced rhinoconjunctival symptoms clearly related to her work: after having molded the confectionery, she sprinkled it with cocoa and dried milk powder, and she suspected that the pathogenetic agent was in one of these two. She felt better after leaving the factory and also when working in a different section. She had no symptoms during weekends and holidays. Apart from rhinoconjunctivitis, she had experienced coughing, wheezing, and dyspnea during the last year, and these symptoms also disappeared when she was not working in the chocolate confectionery department. She drank cocoa and milk without any trouble. By the avoidance as much as possible of workplaces where dried milk powder was present, and with the use of oral antihistamines and the inhalation of disodium cromoglycate, her symptoms disappeared, except for when the level of powder became very high during days of high production.

The physical examination, laboratory tests, and radiographs of her chest were normal. The sinus

radiograph showed a bilateral mucoperiosteal thickening. Her spirometry was normal ($FEV_1 = 107\%$ and $FEV_1/FVC = 101\%$ of predicted normal), but the methacholine test showed a moderate hyperresponsiveness (PD_{20} : 66 UI). The total IgE (PRIST) was 156 kU/l.

Material and methods

Skin tests

A standard prick test was performed with common inhalant allergens and foods, including whole cow's milk, dried milk, cocoa, casein (1 mg/ml), α -lactoglobulin (2 mg/ml), and β -lactalbumin (2 mg/ml). The casein extract was supplied by Alergia e Inmunología Abelló SA (Madrid, Spain), and α -lactoglobulin and β -lactalbumin extracts were obtained by adding PBS to α -lactoglobulin and β -lactalbumin powder (Sigma, St Louis, MO, USA), dialyzing three times against PBS, and filtering through a 0.2- μ m sterilizing filter (Flowpore D 26, Flow Laboratories, Bonn, Germany). Dried milk and cocoa powders used by the patient were also tested. Histamine (10 mg/ml) and saline solution (Dome/Hollister-Stier, Miles, Madrid, Spain) were used as positive and negative controls. All skin tests were read at 20 min.

A prick test end-point titration with α -lactalbumin was also performed, and the following concentrations for conjunctival and bronchial challenge tests were chosen: 0.1, 0.2, 0.25, 0.5, 1, and 2 mg/ml.

Conjunctival challenge test

A drop of PBS, pH 7.2, the solvent used as negative control, and α -lactalbumin at increasing concentrations were applied in the conjunctival fold in both eyes alternatively (11). A test was considered to be positive when pruritus and redness in at least half the bulbar conjunctiva were observed after 20 min. The test was also performed in five nonatopic controls.

Specific bronchial challenge test

The patient was hospitalized during a 12-h period for the performance of this test. The intermittent inhalation, following the method of Townley et al. (15), was performed with a Mark-7 model (Bird Co, Palm Springs, CA, USA) respirator, with PBS as control and the above-mentioned increasing concentrations of α -lactalbumin. Five inhalations of each dilution, from residual functional capacity to total pulmonary capacity, were made. The test was considered to be positive when a greater than 20% FEV_1 decrease was observed. The test was also performed in five nonatopic controls.

A PEFR record was recorded with a Mini-Wright peak-flow meter each hour, within the 12 h after bronchial challenge for the detection of a late asthmatic reaction.

Specific IgE determination

Specific IgE determinations to milk, α -lactalbumin, β -lactoglobulin, casein, and *Dermatophagoides pteronyssinus* were performed with Phadebas RAST (Pharmacia, Uppsala, Sweden).

Results

Skin test

The skin prick test with α -lactalbumin caused a wheal of 12 $\times$ 9 mm (histamine control: 9 $\times$ 7 mm), while the other allergens (even cocoa) and saline control were negative. α -Lactalbumin did not cause any reaction in 100 volunteer controls.

Conjunctival challenge test

The conjunctival challenge test was positive with 0.5 mg/ml of α -lactalbumin extract, while no reaction occurred with PBS and the 2 mg/ml concentration in five nonatopic controls.

Specific bronchial challenge test

The initial value of FEV_1 was 3 l/s (107% of the theoretic value). Ninety seconds after inhalation of the higher concentration of α -lactalbumin extract (2 mg/ml), a 20% FEV_1 decrease was shown (FEV_1 2.4 l/s), recovering after a 200 μ g salbutamol inhalation. No late asthmatic reaction was observed (Fig. 1).

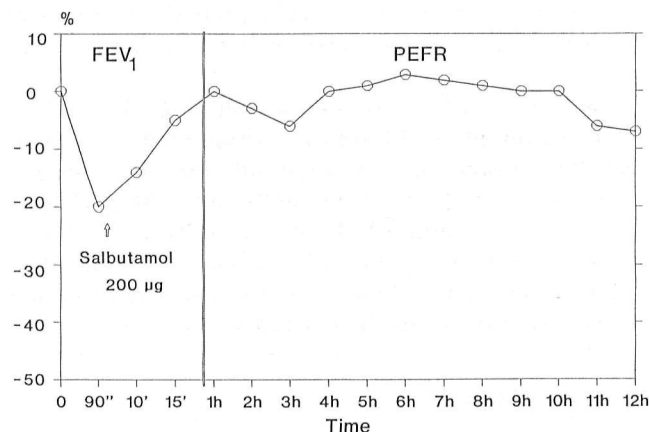


Fig. 1. Lactalbumin bronchial challenge (2 mg/ml): a 20% decrease of FEV_1 that recovers after salbutamol inhalation and peak-flow meter recording for 12 h.

Specific IgE

Specific IgE was detected to milk (4.48 PRU/ml) and α -lactalbumin (0.74 PRU/ml). RAST with β -lactoglobulin, casein, and *D. pteronyssinus* was negative.

Discussion

Various proteins derived from plant and animal products, such as wheat and rye flour, buckwheat, coffee beans, tea, crab, prawn (3), potatoes, green beans, chard (6), garlic, onion, cinnamon (9), bovine seroalbumin (14), egg (2), etc., have been reported to cause asthma through inhalation.

Allergy to cow's milk is well known to be produced by proteins, and at least 16 of them have been reported as potential allergens (7). The most important are β -lactoglobulin, α -lactalbumin, and casein, and specific IgE against these proteins has been demonstrated (7). Few patients sensitized to α -lactalbumin have been reported in the numerous papers published (13). Likewise, cow's milk proteins usually cause gastrointestinal and skin manifestations; very rarely have they been implicated in occupational asthma.

In spite of the wide use of cow's milk proteins in the milk derivatives industry, few cases of occupational asthma have been reported. Moneret-Vautrin et al. (13) reported a case of occupational asthma from lactoglobulin in an employee of the cheese industry, and an IgE-mediated mechanism was demonstrated. The occupational asthma of a tanner with atopic antecedents was found to be caused by the inhalation of casein, as shown by Olaguibel et al. (12).

As our patient tolerated the ingestion of milk, and in view of the cases of these two patients, the importance is borne out of the route of allergen penetration with respect to the type of reaction caused. The respiratory route is the commonest by which foods induce sensitization and symptoms, as has been demonstrated with occupational asthma caused by inhalation of bovine seroalbumin (2, 14).

The conjunctival and bronchial challenge tests confirmed that α -lactalbumin was the pathogenetic agent in our case. As in the study of Olaguibel et al. (12), only immediate reaction was induced by the bronchial challenge test without late asthmatic reaction.

An allergic mechanism has been shown by means

of immediate prick, conjunctival, and bronchial challenge tests and RAST, all of which demonstrate IgE against α -lactalbumin. This agrees with reports indicating an IgE-mediated mechanism in asthma by high-molecular-weight compounds (1, 3). It is very interesting that our patient did not have an atopic condition in spite of the fact that atopy is considered to be a predisposing factor in sensitization among workers handling high-molecular-weight compounds (4).

In conclusion, we report a new case of occupational asthma caused by inhalation of foods in which an IgE-mediated mechanism has been demonstrated.

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