CASE REPORT

Allergy to Cassava: A New Allergenic Food With Cross-Reactivity to Latex

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Abstract

Patients who are allergic to latex (*Hevea brasiliensis*) may exhibit cross-hypersensitivity with foods. We present a case of anaphylaxis due to cassava in a patient suffering from pollinosis, latex allergy, and latex-fruit syndrome. We performed sodium dodecyl sulfate polyacrylamide gel electrophoresis (SDS-PAGE) and immunoblotting with cassava, avocado, chestnut, banana, kiwi, and latex extracts in order to analyze the protein bands and their molecular weights, and identify immunoglobulin (Ig) E-binding bands. Immunoblot inhibition and enzyme-linked immunosorbent assay (ELISA) inhibition were performed with latex in order to assess cross-reactivity. Cassava exhibited numerous protein bands, 5 of which were IgE-binding (89.75, 46.28, 26.68, 21.38, and 19.49 kd). These cassava IgE-binding bands were 100% inhibited by preincubation of the patient's serum with latex extract. The ELISA inhibition between latex and cassava was 23%. Our results confirm cassava as another food with clinical cross-reactivity in patients suffering from latex allergy.

Key words: Cassava. Latex-fruit syndrome. Cross-reactivity.

Resumen

Los pacientes alérgicos al látex (*Hevea brasiliensis*) pueden presentar alergia cruzada con alimentos. Se presenta un caso de anafilaxia por yuca en una paciente con polinosis, alergia al látex y un síndrome látex-frutas. Realizamos electroforesis en poliacrilamida con dodecilsulfato de sodio e inmunotransferencia con extractos de yuca, aguacate, castaña, plátano, kiwi y látex, para determinar las bandas proteicas, sus pesos moleculares y las bandas que fijaban inmunoglobulina (Ig) E. Se realiza inhibición de la inmunotransferencia e inhibición del inmunoanálisis ligado a enzimas (ELISA) con látex, para valorar la reactividad cruzada. La yuca presenta numerosas bandas proteicas de la cuales 5 fijan la IgE (89.75, 46.28, 26.68, 21.38 y 19.49 kd). Estas bandas fijadoras de IgE de la yuca son inhibidas al 100% con un extracto de látex. La inhibición del ELISA entre látex y yuca es de un 23%. Se confirma la yuca como otro alimento con reactividad cruzada clínica en pacientes con alergia al látex.

Palabras clave: Yuca. Síndrome látex-frutas. Reactividad cruzada.

Introduction

In 1991, M'Raihi et al [1] were the first to describe a patient with symptoms of angioedema due to the ingestion of bananas; the patient had suffered an anaphylactic shock during surgery. Afterwards, a patient with allergy to latex, avocado, and banana was described [2], and several patients with cross-reactivity between latex and chestnuts were reported [3]. In 1994, Blanco et al [4] put forward the term "latex-fruit syndrome" based on the fact that 52% of their patients with latex allergy were sensitized to fruits, the most common of which were avocados (36%), chestnuts (36%), bananas (28%), kiwis (20%), and papayas (12%). Subsequently, many authors confirmed the pattern of this syndrome using diagnostic criteria based on clinical histories and/or skin tests [5-8]. Since 1995, numerous studies have described many foods showing cross-reactivity with latex, such as potatoes [9], tomatoes, mangoes, papayas, melons, figs, peaches, and aubergines. In 2003, 3 patients with latex allergy and cross-reactivity with cassava were described [10,11].

Case Description

The patient was a 27-year-old woman with no significant prior medical history or history of substance abuse. A few

months after beginning to work at a restaurant specialized in Cuban food 2 years previously, she developed symptoms of sneezing, nasal pruritus, and watery rhinorrhea that began while she was peeling raw cassava. If exposure continued, she also developed nasal obstruction, flares on the back of the hands, generalized erythema, facial angioedema, dyspnea, dysphonia, and dysphagia, without coughing or wheezing. Later, she exhibited symptoms of abdominal pain, nausea, dyspnea, generalized erythema, facial urticaria, and facial angioedema an hour after eating a ripe banana and itchy gums 15 minutes after eating guacamole (a sauce containing avocados, chilli pepper, onions, and salt), progressing to dyspnea, generalized erythema, abdominal pain, and vomiting. She also reported a mild perennial rhinitis during the last 2 years. She had stopped using condoms because of vaginal pruritus and did not use gloves regularly. She tolerated bread, oranges, onions, tomatoes, mustard, and green bananas. However, she did not like to eat kiwis or chestnuts.

Skin prick tests (SPT) were performed with the 18 most common aeroallergens in our area and with 34 food allergens that were a regular part of our patient's diet. Tests were considered positive when a wheal was obtained that was greater than or equal to 2/3 of the size of the histamine wheal in the case of foods and greater than or equal to the size of the histamine wheal in the case of aeroallergens. In SPT for aeroallergens, positive reactions were observed with *Dermatophagoides pteronyssinus, Dermatophagoides farinae,* and pollen from *Olea europea* and *Chenopodium album.* SPT with food allergens revealed positive reactions to latex, kiwis, oranges, tomatoes, onions, mustard, and gluten. A prick-by-prick test also showed positive results with cassava, banana, and avocado.

The total serum immunoglobulin (Ig) E concentration was 126 U/L. Specific IgE measured by CAP immunoassay (Pharmacia, Uppsala, Sweden) revealed negative values (< 0.35 kU/L) for kiwi, gluten, onion, and mustard, and positive values for tomatoes (0.41 kU/L), chestnuts (0.47 kU/L), avocados (2.89 kU/L), bananas (5.01 kU/L), latex (5.04 kU/L), *D pteronyssinus* (4.78 kU/L), and *Chenopodium* (0.77 kU/L). It was not possible to analyze specific IgE for olive pollen or cassava.

Sodium dodecyl sulfate polyacrylamide gel electrophoresis (SDS-PAGE) and immunoblots were performed with cassava, avocado, chestnut, banana, kiwi, and latex extracts. In SDS-PAGE, the extracts were separated on 12.5% denaturing polyacrylamide gels. In immunoblot experiments, proteins were transferred to a polyvinylidene fluoride membrane (Hybond P, GE Healthcare, Uppsala, Sweden) according to the method described by Towbin et al [12]. The membrane was blocked with phosphate buffered saline (PBS) containing 0.1% Tween for 1 hour at room temperature. The patient's serum was added to the membrane at a 1:4 dilution in blocking buffer and left under agitation overnight at 4ºC. For immunoblot inhibition, the latex extract was preincubated with the patient's serum for 3 hours at room temperature. The mixture was then added to the membrane onto which the cassava extract proteins had been transferred. After several washes, the membrane was incubated with horseradish-peroxidase-conjugated anti-human IgE antibody (DAKO, Barcelona, Spain) for 2 hours at room temperature. Immunodetection was performed using a chemiluminescent detection reagent (Western Lighting Plus, Perkin Elmer, Boston, USA), according to the manufacturer's instructions.

The cassava extract contained multiple protein bands: 96.24, 83.67, 65.52, 57.69, 48.45, 46.44, 32.85, 29.42, 26.97, 19.52, 17.89, and 15.14 kd. SDS-PAGE was then performed with the avocado, chestnut, banana, kiwi, and latex extracts (Figure 1). In addition, Tricine SDS-PAGE was performed in order to show the low-molecular-weight protein bands. Immunoblotting of the cassava extract showed at least 5 IgE-binding bands of 89.75, 46.28, 26.68, 21.38, and 19.49 kd. Immunoblotting of the avocado extract revealed 7 IgE-

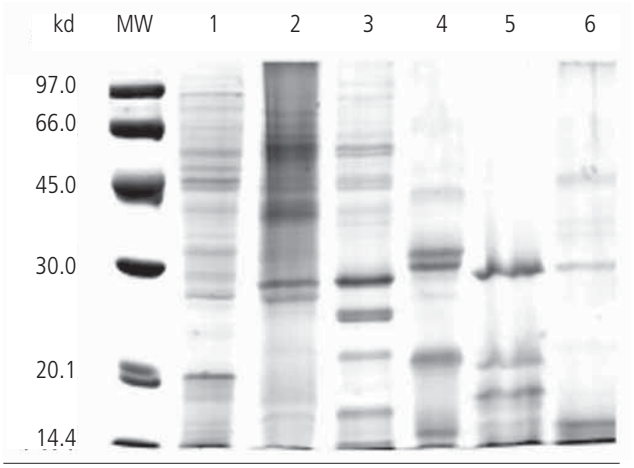

Figure 1. Sodium dodecyl sulfate polyacrylamide gel electrophoresis of cassava (1), avocado (2), chestnut (3), banana (4), kiwi (5), and latex (6) extracts. Cassava extract contains protein bands between 15.14 and 96.24 kilodaltons (kd). MW indicates molecular weight marker.

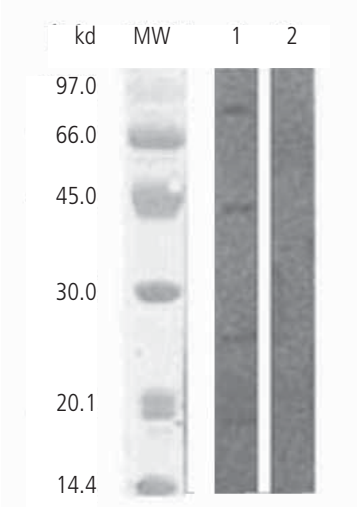

Figure 2. Immunoblot inhibition of casava proteins by latex extract. Lane 1 shows immunoblotting of cassava extract with the patient's serum. Lane 2, immunoblotting of cassava extract with the patient's serum preincubated with latex extract. MW indicates molecular weight marker.

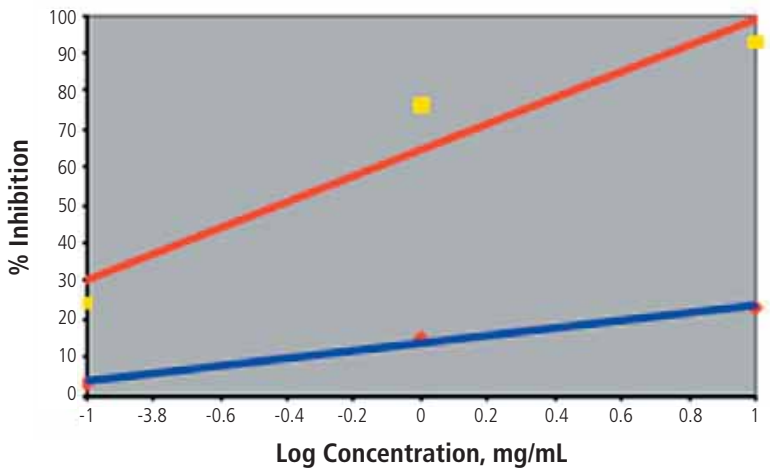

Figure 3. Enzyme-linked immunosorbent assay (ELISA) inhibition. Binding of the patient's serum to latex extract was analyzed following preincubation with cassava or latex extract as the inhibition phase. The graph shows the percentage inhibition with increasing concentrations of inhibition phase. The red line shows ELISA inhibition following preincubation with latex extract (yellow squares), and the blue line, cassava extract (red diamonds) as the inhibition phase. At a concentration of inhibition phase that achieved 100% inhibition with latex extract, 23% inhibition was observed with cassava extract.

binding bands (42.44, 38.06, 24.90, 22.50, 21.00, 19.52, and 16.83 kd), the chestnut extract 6 bands (44.28, 36.37, 25.04, 21.39, 19.55, and 17.59 kd), the banana extract 3 bands (69.33, 60.48, and 30.10 kd), the kiwi extract 2 bands (33.30 and 31.50 kd), and the latex extract 2 IgE-binding bands (33.30 and 31.05 kd). Immunoblot inhibition showed 100% inhibition of the IgE-binding protein bands of cassava with the latex extract (Figure 2).

Enzyme-linked immunosorbent assay (ELISA) inhibition studies were performed as described by Boluda et al [13,14], with some modifications. An ELISA plate was coated with 0.250 mg/mL of latex extract. The patient's serum was preincubated with latex extract or cassava extract for 3 hours at room temperature and added to the wells of the ELISA plate following blocking of the plate with assay buffer (1% bovine serum albumin in PBS containing 0.05% Tween). Binding of IgE was detected with a monoclonal anti-human IgE antibody (1:1000; 50 μL/well; Operon, Zaragoza, Spain) followed by incubation with a biotinylated anti-mouse IgG antibody (1:5000; 50 μL/well; Sigma, St Louis, USA) and finally streptavidin-peroxidase (1:1000; 50 μL/well; Sigma). Finally, detection was performed with 3,3',5,5'-tetramethylbenzidine solution (50 μL/well; Sigma) and the color reaction was read on a spectrophotometer at a wavelength of 450 nm. Binding of the specific IgE in the patient's serum was compared in samples with or without preincubation with latex or cassava extract to assess inhibition. At a concentration that achieved 100% inhibition of IgE binding following preincubation of the patient's serum with latex extract, 23% inhibition of binding to the latex solid phase was observed when cassava extract was used as the inhibition phase (Figure 3).

Discussion

Cassava, also known as manioc, mandioca, yucca, or tapioca, is the common name for the tuber *Manihot esculenta* Crantz, which belongs to the *Euphorbiaceae* family from the West Indies, Latin America, and Africa. It is a staple food in regions of South America and Africa and is eaten cooked, fried, or in the form of flour for bread, pastry, and cakes. It is necessary to remove the skin and then grind the flesh, soak it repeatedly, and cook it in order to avoid an excess of hydrocyanic acid. It has been reported that the ingestion of poorly processed cassava may cause tropical ataxic neuropathy, tropical pancreatic diabetes, and goitre [15].

Cassava has only recently been introduced into the diet in Spain. In 2003, the Brazilian researchers Galvao et al [10] described 2 patients with latex allergy who suffered from anaphylaxis following the ingestion of boiled cassava. Later, Gaspar et al [11] published the case of a woman with latex-fruit syndrome who suffered from 2 episodes of anaphylaxis following ingestion of boiled cassava and ingestion of raw cassava flour. Immunoblotting with raw cassava showed 3 IgE-binding bands (35, 42-44, and 50 kd) and radioallergosorbent test inhibition with latex in the solid phase showed 83% inhibition with raw cassava extract, with total inhibition in the 42-44 kd band. That protein band was found to be similar to Hev b7 or patatin-like protein, explaining the cross-reactivity between potatoes and tomatoes.

In our patient, the cross-reactivity between cassava and latex could also be attributed to a chitinase, since class I chitinases, which are plant defense proteins with an N-terminal domain similar to that of prohevein (Hev b 6) in latex, have been particularly implicated in the extensive cross-reactivity in latex allergy. These chitinases have been identified in banana, avocado, and chestnut, and have been considered to be the "panallergens" responsible for the latex-fruit syndrome [9,16-20].

To date, 2 Brazilian patients [10] and 1 African patient (Mozambique) [11] have been described with allergy to cassava and latex. All of them were first diagnosed with allergy to latex and subsequently to cassava (digestive sensitization). Our patient is the first reported case of allergy to cassava in Europe, and her sensitization sequence began with pollinosis, continued with allergy to latex and cross-allergy to fruits and vegetables (latex-fruit syndrome), and ended with sensitization to cassava due to occupational exposure.

Globalization facilitates the entry and consumption of new foods in Europe. In Spain, food from other continents like South America and Africa, such as cassava and tropical foods like lychee, papaya, and passion fruit are now being consumed. Consequently, we can expect an increasing number of cases of allergy to cassava in the coming years.

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