

Latex-vegetable syndrome due to custard apple and aubergine: new variations of the hevein symphony

P. M. Gamboa¹, R. Sánchez-Monge², A. Díaz-Perales², G. Salcedo², I. Ansótegui¹ M. L. Sanz³

¹Servicio de Alergía. Hospital de Basurto. Bilbao. Spain.

²Unidad de Bioquímica. Departamento de Biotecnología. E.T.S. de Ingenieros Agrónomos. Madrid. Spain.

³Departamento de Alergología e Inmunología Clínica. Clínica Universitaria. Universidad de Navarra. Pamplona, Spain

Abstract. An increasing number of vegetables with crossreactions to latex are being described in patients with latex-vegetable syndrome. We present two of these vegetables, custard apple linked in two previous cases with latex sensitisation, and aubergine, that had not been described up to now in patients with latex sensitisation. The diagnosis of both cases was based on the clinical history, positive skin prick test (SPT) and specific IgE to the offending vegetables, as well as to positive SPT and specific IgE levels to latex and the major fruits involved in the latex-fruit syndrome (avocado, banana, and chestnut). Further, crude extracts from latex, custard apple and aubergine, as well as the purified allergens Hev b 6.02 and Prs a 1 were used in *in vitro* and *in vivo* assays: IgE immunodetection, histamine release (HRT) and basophil activation (BAT) tests and skin prick tests.

In case 1, both purified Hev b 6.02 and Prs a 1 induced positive responses in skin prick tests, high levels of basophil activation and histamine release. Specific IgE immunodetection uncovered a reactive band of 45 kd in the crude custard apple extract, which was also recognized by anti-chitinase monospecific antibodies. The serum from patient 1 also detected Prs a 1 in immunodetection.

Hev b 6.02 produced positive skin responses and showed high biological activity in HRT and BAT in the case of patient 2. However, Prs a 1 was reactive neither in SPT nor in IgE immunodetection. In fact, no band was detected using the serum of patient 2 in avocado or aubergine extracts. By contrast, Prs a 1 reached high values of basophil activation and over 10 % of histamine release in case 2.

Key words: Latex-vegetable syndrome, Custard apple, Aubergine, Hevein.

Introduction

A high percentage of patients allergic to latex, ranging from 21 to 58% of the cases, are also sensitised to foods, especially fruits, forming the so called latex-fruit syndrome or the more generic latex-vegetable syndrome. The most frequently involved foods in these crossreactions are banana, avocado, chestnut and kiwi [1]. Fruit class I chitinases with an N-terminal hevein-like domain and latex hevein (Hev b 6.02) have been identified as the main allergens responsible for such crossreactions [2]. Nevertheless, an increasing number

of vegetables with crossreactions to latex are being described. We present two of these vegetables, custard apple linked in two previous cases with latex sensitisation [3,4], and aubergine, that had not been described up to now in patients with latex sensitisation.

Material and Methods

The diagnosis of both cases was initially based on the clinical history, a positive skin prick or prick-prick test response, and significant specific IgE levels (CAP-

Table 1. Results of the *in vivo* and *in vitro* determinations performed in both patients.

	Latex	Custard	Aubergine	Hev b 6.02	Prs a 1	Avocado	Banana	Chestnut
Case 1								
SPT (mm)	10 x 8	10 x 4	ND	15 x 10	6 x 5	6 x 5	3 x 3	5 x 4
IgE (kU/I)	43.1	ND	ND	ND	ND	2.16	1.61	1.12
HRT %	44	36	ND	88	3	55	18	49
BAT (% activated basophils)	98	96	ND	94	98	85	84	95
Immuno-Detection	+ (45 Kda)				+			
Case 2								
SPT Prick by Prick (mm)	12 x 9	ND	13 x 7	18 x 7	neg	6 x 4	10 x 8	5 x 6
IgE (KU/l)	19.8	ND	0.36	ND	ND	2.91	0.82	1.48
HRT%	91	ND	65	91	11	11	15	68
BAT (% activated basophils)	98	ND	97	99	97	88	83	91
Immuno-Detection			neg		neg			

Concentration of the antigen used in BAT (Basophil activation test) and HRT (Histamine release test): **Latex** 30 µg/ml, **Custard apple** 300 µg/ml, **Aubergine** 300 µg/ml, **Hev b 6.02** 0.025 µg/ml, **Prs a 1** 0.025 µg/ml, **Avocado** 300 µg/ml, **Banana** 300 µg/ml, **Chestnut** 300 µg/ml. ND: Not done. SPT: Skin prick test. HRT: Histamine Release Test. BAT: Basophil Activation Test.

Concentration of purified allergens in SPT: Hev b 6.02 6 µg/ml and Pers a 1 40 µg/ml.

FEIA System; Pharmacia Diagnostic) to latex and the offending vegetable (Table I). Further, crude extracts from latex, custard apple and aubergine, as well as the purified allergens Hev b 6.02 (latex hevein) and Prs a 1 (avocado class I chitinase) were used in *in vitro* and *in vivo* assays. Both latex hevein and Pers a 1 were isolated as previously

described [2]. These assays included IgE immunodetection, histamine release (HRT) and basophil activation (BAT) tests and skin prick tests (Table I and Fig. 1), performed according to previously described methods [5-7]. The reliability of HRT and BAT in the allergologic diagnosis, including latex allergy, has been previously proven [6,7].

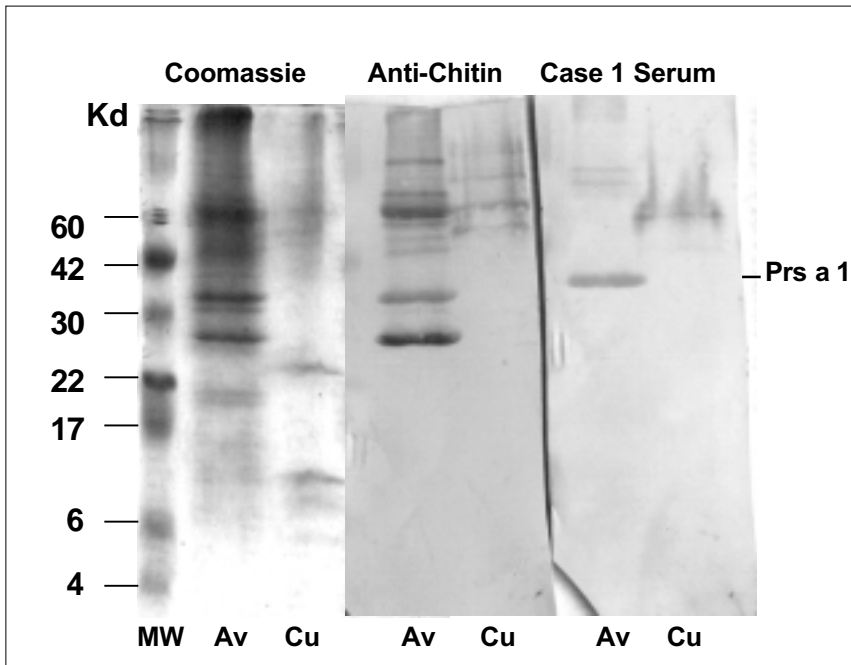


Figure 1. Protein staining (Coomassie), immunodetection with rabbit anti-chitinase antibodies, and IgE immunodetection with Case 1 serum of crude extract from avocado (Av) and custard apple (Cu). Position of Prs a 1 and the 45 kd reactive band are indicated.

Case 1

Twenty-eight year old woman, with neither medical background of interest nor previous surgery. Lawyer. With previous diagnosis of latex-fruit syndrome due to presenting with rhinitis and urticaria after contact with latex and after eating kiwi. Anaphylaxis after eating banana (initial symptom previous to latex sensitisation), and rhinitis after eating chestnut. Subsequently, the patient presented with eyelid, lip and palate angioedema, hives in upper limbs, as well as rhinitis, one hour after eating custard apple. The results of the *in vivo* and *in vitro* studies are shown in Table I and Figure 1.

Case 2

Thirty-one year old woman with bronchial asthma induced by cat dander allergy. Previous medical background: a single reduction mammoplasty surgery. Housewife. Previous diagnosis of latex-fruit syndrome after presenting with rhinitis, skin and pharyngeal pruritus after eating chestnut (initial symptom). Three years later, anaphylaxis after eating banana and subsequently, after minimum environmental expositions to latex, bronchial asthma, rhinoconjunctivitis and urticaria. Also, immediately after ingestion of aubergine, the patient presented with facial and hands angioedema, conjunctivitis, generalised pruritus and glottis difficulty to breath. The patient tolerates ingestion of other solanaceous vegetables, such as potatoes and tomatoes. The data of the *in vivo* and *in vitro* tests are shown in Table I.

Discussion

The allergic reactions induced by sensitisation to custard apple and aubergine are really rare, and their presentation as latex-vegetable syndrome is exceptional. This presentation was strongly indicated in both cases by positive skin responses to custard apple and aubergine, respectively, as well as to positive SPT and specific IgE levels to latex and the major fruits involved in the latex-fruit syndrome (avocado, banana, and chestnut). Moreover, biological tests (HRT and BAT) using the corresponding crude extracts fully confirmed these results (Table I). BAT showed higher values than HRT in both cases, probably due to the greater sensitivity of BAT [7].

The involvement of latex hevein and fruit class I chitinases as main crossreacting allergens was supported by several lines of evidence in case 1. Both purified Hev b 6.02 and Prs a 1 induced positive responses in skin prick tests, as well as high levels of basophil activation and histamine release (in the case of Hev b 6.02) (Table I). Specific IgE immunodetection uncovered a reactive band of approximately 45 kd in the crude custard apple extract, which was also recognized by rabbit anti-chitinase monospecific antibodies [5] (Figure 1). The serum from patient 1 also detected Prs a 1 in immunodetection.

Hev b 6.02 produced positive skin responses and showed high biological activity in HRT and BAT in the case of patient 2. However, Prs a 1 was reactive neither in SPT nor in IgE immunodetection. In fact, no band was detected using the serum of patient 2 in avocado or aubergine extracts (not shown). By contrast, Prs a 1

reached high values of basophil activation and over 10 % of histamine release in case 2. Low levels of class I chitinases in the aubergine extract analyzed and/or the presence of allergenic proteins with hevein-like domains (i.e. proheveins, lectins) not related with chitinases could explain the above mentioned results. Another possible explanation is that, as stated by other authors [8], allergen-specific IgE antibodies capable of binding to FcRI and biological sensitivities are not necessarily associated.

In our cases, in order to confirm the sensitisation, we used for the first time a new technique (BAT) that has been successfully used in the diagnosis of different kinds of allergic diseases [7,9,10]. In this occasion it was useful to determine in a quantitative manner the intensity of the allergic reaction to latex and to the rest of foods involved. In fact, this is the main commercialised *in vitro* technique that allows a precise knowledge of the patients' sensitisation pattern to the different latex allergens by using purified or recombinant allergens, and this way it enables to foresee the possible crossreactivity with vegetables.

References

1. Blanco C, Carrillo T, Castillo R, Quiralte J, Cuevas M. Latex allergy: clinical features and crossreactivity with fruits. *Ann Allergy* 1994; 73: 309-14.
2. Diaz-Perales A, Sanchez-Monge R, Blanco C, Lombardero M, Carrillo T, Salcedo G. What is the role of the hevein-like domain of fruit class I chitinases in their allergenic capacity? *Clin Exp Allergy* 2002; 32: 448-54.
3. Sánchez-Morillas L, Moneo I, Sedano A, Iglesias ML, Caballero ML, Rodríguez M. Oral allergy syndrome after ingestion of custard apple. *Allergy* 2003; 58: 260.
4. Sanchez-Guerrero MI, Escudero AI, Tortosa JA, Lombardero M. Anaphylaxis to cherimoya. *Allergy* 2000; 55: 976-7.
5. Díaz-Perales A, Collada C, Blanco C, Sanchez-Monge R, Carrillo T, Aragoncillo C, Salcedo G. Cross-reactions in the latex fruit syndrome: A relevant role of chitinases but not of complex asparagine-linked glycans. *J Allergy Clin Immunol* 1999; 104: 681-7.
6. Sanz ML, Prieto I, Oehling A. The Histamine Release Test as an important complement in the diagnosis of allergic diseases. *ACI News* 1995; 7: 56-61.
7. Sanz ML, Gamboa PM, García-Avilés C, Vila L, Dieguez I, Antepara I, de Weck AL. Flow-cytometric cellular allergen stimulation test in latex allergy. *Int Arch Allergy Immunol* 2003; 130: 33-39.
8. Purohit A, Laffer S, Metz-Favre C, Verot A, Kricsek F, Valenta R, Pauli G. Poor association between allergen-specific serum immunoglobulin E levels, skin sensitivity and basophil degranulation: a study with recombinant birch pollen allergen Bet v 1 and an immunoglobulin E detection system measuring immunoglobulin E capable of binding to Fc epsilon RI. *Clin Exp Allergy*. 2005 Feb;35(2):186-92.
9. Sanz ML, Sánchez G, Gamboa PM, Vila L, Uasuf C, Chazot M, Diéguez I, de Weck AL. Allergen-induced basophil activation: CD63 cell expression detected by flow cytometry in allergic patients to *Dermatophagoides pteronyssinus* and *Lolium perenne*. *Clin Exp Allergy* 2001; 31: 1007-13.
10. Sanz ML, Gamboa PM, Antepara I, Uasuf C, Vila L, García-Avilés C, Chazot M, de Weck AL. Flow cytometric basophil activation test by detection of CD63 expression in patients with immediate-type reactions to betalactams antibiotics. *Clin Exp Allergy* 2002; 32: 277-86.

Prof. Dr. María L. Sanz

Department of Allergology and Clinical Immunology
 University Clinic of Navarra
 Apartado 4209
 31080 Pamplona, Spain
 Tel.: ++ 34 948 25 54 00
 Fax: ++ 34 948 29 65 00
 E-mail: mlsanzlar@unav.es