Custard Apple Allergy With Glycosyltransferase as the Culprit Allergen

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J Investig Allergol Clin Immunol 2022; Vol. 32(1): 73-74
doi: 10.18176/jiaci.0711

Key words: Custard apple. Oral allergy syndrome. Glycosyltransferase. Latex.

Palabras clave: Chirimoya. Síndrome de alergia oral. Glicosiltransferasa. Látex.

Custard apple, also known as cherimoya, is a tropical fruit that belongs to the Annonaceae family. Although it originates from Central America, Spain is the leading producer in Europe. Its consumption has been increasing in recent years owing to the fruit's nutritional composition, its content in specific phytochemical compounds, and its beneficial effect on health [1]. Nevertheless, hypersensitivity to cherimoya is infrequent [2]. Few cases of allergy to cherimoya have been reported, and most are related to cross-reaction with latex due to class I chitinase proteins [3]. The first report of custard apple allergy revealed the presence of a 20- to 25-kDa protein as the culprit [1], and subsequent studies detected cross-reactivity between latex and cherimoya involving allergenic proteins of around 40-45 kDa [2,4,5]. The most recent case report describes an IgE-binding band of 14 kDa that displays cross-reactivity with latex, papaya, and avocado as a new allergen involved in cherimoya and latex cross-reaction [3].

We present the case of an 11-year-old child diagnosed with rhinoconjunctivitis due to *Cupressus arizonica* pollen. She had previously experienced 2 episodes of oral allergy syndrome after eating custard apple. She presented no symptoms with latex or other fruits, including peach, avocado, papaya, and banana.

Skin prick testing (SPT) was performed with commercial extracts of latex, common inhalants, palm pollen profilin (Pho d 2), and peach lipid transfer protein (LTP) and prick-by-prick testing with fresh custard apple (peel and pulp). The results of the SPT were positive (mean wheal diameter ≥3 mm) to *Cupressus arizonica* pollen and to custard apple (peel and pulp) only. Total and specific IgE were assessed using the CAP system (Phadia). Total IgE was 859 kU/L. Determination of sIgE to Pru p 3, profilin, latex, and recombinant latex proteins (rHeb v 1, rHeb v 3, rHeb v 5, and rHeb v 6.01) was negative (<0.1 kU_A/L).

Protein extracts from cherimoya pulp and peel were prepared by homogenization in phosphate-buffered saline, followed by centrifugation and dialyzation. SDS-PAGE IgE immunoblotting assays revealed IgE reactivity with a band of 50 kDa in the peel (Figure, A). Proteins from the peel were separated using 2-dimensional gel electrophoresis run with a pH gradient of 4 to 8 (Figure, B) and subsequently transferred to a nitrocellulose membrane for incubation with the patient's serum. A single peel protein (approximately 50 kDa) was recognized by IgE with a point isoelectric protein (pI) value of 5-5.8 (Figure, C). The 50-kDa IgE binding spot was manually excised from the Coomassie blue–stained gel for tryptic digestion according to Martínez-Alonso et al [6].

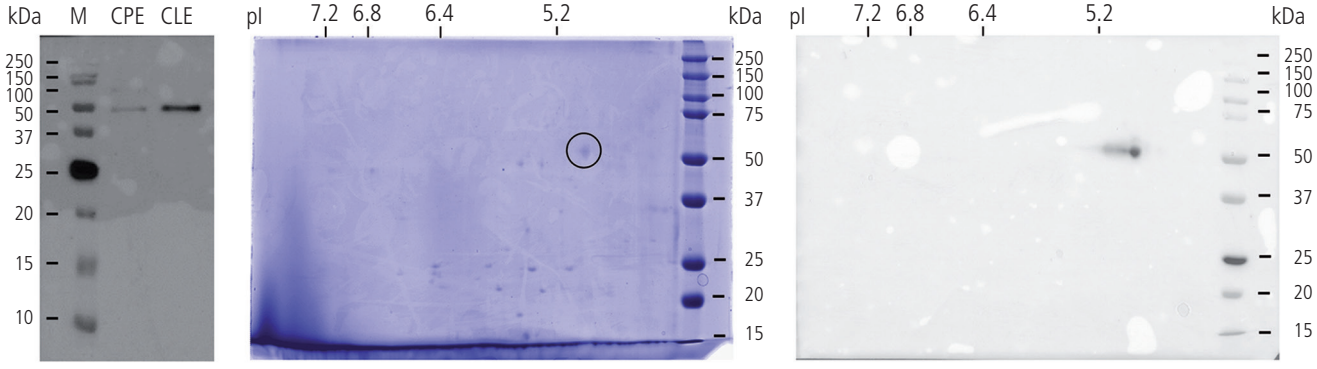

Figure. In vitro studies with custard apple extract. A, Immunoblot. IgE binding to custard apple extract in serum from an allergic patient. B, 2D PAGE protein profile of CPE. C, 2D immunoblot analysis of custard apple with skin extract developed with the patient's serum. The protein spot was used for peptide mass print analysis and protein identification. CLE indicates cherimoya peel extract; CPE, cherimoya pulp extract; M, molecular weight marker; pI, point isoelectric.

After digestion, peptide mass fingerprinting was analyzed using MALDI-TOF mass spectrometry to identify proteins as previously described [6]. Additionally, when available, and for confirmation of protein identity, peptide fragmentation was performed by MS in tandem with MALDI LIFT TOT/TOF. Based on comparison with a database, the resulting peptides were analyzed using mass spectrometry and tandem mass spectrometry, which revealed high homology with the glycosyltransferase of *Capsicum baccatum* in the peel.

Glycosyltransferases comprise a large family of enzymes that catalyze formation of glycosidic bonds to a variety of acceptor molecules (eg, proteins, lipids, polysaccharides, nucleic acids, and small organic molecules) using sugar donors containing a nucleoside phosphate or a lipid phosphate leaving group [7]. As result, these enzymes, which are located in the Golgi apparatus, generate a significant and diverse amount of glycoconjugates that are important for biological processes, such as cell signaling, cell–pathogen interactions, and maintenance of the cellular architecture and metabolism [7]. Among the glycosyltransferases, the enzyme ß1,2-xylosyltransferase adds xylose to glycoprotein and may play a critical role in allergenicity by regulating the structure of the oligosaccharide chains and targeting these proteins to various organelles such as storage bodies [8]. In vitro reports have shown that IgE from sera of allergic individuals recognize core α-3-fucosyltransferase in the prostate glands of snails, and it has been suggested that this protein could be allergenic [9]. Subsequent studies have demonstrated that complex plant *N*-glycans constitute a major class of the so-called carbohydrate cross-reactive determinants, which react with IgE antibodies in the sera of many allergic patients [10]. However, their real implication in clinical practice has not been demonstrated to date.

We report a case of IgE-mediated allergy to custard apple with a glycosyltransferase as the allergen involved. It is important to remember that theoretically low-allergenic foods are always likely to cause problems. In addition, when evaluating an allergic patient, we must assess allergenic sources other than those already known in order to be able to make the appropriate avoidance recommendations.

Funding

The authors declare that no funding was received for the present study.

Conflicts of Interest

The authors declare that they have no conflicts of interest.

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Manuscript received April 12, 2021; accepted for publication May 25, 2021.

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