Anaphylaxis After Mango Fruit Intake: Identification of New Allergens

Ortega-Martín L[1], Sastre B[2,3], Rodrigo-Muñoz JM[2,3], Cañas JA[2,3], Valverde-Monge M[1], Del Pozo V[2,3]
[1]*Department of Allergy, Fundación Jiménez Díaz, Madrid, Spain*
[2]*Department of Immunology, Instituto de Investigación Sanitaria (IIS) Fundación Jiménez Díaz, Madrid, Spain*
[3]*CIBER de Enfermedades Respiratorias (CIBERES), Madrid, Spain*

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Mango fruit allergy is a rare entity. *Mangifera indica* belongs to the *Anacardiaceae* family, along with pistachio and cashew [1]. Spain is the leading producer of mango in the European Union. According to the National Tax Agency, consumption of mango in Spain has almost tripled in the last 5 years [2]. This finding suggests that, in the coming years, the frequency of mango allergy will increase in line with consumption.

We report a case of anaphylaxis after mango fruit intake in which the sensitizing allergens were shown to be thioredoxin-dependent peroxiredoxin, inositol-3-phosphate synthase, Man i 1, Man i 2, and proteins with molecular weights of 50 and 75 kDa.

A 29-year-old man with no personal or family history of atopy was referred to the allergy department after experiencing 4 episodes of symptoms suggestive of allergy on intake of mango fruit. The episodes were characterized by lingual, uvular, palpebral, facial, and genital angioedema, as well as generalized itchy and erythematous rash, minutes after eating mango fruit. During the most recent episode, he was admitted to the emergency department, where he received parenteral antihistamine and corticosteroid therapy, and his symptoms resolved. Therefore, the patient fulfilled the diagnostic criteria for anaphylaxis and was sent to the allergy department for evaluation. The patient gave his written informed consent for publication.

After taking a detailed history, we concluded that the 4 episodes occurred minutes after the intake of mango fruit in different presentations (raw fruit, sushi containing mango, and a mango-flavoured yogurt without portions of fruit). He tolerates all other fruits and nuts, including cashew and pistachio. In the test we requested, the complete blood count was normal. Negative results were recorded for IgE antibodies to mango fruit (0.01 kU/L), pistachio (0.02 kU/L), cashew (0.00 kU/L), latex (0.01 kU/L). Similarly, the results for several recombinant allergens assessed using ImmunoCAP

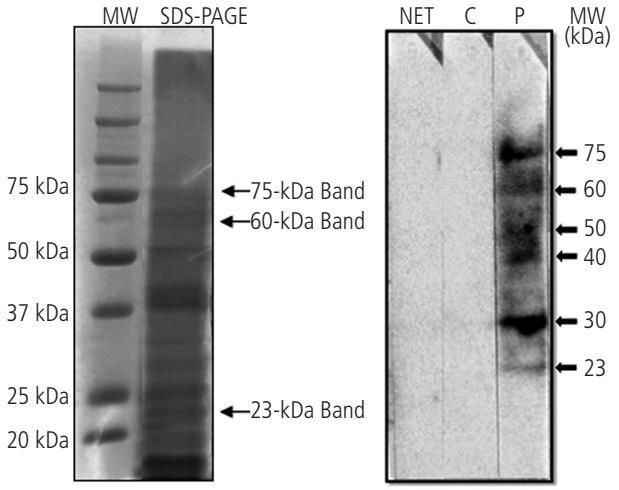

Figure. SDS-PAGE of the mango fruit extract (left) and IgE-immunoblotting of mango fruit with the patient's serum (right). MW indicates molecular weight; SDS-PAGE, mango fruit extract; NET, negative control; C, nonatopic individual serum; P, patient serum.

(Thermo Fisher Scientific) were all negative (<0.35 kU/L). However, given that the result of skin prick testing (prick-by-prick) with mango pulp was positive (4 mm), the patient was confirmed as being sensitized to mango pulp.

The patient was advised to avoid mango fruit and prescribed antihistamines, corticosteroids, and an adrenaline autoinjector in case of a reaction. A challenge with mango was not performed owing to the severity of the reaction and sensitization to that fruit.

An in vitro experiment was performed with complete mango extract manufactured by us from the fruit of the variety "TOMMY ATKINS", which was defatted with ether. SDS-PAGE and an immunoblotting assay were then performed, revealing several bands recognized by the patient's IgE (75 kDa, 60 kDa, 50 kDa, 40 kDa, 30 kDa, 23 kDa) (Figure).

According to published data, the 4 allergens described in mango pulp are Man i 1 (glyceraldehyde 3-phosphate dehydrogenase, 40 kDa), Man i 2 (30 kDa), Man i 3 (profilin, 14 kDa), and Man i chitinase (46 kDa), with Man i 1 and Man i 2 being considered major allergens [3]. In 2010, Paschke et al [4] performed immunoblotting with the sera of 52 patients sensitized to mango. IgE binding was identified in sera with the following protein bands: 40 kDa, 30 kDa, 67 kDa, 43 kDa, 50 kDa, 14 kDa, 25 kDa, and 16 kDa [4].

As a novel finding, we observed sensitization to mango pulp proteins of approximately 75 kDa, 60 kDa, and 23 kDa, although the 23-kDa protein could be the same as the 25-kDa protein described by Paschke et al [4]. We also observed sensitization to the 50-kDa protein and the Man i 1 and Man i 2 allergens. Therefore, the bands of 23 kDa, 60 kDa, and 75 kDa from the mango extract were analyzed using matrix-assisted laser desorption/ionization-time-of-flight (MALDI-TOF) mass spectrometry (MALDI TOF MS). A search of a nonredundant protein sequence database (National Center for Biotechnology Information) using the Mascot program (http://www.matrixscience.com) revealed the 23-kDa protein to be a thioredoxin-dependent peroxiredoxin (score, 161; protein sequence coverage, 51%), the 60-kDa band to be inositol-3-phosphate synthase (score, 312; protein sequence coverage, 26%), and the 75-kDa protein to be an uncharacterized protein (score, 255; protein sequence coverage, 31%). The 50-kDa, 40-kDa, and 30-kDa proteins were not analyzed because they had previously been reported in the literature [3,4]. Peroxiredoxins and inositol phosphate synthase have multiple functions in the antioxidant defence signaling pathway of the cell [5,6].

Based on these results, we confirmed a diagnosis of allergy to mango fruit due to sensitization to Man i 1, Man i 2, thioredoxin-dependent peroxiredoxin, inositol-3-phosphate synthase, and proteins with molecular weights of 50 and 75 kDa.

Although there are no specific epidemiology data on mango allergy, this rare entity seems to be increasingly common [7,8]. Until the present study, few mango allergens had been identified, and none are available in the most widely used diagnostic platforms in clinical practice, such as ImmunoCAP Specific IgE and ImmunoCAP ISAC [9].

When treating a patient with a systemic reaction who is sensitized to mango fruit, physicians should consider that other proteins might be involved. For this reason, the study of food allergy by skin tests and detection of specific IgE may be insufficient, and an in vitro study such as immunoblotting may be required to identify the specific proteins that cause the reaction. With the description of new mango fruit allergens, we think that the range of proteins used to accompany skin testing should be extended and recommend more widespread application of laboratory in vitro tests such as Western blot in the diagnosis of allergies. Our study is limited by the fact that we did not use other techniques, such as the basophil activation test, which could be applied to larger numbers of patients with mango fruit allergy. This approach would enable us to indicate the most appropriate treatment, evaluate cross-reactivity with other foods, and foresee the type or severity of future events.

The clinical case we report is a significant contribution to the literature because it is the first time that a thioredoxin-dependent peroxiredoxin, inositol-3-phosphate synthase, and an unknown 75-kDa protein have been described as mango fruit allergens.

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Conflicts of Interest

The authors declare that they have no conflicts of interest.

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Victoria del Pozo
E-mail: VPozo@fjd.es

