

Allergy to pomegranate (*Punica granatum*)

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Key words: food hypersensitivity; fruit allergy; pomegranate; *Punica granatum*.

• THE pomegranate is the fruit of the *Punica granatum*, a tree native to southwest Asia and widely cultivated in the Mediterranean area. The pulp of the fruit is composed of a cluster of fleshy, red-violet seeds. Several adverse reactions to pomegranate, including severe symptoms such as anaphylactic shock or laryngeal edema, have been described in recent years (1, 2).

Case 1. A 25-year-old woman developed generalized pruritus, urticaria, and bronchospasm 1 h after ingesting half a pomegranate. Two weeks later, after accidental intake of a few pomegranate seeds, she developed oropharyngeal pruritus. Her personal history included allergic rhinitis and

bronchial asthma, pruritus, and vomiting after eating peach, grapes, banana, and mustard, and oral allergy syndrome after the ingestion of nuts. The prick-prick test was positive for all the above fruits. Skin prick tests with a battery of common allergens were positive for *Phleum*, *Artemisia*, *Parietaria*, and *Dermatophagoides pteronyssinus*.

Case 2. A 25-year-old woman presented abdominal pain, itching, and generalized urticaria 10 min after eating a pomegranate. She had had several previous episodes of urticaria and angioedema after ingesting pear and peach, and oral allergy syndrome when eating apple. Skin prick tests to common inhalants were positive to grass pollen.

Case 3. A 3-year-old girl developed facial angioedema, generalized urticaria, and shortness of breath immediately after the ingestion of some pomegranate seeds. It was the first time she had eaten pomegranate. She had previously suffered urticaria after the ingestion of peanuts, almonds, and figs. Skin prick tests were positive to mites, mustard, peanut, almond, fig, peach, corn, and rice.

Skin tests (prick-prick) were performed in the three patients with fresh fruit. A pomegranate was peeled and the pulp homogenized in Björkstén et al.'s solution (3). IgE antibody was determined with Phadenzym RAST reagents, as

previously described (4). SDS-PAGE was performed in 12.5 % gel by Laemmli's procedure (5). Separated protein bands were electrophoretically transferred to PVDF membranes (6) and incubated with 0.5 ml of undiluted human serum (16 h at 4°C). The blots were then incubated with 1:10000 diluted rabbit immunoglobulins to human ϵ -chains conjugated to peroxidase. Blots were developed by chemiluminescence (Lumigen PS-3).

Prick-prick tests using fresh pomegranate samples were positive in the three patients, and specific IgE was positive in patients 1 and 3 (3.21 and 0.75 PRU/ml, respectively). SDS-PAGE immunoblotting of pomegranate extract incubated with patient sera is shown in Fig. 1. Only one IgE-binding component of 29 kDa was detected by image analysis (Bio-Image System, Millipore) in the three sera.

Fruit allergy is one of the main causes of adult food allergy in southern Europe and is often associated with pollen allergy. The pomegranate ripens in autumn and is consumed from September to December. In 1992, we reported the presence of specific IgE (prick test and RAST) against pomegranate in a 7-year-old girl who presented immediate bronchospasm after the ingestion of pomegranate (1). Patients with pomegranate allergy are often sensitized to other allergens.

A 29-kDa protein allergen has been identified in this common Mediterranean fruit.

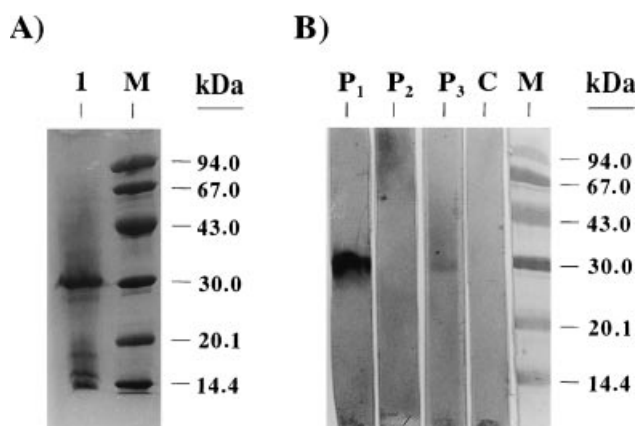


Figure 1. Pomegranate extract electrophoretic results and immunoblotting. A) SDS-PAGE after Coomassie brilliant blue R-250 staining. Lane 1) pomegranate extract; M) molecular mass marker. B) SDS-PAGE immunoblotting; Lane P₁) patient 1; P₂) patient 2; P₃) patient 3; C) control serum (pool from nonatopic subject sera); M) molecular mass marker.

In a study of 15 patients allergic to pomegranate, 13 had sensitivity to pollens, 10 to nuts, and eight to peach (2). The three patients of the present study were also sensitized to pollens, mites, fruits, and nuts. Patient 3 is particularly interesting owing to the early onset of her sensitization and because her mother stated that she had never previously ingested pomegranate. Nevertheless, her mother had frequently eaten this fruit while breast-feeding her daughter. In this case, maternal milk could have been the source of the child's sensitization. Patient 2 had a negative RAST despite her clinical history and the presence of the 29-kDa band in the blot. Perhaps IgE against pomegranate extract could have been detected by a more sensitive method of specific IgE detection, such as the CAP System. SDS-PAGE immunoblotting showed a low-molecular-weight protein (29 kDa) that bound IgE in the sera of the three patients, as detected by image analysis. To our knowledge, this is the first report of an allergen involved in pomegranate allergy. All three patients suffered multisystemic reactions after the ingestion of pomegranate. Type I hypersensitivity was strongly suggested by the positivity of the skin prick test and demonstration of specific IgE antibodies to pomegranate in patient sera. The presence of specific IgE that recognizes epitopes present in a 29-kDa protein confirmed this hypersensitivity. Pomegranate should be considered a potential allergen in patients suffering anaphylaxis in autumn and living in countries where this fruit is consumed.

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References

1. Gaig P, Botey J, Gutiérrez V, Pena M, Eserverri JL, Marín A. Allergy to pomegranate (*Punica granatum*). *J Invest Allergol Clin Immunol* 1992;2:216-218.

2. García J, Carreño A, Contreras L, et al. Alergia a la granada. Revisión de nuestra casuística. *Rev Esp Alergol Inmunol Clin* 1996;11 Suppl 2:146.
3. Björkstén F, Halmepuro L, Hannuksela M, Lahti A. Extraction and properties of apple allergens. *Allergy* 1980;35:671-677.
4. Jiménez A, Moreno C, Martínez J, et al. Sensitization to sunflower pollen: only an occupational allergy? *Int Arch Allergy Immunol* 1994;105:297-307.
5. Laemmli UK. Cleavage of structural proteins during the assembly of the head of bacteriophage T. *Nature* 1970;227:680-685.
6. Towbin H, Staehelin I, Gordon J. Electrophoretic transfer of proteins from polyacrylamide gels to nitrocellulose sheets: procedures and some applications. *Proc Natl Acad Sci U S A* 1979;76:4350-4354.

Anaphylactic reactions to buflomedil

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Key words: anaphylactic reaction; buflomedil.

● BUFLOMEDIL chlorhydrate (BC), a hemorheologic drug used in a wide range of dermatoses (1), exerts a peripheral vasodilatory action, increases perfusion to impaired vascular beds of the microcirculation, and increases arterial perfusion with minimal effects on central hemodynamics (2). BC increases intracellular levels of cAMP, secondary to adenylate cyclase stimulation. The efficacy of BC in reducing the mean daily frequency and severity of winter ischemic attacks has been demonstrated (3). Here we report a case of anaphylactic reaction to BC in which clinical evaluation and positive skin prick test (SPT) suggest an IgE-mediated hypersensitivity mechanism.

A 53-year-old woman treated for Raynaud's phenomenon developed urticarial rash,

systemic pruritus, and hypotension 10 min after parenteral administration of BC. She did not lose consciousness. The patient was treated with corticosteroids and had a remission within 6 h. Six months after the occurrence of the adverse reaction, the patient was admitted to our ward for further investigation. There was no family or personal atopic history. Total IgE was 104 kU/l, and specific IgE to inhalants or food allergens was negative. Concentrations used for skin testing had been previously established in a negative group of three subjects in order to rule out irritant responses. Skin test with BC dissolved in water at concentrations of 0.001, 0.01, 0.1, and 1 mg/ml was performed. Intradermal tests were carried out at the same concentration. The positive and negative tests were histamine and saline solution, respectively. An immediate positive response was obtained at concentration levels of 1 mg for SPT (wheal 4×4 mm, flare 6×8) and at 0.1 mg/ml for the intradermal skin test (wheal 7×8 mm, flare 13×11 mm). Our patient was challenged with another hemorheologic drug (pentoxifylline). A therapeutic dose of 100 mg was well tolerated.

Patients with allergic or pseudoallergic reactions resulting from BC therapy have never been described in the literature.

In conclusion, we report a case of anaphylaxis caused by BC. The positive skin test response suggests a type-1 immunologic hypersensitivity mechanism.

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References

1. Redondo P, Garcia-Foncillas J, Espana A, Cuevillas F, Quintanilla E. Differential modulation of IL-8 and TNF-alpha expression in human keratinocytes by buflomedil chlorhydrate and pentoxifylline. *Exp Dermatol* 1997;6:186-194.