

Exercise-induced anaphylaxis to grape

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Key words: exercise-induced anaphylaxis; food allergy; grape.

● EXERCISE-induced anaphylaxis (EIA) is characterized by airways obstruction, urticaria, and hypotension following physical exercise, and it can be associated with food allergy (1, 2). We describe one case of EIA due to ingestion of grape, which rarely causes allergic reactions.

A 33-year-old woman, with allergic rhinoconjunctivitis due to *Parietaria* and mugwort, reported in the past year facial flushing, edema of the lips, and dyspnea after drinking white or red wine, although she could eat fresh grapes without problem. The symptoms were reproducible and clearly related to wine; therefore, she was advised to avoid it. One month before, after eating white grapes, she had gone jogging. After the exercise, urticaria, facial/pharyngeal edema, abdominal pain, and dyspnea appeared and rapidly worsened. At the emergency department, profound hypotension was found: her blood pressure was 70/52 mmHg, heart rate 130 bpm, and respiratory frequency 24/min. She received epinephrine, plasma expanders, and corticosteroids/antihistamines, and recovered within 3 h.

We suspected EIA associated with grape allergy, and performed a detailed diagnostic procedure. The skin prick tests with commercial extracts (Stallergènes, Antony Cedex, France) with inhalants and foods were negative except for *Parietaria* and mugwort. Molds (*Aspergillus fumigatus*, *Cladosporium herbarum*, *Alternaria*

alternata, *Penicillium notatum*, and *Botrytis*), which can be present on grape surfaces, were negative as well. The prick-to-prick tests with juice from white and red grapes were positive. The arithmetic means of wheal diameters were as follows: 8 mm for white grape, 5 mm for red grape, and 4 mm for histamine HCl 0.1%. The oral single-blind challenge with metabisulfite using increasing doses up to 75 mg (Test Dose, Lofarma, Milan, Italy) was negative. An *in vivo* challenge (food plus exercise) was not performed for ethical reasons. Serum tryptase (Tryptase UniCAP, Pharmacia, Uppsala, Sweden) in a blood sample obtained within 1 h after the onset of EIA was increased (18.2 ng/ml, normal value <15 ng/ml).

A grape extract was prepared for immunologic studies. Grape was homogenized and extracted at 10% w/v in 0.1 M potassium phosphate buffer, pH 7, for 1 h. After removing the particulate by centrifugation, the supernatant was dialyzed against 5 mM ammonium bicarbonate, lyophilized, and resuspended in 1/10 of the initial volume. Electrophoresis of the extract (12 µg/lane) was performed in a 10% polyacrylamide gel (Nupage Sis-Tris, Prodotti Gianni, Milan, Italy) at 180 mA for 1 h. The resolved proteins were stained with 0.1% Coomassie brilliant blue and transferred to a nitrocellulose membrane (Protann BA, 85, Scheicher and Schuell, Milan, Italy). The membrane was saturated with 5% defatted dried milk before incubation with patient's serum or control sera diluted 1:2. Bound specific IgE was then detected by peroxidase-conjugated antihuman IgE serum. No grape-specific IgE could be demonstrated in the patient's serum by the CAP-RAST technique. However, the assessment of IgE reactivity of serum against grape extract provided a positive result. The SDS-PAGE profile of grape extract showed the presence of a well-resolved band at about 67 kDa and a diffuse stain between 25 and

35 kDa. Immunoblotting showed that the patient's serum had IgE antibodies against one specific component of the extract (approximate molecular mass 30 kDa), whereas control sera also reacted to the 67-kDa band.

IgE-mediated reactions to grape have been rarely reported (2, 3–6). The case herein described was a true food-associated EIA, since the patient remained asymptomatic when eating at rest great amounts of the sensitizing food. The prick-to-prick positivity and the increase of serum tryptase confirmed the mast-cell activation. Moreover, the immunoblot analysis suggested that the patient had specific IgE reacting to one component of the grape extract, despite the negativity of the CAP-RAST assay.

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TGF-β1 gene polymorphisms

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● ASTHMA, hay fever, and eczema are part of a syndrome of allergic diseases known as atopy. Genome-wide screens, linkage analysis, and studies of polymorphisms in candidate genes have all identified genetic factors likely to contribute to the allergic pathogenesis (1). Recently, some studies have indicated a role for TGF-beta in the etiopathogenesis of allergic diseases, and its increased levels were found in asthmatic and rhinitis patients. The coding gene is located on chromosome 19q13.1–13.3 (2), and several polymorphic variants have been identified in this gene. The C/T base exchange in position –509, which is present in a region of the promoter associated with negative transcription regulation, was previously shown to be associated with elevated total serum IgE levels (3). The aim of our study was to determine whether atopic asthma or other atopic diseases (or possibly related phenotypes) are associated with selected mutations (polymorphisms) in the TGF-beta 1 gene also in the highly homogeneous Czech population.

Caucasian subjects of exclusively Czech ethnicity ($n=288$) were included in this study. DNA taken from subjects with clinically manifested asthma and other atopic diseases ($n=170$, 90 men and 80 women, aged 25.4 ± 11.5 years [mean $\pm$ SD]) and reference ethnically and age-matched unrelated subjects ($n=118$, 61 men and 57 women, aged 29.3 ± 7.9 years) was examined for base substitutions in the TGF-beta 1 gene.

Atopy (defined as enhanced IgE responsiveness) was recognized by specific IgE (>0.35 kU/l) or a positive skin prick test to any one or more allergens, as described previously (4).

Project approval was granted by the local ethics committee at the Medical Faculty, MU Brno, and written informed consent for genetic analysis was obtained from all subjects.

After DNA extraction, three polymorphisms located in the 5' region at position –988 (C/A), –800 (G/A), and –509 (C/T) and two polymorphisms located at codons 10 (L10P) and 25 (R25P) of exon 1 were investigated by PCR methods, as described earlier (5).

The TGF-beta 1 –988 A variant was not present in our subjects (all patients and reference subjects had only the CC genotype for this mutation). We found no association between any of the four polymorphisms in the TGF-beta 1 gene and clinical manifestation of atopic diseases ($P>0.05$ in all cases) (Table 1). In atopic subjects, there were no significant associations among TGF-beta 1 genotypes and a number of quantitative traits investigated in our study, including total serum IgE levels (TGF –509: wild type [CC genotype] – IgE: 294 ± 50.9 [mean $\pm$ SEM], heterozygote [CT] – IgE:

Table 1. Genotype distributions (%) and allele frequencies of four polymorphisms in TGF-beta 1 gene

		–800G/A polymorphism					
		GG (%)	GA (%)	AA (%)	G allele	A allele	P
Atopic patients	($n=170$)	153 (90.0)	16 (9.4)	1 (0.6)	0.947	0.053	
Reference group	($n=118$)	100 (84.7)	18 (15.3)	0 (0)	0.924	0.076	>0.05
		–509C/T polymorphism					
		CC (%)	CT (%)	TT (%)	C allele	T allele	P
Atopic patients	($n=170$)	85 (50.0)	66 (38.8)	19 (11.2)	0.694	0.306	
Reference group	($n=118$)	63 (53.4)	43 (36.4)	12 (10.2)	0.716	0.284	>0.05
		+869 T/C (L10P) polymorphism					
		TT (%)	TC (%)	CC (%)	T allele	C allele	P
Atopic patients	($n=167$)	65 (38.9)	71 (42.5)	31 (18.6)	0.602	0.398	
Reference group	($n=117$)	46 (39.3)	51 (43.6)	20 (17.1)	0.611	0.389	>0.05
		+915 G/C (R25P) polymorphism					
		GG	GC	CC	G allele	C allele	P
Atopic patients	($n=167$)	143 (85.6)	23 (13.8)	1 (0.6)	0.925	0.075	
Reference group	($n=117$)	98 (83.8)	19 (16.2)	0 (0)	0.919	0.081	>0.05

P values refer to both genotype and allele distribution.