

Ethanol-induced anaphylaxis following ingestion of overripe rock melon, *Cucumis melo*

Dominic F J Mallon, MD and Connie H Katelaris, MD, PhD

Background: Anaphylactic reactions to ethanol are rare with only seven cases reported in the literature. All previous cases have occurred following ingestion of alcoholic beverages or food to which an alcoholic beverage has been added. To date there are no cases in the literature of ethanol-induced anaphylaxis caused by the accumulation of endogenous ethanol in overripe fruit.

Methods: We report a patient with ethanol-induced anaphylaxis who developed anaphylaxis following ingestion of overripe, but not fresh rock melon (*Cucumis melo*). The patient is a 24-year-old, previously well woman who experienced five episodes of acute anaphylaxis following ingestion of various alcoholic beverages and, on one occasion, following ingestion of overripe rock melon to which no ethanol was added. Ethanol-induced anaphylaxis was confirmed on blinded challenge; however, challenge with freshly prepared rock melon was negative. The patient declined further challenges.

Conclusion: Ingestion of overripe fruits may cause anaphylaxis in patients with ethanol-induced anaphylaxis. These patients should therefore, be advised to avoid ingestion of overripe fruits.

Ann Allergy Asthma Immunol 1997;78:285–6.

INTRODUCTION

Allergic reactions to foods and beverages containing ethanol are uncommon. The majority of allergic reactions to food consist of anaphylactoid reactions to yeasts, salicylates, coloring agents, and preservatives (principally metabisulfites) found commonly in alcoholic beverages.² Anaphylactic reactions to ethanol itself are rare with only seven adequately documented cases in the literature.^{1–7}

The possibility of an anaphylactic reaction occurring due to endogenous ethanol in overripe fruit has not been reported previously. We present a case of ethanol-induced anaphylaxis in which one episode of anaphylaxis was precipitated by ingestion of overripe rock melon.

CASE PRESENTATION

A 24-year-old woman was referred to the allergy service at Westmead Hos-

pital with six episodes over 4 months of rapid onset angioedema affecting her lips, mouth, and periorbital regions associated with urticaria. On four occasions, the symptoms resolved spontaneously within hours. On two occasions, her symptoms were associated with wheeze and near-syncope prompting her attendance at the emergency department of her local hospital where her symptoms responded to oral H₁ antagonists and inhaled salbutamol. Spirometry was not performed. Four of the six episodes occurred within 25 minutes of ingesting various alcoholic beverages and two episodes occurred following ingestion of foods (overripe rock melon prepared at home and tomato puree served at a restaurant) to which ethanol had not been added.

The patient had no personal history of atopic disease. She was taking an oral contraceptive pill but no other medications, and was constitutionally well. Physical examination revealed a fit young woman with no relevant findings.

Skin prick tests to a panel of common allergens resulted in a 5-mm

wheel to plantain, a 5-mm wheel to *D. farinae*, and 4-mm to *D. pteronyssinus* but were negative to a number of common food allergens including cow milk, egg, wheat, peanut, fish, baker's and brewers yeasts, and tomato.

The patient was prescribed a diet low in natural salicylates and amines, preservatives, and additives (metabisulfite, monosodium glutamate, and benzoates). Compliance was excellent. When on this diet, she experienced one episode of urticaria and angioedema within 15 minutes of swallowing a small mouthful of vodka. Randomized, double-blind capsule challenges to metabisulfite, salicylate, monosodium glutamate, phenylethylamine, tyramine hydrochloride, and benzoates did not reproduce her symptoms.

Skin prick tests to rock melon, tomato puree, 10% acetaldehyde, 10% and 99.9% ethanol were negative. A 5-mm wheal developed following skin prick testing to 1% and 10% acetic acid that was not elicited by prick testing a nonatopic volunteer. As the patient had recently ingested vinegar in a salad dressing without adverse effect, we decided to include an oral challenge with acetic acid in her workup. Unblinded challenges to fresh rock melon, a commercial brand of tomato puree, and 50 mL of 2% acetic acid did not reproduce the patient's symptoms. Single blind challenges with 50 mL of 0.02% and 0.2% absolute ethanol solutions (diluted with orange juice) were similarly negative; however, within 15 minutes of ingesting a similar preparation of 50 mL of 2% ethanol, the patient complained of pruritus of her mouth and gums, which was associated with urticaria of her face and neck and a 25% reduction in her prechallenge FEV₁. Her symptoms responded to oral terfenadine and in-

From the Department of Immunology, Westmead Hospital, New South Wales, Australia.

Received for publication February 28, 1996.

Accepted for publication in revised form April 24, 1996.

haled salbutamol. The patient refused further challenges to overripe rock melon.

The patient was diagnosed as having immediate type hypersensitivity to ethanol and was advised to avoid beverages and foods containing ethanol, and to avoid overripe fruits. The patient was also prescribed self-injectable epinephrine.

DISCUSSION

The principal manifestations of ethanol-induced anaphylactic reactions reported in the literature are urticaria and angioedema following ingestion of alcoholic beverages,¹⁻⁷ confirmed by reproduction of urticaria and angioedema following blinded challenges to pure ethanol. This syndrome is to be distinguished from the more common "antabuse" syndrome of flushing, headache, and hypotension due to inherited or acquired impairment of aldehyde dehydrogenase activity.

The pathogenesis of this syndrome is unclear. Ethanol-specific IgE has not been demonstrated but, if present, would be directed to ethanol conjugated to a protein. An alternative explanation would be that ethanol itself acts as a mast cell degranulator in these predisposed individuals. Again, there are no data to support this hypothesis. The involvement of preformed mediators released by mast cells in the pathogenesis is suggested by the nature and rapidity of onset of the symptoms. In addition, mast cell degranulation has been demonstrated on skin biopsy in one case where biopsy was performed,⁶ and elevations in plasma histamine have been documented in two further patients.^{5,6}

Theoretically, the reactions may be triggered by ethanol or by one of its metabolites (acetaldehyde or acetic acid). Urticaria provoked by oral acetic acid challenge was documented in one patient in whom skin tests were not

performed,² and positive skin prick tests were found in two others.^{3,7} In one of these patients, the authors claimed this as evidence that a reaction to acetic acid was the cause of the patient's symptoms,³ but in our patient, a positive skin prick test for acetic acid failed to predict a positive challenge. In another case, positive skin prick testing to acetic acid was not associated with a history of adverse reactions to vinegar.⁷ Skin prick tests are thus unreliable in identifying clinically significant triggering agents in these patients, and should be confirmed by oral challenges where possible.

The patient presented in this report is the first we are aware of where symptoms associated with ethanol-induced anaphylaxis may have been provoked by a build-up of endogenous ethanol in overripe fruit. The rock melon that provoked our patient's symptoms was prepared at home with no added ethanol and was described as being overripe with a pungent odour, whereas that with which she was challenged in our clinic was fresh with no odour. The concentration of ethanol in rock melon (*Cucumis melo*) has been shown to increase in parallel with the concentration of volatile esters with time after harvest.⁸ Unfortunately, there are no data in the literature on the absolute concentrations of ethanol achieved in melons during the ripening process to correlate with the results of the titrated blinded challenge with pure ethanol in our patient.

We hypothesize that the concentration of ethanol in the overripe rock melon prepared at home that triggered urticaria and angioedema in our patient was sufficient to cause her symptoms. Ethanol may also be found in tomato products, usually in very small concentrations (up to 6 ppm), with the concentration varying according to the variety, ripeness at harvest, and the

method and length of storage.⁹ Whether the tomato puree that provoked angioedema in our patient had sufficient endogenous ethanol to cause these symptoms or whether there was contamination with exogenous ethanol during preparation in the restaurant where it was served remains speculative. Nevertheless, this case underlines the potential hazard caused by elevated levels of endogenous ethanol in overripe fruit in patients with ethanol-induced anaphylaxis.

REFERENCES

1. Hicks R. Ethanol, a possible allergen. *Ann Allergy* 1968;26:641-3
2. Karvonen J, Hannuksela M. Urticaria from alcoholic beverages. *Acta Allergologica* 1976;31:167-70
3. Przybilla B, Ring J. Anaphylaxis to ethanol and sensitisation to acetic acid. *Lancet* 1983(i):483
4. Ormerod AD, Holt PJA. Acute urticaria due to alcohol. *Br J Dermatol* 1983;108:723-4
5. Elphinstone PE, Kobza Black A, Greaves MW. Alcohol-induced urticaria. *J Royal Soc Med* 1985;78:340-1
6. Ting S, Rauls DO, Ashbaugh P, Mansfield LE. Ethanol-induced urticaria: a case report. *Ann Allergy* 1988;60:527-30
7. Kelso JM, Keating MU, Squillace DL, et al. Anaphylactoid reaction to ethanol. *Ann Allergy* 1990;64:452-4
8. Yabumoto K, Yamaguchi M, Jennings WG. Production of volatile compounds by muskmelon, *Cucumis melo*. *Food Chem* 1978;3:7-16
9. Nelson PE, Hoff JE. Tomato volatiles: Effect of variety, processing and storage time. *J Food Sci* 1969;34:53-7

Request for reprints should be addressed to:
Dr D F J Mallon, MD
c/-MacFarlane Burnet Centre for Medical
Research
Yarra Bend Rd
Fairfield, Victoria
3078 Australia