

Grapple® Allergy: The Grape or the Apple?

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Key Words

Apple • Food allergy • Grapple

Abstract

Background: Many foods can cause food allergies. Grapple® is just one of many new fruits recently introduced into grocery stores. **Objective:** To describe 2 unique patients with food allergies after consuming a unique food, a Grapple. **Methods:** Commercial skin prick testing, fresh fruit prick-prick and radioallergosorbent testing were used to characterize the food allergy reaction. **Results:** Clinical history and appropriate testing confirmed the Grapple food allergy. **Conclusions:** To our knowledge, these are the first 2 case reports of food allergy to a new fruit called Grapple. These cases illustrate the importance of consumer labeling laws and careful identification of component ingredients by food-allergic individuals.

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Introduction

While the prevalence of food allergy is less common in adults than in children, food allergies affect nearly 2% of individuals in the United States [1]. A careful history is frequently required to identify the culprit food allergen. Studies of food-allergic individuals and their families found that allergenically dangerous ingredients were correctly identified by parents only part of the time, varying from 7% for milk to 93% for egg products [2]. As such, it is not surprising that a survey of 15,000 United Kingdom households found that approximately 20% of the population alters their diet for a perceived adverse reaction to food [3].

Food allergies have been recognized since the time of Hippocrates when the ancient Romans noted that some people could tolerate foods that others could not [1]. Irrespective of the expansion of the Roman Empire of its day, our global economy is unparalleled. The variety in food shipped in from all over the globe into local supermarkets of the United States is unprecedented. Because of this wider variety in food supply, the likelihood that an individual will come into contact with an allergy-inducing food has increased over the past 2 decades. The reasons suggested are multifactorial, but the implications are clear [4].

The views expressed in this article are those of the authors and do not reflect the official policy of the Department of Defense or other Departments of the US Government. The voluntary, fully informed consent of the subjects involved in this research was obtained as required by 32 CFR 219 and AFI 40-402.

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1018–2438/07/1433–0211\$23.50/0

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Fig. 1. Grapple used for prick-prick skin testing.

With the globalization of food production, shipping and processing, there is an increased risk of being sensitized to new food antigens previous generations were not exposed to. Decision tree approaches to assess the allergenic potential of foods were developed by the United Nation's Food and Agricultural Organization/World Health Organization (FAO/WHO) consequent to the finding that a genetically modified (GM) soybean expressed a protein from the Brazil nut [5]. The FAO/WHO Joint Committee recommended decision tree approaches, dividing new foods into two categories, GM and non-GM foods. For novel non-GM foods, the assessment of the allergenic potential is more subjective. Where protein is present in the novel non-GM food, hazard and risk assessments need to be made. The US Food and Drug Administration (FDA) has recognized the importance of and is currently developing approaches to evaluating allergic reactions to major food allergens [6].



Fig. 2. Grapple used for prick-prick skin testing.

We present 2 adult patients with food allergy to a novel food called Grapple® (pronounced 'grape-L'), which have not been reported previously. Grapple (fig. 1 and 2) is a new food introduced into US markets in autumn 2004 [7]. It is advertised as a healthy snack that 'Looks like an apple. Tastes like a grape.'™ According to the website, it has made the front page of the USA Today Lifestyle section as well as being a Jeopardy game question. The marketing cites that 'With childhood obesity increasing at alarming rates... Isn't it time for your whole family to enjoy this exceptional fruit treat?' We conducted a thorough literature search (PubMed and Ovid) of articles published between 1966 and March 2006 with the following keywords: grapple + food allergy, genetically modified food + allergy, apple allergy + grape allergy, food allergy + apple, processed food + allergy, hybrid food + allergy, novelty foods + allergy and methyl anthranilate, 2-aminobenzoic acid methyl ester + allergy. The relevance of over 300 articles was reviewed for reports of previous Grapple allergy. While other unique fruits, such as jackfruits and Sharon fruit, have been previously presented [8, 9], it is apparent that these are the first 2 cases of Grapple allergy reported in the literature.

Case Reports

Patient 1 was a 29-year-old female referred for allergy evaluation with a chief complaint of adverse food reactions. The patient reported an acute episode of oropharyngeal pruritus (the same she experienced with almonds) that progressed to globus, perior-

bital swelling and chemosis where she had rubbed her eye after eating shrimp and a Grapple she bought from the local grocery store. She called a nurse helpline and was instructed to go to the emergency department. Once there, she was given diphenhydramine and discharged home with an EpiPen. She denied prior adverse reactions to apples, grapes or shrimp and had avoided these products since her reaction. She had never before eaten a Grapple. She tolerated certain almonds and all hazelnuts, pistachios, Brazil nuts, pecans, pinenuts and Macadamia nuts. She denied seasonal or perennial rhinoconjunctivitis over the last year. She did report rhinitis symptoms with heavy dusting, cat exposure and irritants but denied symptoms with dogs or cutting grass.

Skin prick testing (SPT) was positive to commercial apple, almond and birch extract. Fresh fruit prick-prick skin testing was also positive to fresh Grapple, Red Delicious apple and grape. Radioallergosorbent testing was class 0 to grape and class 2 to apple. Investigation into the Grapple revealed that this was a Fuji apple 'dipped into a combination of pure water and Concord grape flavoring for a short time' [7]. A list of ingredients of the flavoring was requested from the manufacturer in order to determine whether there was any grape protein in the fruit. Information from the manufacturer revealed no actual grape protein but only water and flavoring consisting of methyl anthranilate, 2-aminobenzoic acid methyl ester (chemical family: aromatic acid ester + inert ingredients, 24.4% methyl anthranilate, 73.6% inert ingredients; GRAS Registry No: USFDA 21 CFR 182-10 No. 2682).

Grapple, apple and grape (prior to our realization that there was no actual grape protein in the Grapple) avoidance and a Medic Alert bracelet were recommended. She was also encouraged to become a member of the Food Allergy and Anaphylaxis Network. At the 1-year follow-up, the patient was tolerating red and green grapes as well as cooked apples but continued to avoid raw apples.

Three months later, another patient was referred for allergy evaluation. The patient was a 25-year-old female who was referred for an adverse reaction after eating a Grapple. She reported immediate pharyngeal pruritis, lightheadedness, metallic taste and cough after the ingestion of this fruit. She stated that previous apple and nectarine ingestion caused similar reactions in the past, and that she had eaten grapes after this event without adverse reaction. She had also consumed other Rosaceae food items, e.g. strawberry, carrot, potato, almonds and celery over this time without adverse reactions and she tolerated apple juice without difficulty. She reported a history of rhinoconjunctivitis triggered by dogs, cats, dusting, vacuuming, cutting grass, irritants and raking leaves.

Commercial SPT was positive to birch, and fresh fruit prick-prick skin testing was positive to Grapple and apple. She was diagnosed with apple and nectarine allergy, instructed on avoidance measures and provided with an EpiPen.

Discussion

There are several types of new foods appearing in our local markets. Both GM as well as non-GM foods such as hybrid foods, regional/ethnic foods and processed foods

are being shipped to non-local regions [5]. The Grapple represents a type of non-GM, processed food category that has yet to be presented. Grapple is truly an apple with the chemical additive of methyl anthranilate (chemical name is 2-aminobenzoic acid methyl ester with the empirical formula $C_8H_9NO_2$) [10]. Methyl anthranilate is one of the first artificial flavor compounds to be discovered and is responsible for the characteristic aroma of the Concord grape. Methyl anthranilate is an ester, not a protein, that is catalyzed from methanol by anthraniloyl-coenzyme A: methanol acyltransferase [11]. Methyl anthranilate is neither found on the FAO/WHO 2005 Codex Alimentarius list of food additives nor has it previously been described as being related to any food-related allergic disorder [12]. A large number of different flavoring substances are used in foods. Many formulations used for flavoring contain literally hundreds of different chemical compounds. Typically natural and artificial flavors appear as the final ingredient on food labels as they are the least prevalent component. There are few reports of allergic reactions to flavors alone. IgE-mediated reactions to flavoring ingredients in typical food products are even rarer. Thus, food additive-induced sensitivities seem to occur rarely in the overall population [13]. When reactions occur due to flavoring, it is frequently the result of nonspecific labeling or processing contamination, such as labeling a flavor as 'non-dairy flavoring' when the foods do indeed contain trace amounts of milk or casein protein [14].

Food processing techniques are primarily designed for the stabilization and preservation of protein while enhancing their digestibility, not for their epitope destruction. Among the eight food groups that cause more than 80% of IgE-mediated reactions in children, resistance and allergenicity varies widely. Many foods, including vegetables, have heat-resistant antigens [15].

The allergenicity of apples appears to be dependent on storage conditions. One study found that only severe heat treatment of apples caused a significant decrease in the allergenicity of Mal d 3, one of the major apple allergens [16]. Store-purchased apples contained higher concentrations of another major apple allergen, Mal d 1, than freshly picked apples and apples stored at low temperatures [15]. Prick-prick testing with fresh apples has been shown to be a reproducible method of assessing the allergenicity of apples. Thus, both the selection of apple cultivars and the storage conditions of the apples are both viable strategies for the reduction in symptoms in patients with apple allergies [17].

Commercially prepared extracts are often inadequate when evaluating possible fruit and vegetable allergy due to the lability of the responsible allergen. Therefore, it is recommended that fresh food be used for testing whenever possible [18]. While a negative SPT essentially rules out an IgE-mediated reactivity (negative predictive accuracy >95%), a positive SPT does not necessarily prove that the food is causal due to false-positive results in 50% [19]. This false positivity was demonstrated in patient 1 who was SPT positive to grape before we knew there was no grape protein in the Grapple and then went on to tolerate grapes without adverse reaction. A recent and clear clinical history by a knowledgeable specialist is still important and then combined with a positive SPT may be considered confirmatory of a food-induced allergic reaction to the tested food. In both of our case reports, the patients tested positive to fresh Grapple and fresh apple prick-to-prick skin testing.

Key to the treatment of food allergies, like other allergic reactions, is avoidance, avoidance and avoidance. However, as introduced above, that can be exceedingly difficult. The new FDA labeling law for both domestically produced foods and imported foods sold in the US took effect on the 1st of January 2006. It is designed to improve the ability of the consumer to recognize potentially dangerous food allergens [20]. Consumers will still have to stay vigilant, however, and continue to critically read each product's packaging. As in these 2 cases, it should be recommended to the patient to obtain a Medic Alert bracelet as well as to join the Food Allergy and Anaphylaxis Network. Additionally, appropriate auto-injectable epinephrine should be taught and demonstrated.

In a society of ready-made meals, junk-food junkies and burgeoning childhood obesity, food producers, distributors and groceries are trying to find new foods for consumers to keep up with our demanding appetites. Some of these will be healthy alternatives to snack foods, such as the Grapple. In this case, the food was a healthy apple with artificial flavoring marketed to appear as a unique food.

Food manufacturers continue to try to find new ways to make food taste better either through genetic modification, hybridization or artificial flavoring for improved taste and enhanced nutrition. Some new foods will be GM. Scientists are currently working on a GM pig whose meat will have omega-3 fatty acid, a fatty acid that raises high-density lipoprotein [21]. Other new foods will be processed foods, ethnic/regional or hybrids. Hybrids, like the tangelo (tangerine + orange) or the pluot (a plum crossed with an apricot), have also been implicated in

food allergies. More processed foods also increase the risk of processing contamination of unintentional substances, such as milk protein in hot dogs [14]. As food manufacturers find new and novel ways to make existing food taste better, there may be added allergen diversity in the food pool.

In today's increasingly global markets, allergists will be compelled to do more detective work to identify these truly unique food allergies. The US FDA and FAO/WHO are developing policies for foods with the potential of enhanced allergenicity. As clinicians, allergists must identify the culprit food with a good history and physical and appropriate testing to avoid diets that are overly restrictive.

In summary, these are the first cases of a unique Grapple allergy in the literature. Consumers have to bear in mind that all foods and especially newer foods may present an allergic potential. Furthermore, allergists play a critical role in the analysis of these new foods in order to make information readily available to the public to help food-allergic patients determine whether or not the food in question is allergenically safe for them to consume.

Acknowledgments

We appreciate the clinical updates and opportunities learned from the patients with Grapple allergy in this study.

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