

A nurse with anaphylaxis to stone fruits and latex sensitivity: potential diagnostic difficulties to consider

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Background: There have been several recent reports describing a cross-reactivity between latex and antigens derived from a number of fruits, including those of the stone fruit family. The relationships between the allergic reactions to the antigens from these plant products are still being defined.

Objective: To characterize the IgE reactivity of a patient who had anaphylactic reactions following the ingestion of several members of the stone fruit family (ie, plum, peach, and nectarine) and had a positive clinical history for latex allergy.

Methods: The patient's serum was tested for the presence of specific IgE for latex, stone fruits, and a panel of other foods reported to be cross-reactive with latex. Prick testing was also performed with freshly prepared extracts from the implicated fruits. Finally, the immunochemical relationship between this patient's fruit and latex sensitivity was investigated by RAST inhibition.

Results: The patient had strongly positive skin tests to the freshly prepared fruit extracts but the in vitro food-specific IgE tests were equivocal or very low positive. In vitro latex-specific IgE tests were strongly positive. The stone fruit extracts were shown to be inhibitors of the patient's latex specific IgE by RAST inhibition.

Conclusion: Skin testing with freshly prepared fruit extracts was more sensitive than the in vitro tests with this patient. The inhibition data support an immunochemical relationship between the patient's latex allergy and sensitivity to stone fruits.

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INTRODUCTION

In the early 1990s several European investigators reported that many common fruits contained proteins that cross-react with structurally related proteins found in natural latex.^{1,2} Several early studies focused on the cross-reactivity between latex and banana, kiwi, chestnut, and avocado.^{3,4} The list of foods with cross-reactivity to latex continues to increase with substantial cross-reactivity also reported for hazelnut, peanut, celery, melons, potato, pa-

paya, figs, passion fruit, tomato, grape, pineapple, cherry, and peaches.^{5,6} Peaches are a member of the subfamily Prunoideae. The main members of this subfamily also include: apricot, plums, and cherry. These fruits are commonly referred to as stone fruits. A recent paper⁷ described extensive clinical cross-reactivity in members of the Prunoideae subfamily due to a common 13-kD, IgE-binding component.

The present case is that of a nurse working in the intensive care unit of our hospital. In the course of 1 year she experienced three severe anaphylactic events following the ingestion of peaches, nectarines, or plums. She was admitted to our hospital after her third and most severe allergic reaction. Prior to these episodes she had ingested these foods without difficulty. She had a history of mild symptoms of latex

hypersensitivity at work for several years preceding her hospitalization.

We attempted to establish that this patient's severe anaphylactic reactions to stone fruits were related to latex hypersensitivity. This was done by in vitro studies to latex and the involved fruits. The three stone fruits implicated in the patient's episodes of anaphylaxis were also tested by prick skin tests using fresh fruits as the source of the antigen. Cross-reactivity between the involved stone fruits and latex was established by RAST inhibition studies done with the patient's serum and fruit extracts prepared from the fresh fruits.

CASE REPORT

The patient is a 32-year-old married female registered nurse working in our neonatal intensive care unit. On the date of her admission she ingested a fresh plum prior to leaving work. Within 30 minutes she began to experience vaginal pruritus, generalized erythema, facial swelling, shortness of breath, and the sensation of a tightening in her throat. The patient self administered an Epi-Pen without relief. Paramedics were called to the scene and proceeded to administer to the patient two additional subcutaneous epinephrine injections, diphenhydramine, methylprednisolone, aerosolized albuterol, and intravenous epinephrine.

The patient was transferred to our institution after stabilization in the field, and in another hospital's emergency room. Her anaphylactic episode was initially complicated by frequent runs of ventricular premature beats. This was believed to be secondary to the epinephrine administered to her.

Further questioning about her past medical history revealed two prior al-

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lergic reactions to fresh fruits. One year prior to her hospitalization, after eating a peach, she developed generalized pruritus, a sensation of a "thick" tongue, and difficulty in swallowing and breathing. She was driven to a local emergency room and treated aggressively for food-induced anaphylaxis. She has eaten canned peaches since that episode without difficulty. One month prior to her hospitalization she presented to the emergency room of our hospital after eating a fresh nectarine 30 minutes earlier. Her presenting complaints included acute shortness of breath, a swollen tongue, and generalized pruritus. She was treated in the emergency room for anaphylaxis and after four hours discharged to home with an Epi-Pen. Two hours later she developed a recurrence of tightness in her chest and throat and used her Epi-Pen successfully.

Our patient's occupational history was significant for a 5-year history of contact urticaria from latex gloves. To avoid this problem she used non-latex gloves most of the time, but not exclusively. She denied a history of glove-associated contact dermatitis. Her glove allergy progressed to include swollen and itchy eyes when co-workers used "powdered" gloves during the 2 years preceding her hospitalization. She also described mild symptoms of allergic rhinitis during that 2-year period. This was primarily manifested as intermittent sneezing. She did not use any medications to treat these symptoms. Her only episodes of bronchospasm were associated with her fresh fruit ingestion.

The patient had a family history of atopy. She denied a history of inhalant allergies or drug allergies. Her only regular medication was Synthroid for hypothyroidism.

During her hospitalization, laboratory evaluation revealed a normal complete blood cell count and differential. Her blood chemistries and thyroid functions were normal. The serum IgE was 264 IU/mL, which is significantly above the normal upper limit of 100 IU/mL.

MATERIALS AND METHODS

Allergen-Specific IgE

The concentration of food allergen-specific IgE in the patient's serum were determined by the Pharmacia ImmunoCAP method except for the nectarine-specific IgE where the standard RAST was used (Table 1). The presence of latex-specific IgE was evaluated by three different assays: the AlaSTAT latex test by Diagnostic Products Corporation (DPC), the latex RIA by IBT Reference Lab, and the Pharmacia Diagnostics *H. brasiliensis* latex ImmunoCAP (Table 2). The latex antigens in the DPC and Pharmacia tests are both prepared from nonammoniated latex. Three different antigen sources are used in the latex RIA test: an ammoniated latex antigen, a non-ammoniated latex (E-5) protein preparation, and a glove extract antigen.⁸

Skin Prick Testing with Fresh Extracts

Prick testing was done with fresh fruits (Table 3). Fresh fruit was used instead of commercial extracts due to the lack of strongly positive reactions to the fruits by the in vitro specific IgE tests. The prick testing was done by placing a lancet into the fruit and then pricking the patient's forearm. A positive control using histamine produced 22 mm of erythema and an 8-mm wheal. A prick test using saline was negative. One of the authors (SW), who is nona-

topic was used as a nonallergic control for the fresh fruit material tested on the patient. He reacted appropriately to the positive histamine control and did not react to the skin prick tests using the fresh fruits.

RAST Inhibition

Extracts for the RAST inhibition studies (Table 4) were prepared from several fruits (ie, plum, peach, nectarine, and avocado) by extraction at a 1:1 ratio for 45 minutes at room temperature in 0.85% NaCl, 2% polyvinylpyrrolidone, 0.002M EDTA, and 0.01M sodium diethyldithiocarbamate. The resulting suspension was centrifuged at 3,000 rpm for 20 minutes in a RT6000 (Sorvall Instruments). The supernate was filtered through a 0.45-micron filter and the protein concentrations were determined by the method of Lowry.⁹ The RAST inhibition was performed as previously described.¹⁰ Briefly, 50 μ L of a 1/10 dilution of the patient's serum was incubated for one hour with 20 μ L of the extract/inhibitor. Subsequently, a 50- μ L aliquot was added to a microtiter well coated with latex antigen (E-5 from the FDA). This mixture was incubated at room temperature for five hours and then washed. Radiolabelled anti-IgE was added and the counts bound after an overnight incubation were measured.

Table 1. Food Allergen-Specific IgE Testing

Allergen	Result, kU/L	Class Score	Interpretation
Celery	<0.10	0	Negative
Hazelnut	<0.10	0	Negative
Peach	0.27	0/1	Equivocal
Kiwi	<0.10	0	Negative
Cherry	<0.10	0	Negative
Banana	0.14	0/1	Equivocal
White Potato	<0.10	0	Negative
Tomato	<0.10	0	Negative
Melons	<0.10	0	Negative
Avocado	0.73	2	Moderate Positive
Pear	<0.10	0	Negative
Papaya	<0.10	0	Negative
Apple	<0.10	0	Negative
Nectarine	0.27	0/1	Equivocal
Plum	0.35	1	Low positive

Table 2. Latex-Specific IgE

Test Method	Result	Score and Interpretation
AlaSTAT latex test	> 30IU/mL	Class 4, Strongly positive
Latex RIA		
Ammoniated latex antigen	>200U/mL	Class 5, Strongly positive
Nonammoniated latex antigen	>200U/mL	Class 5, Strongly positive
Latex glove antigen	>200U/mL	Class 5, Strongly positive
ImmunoCAP™H. brasiliensis latex	11.0 kU/L	Class 3, High positive

Table 3. Comparison of Skin Tests with Freshly Prepared Extracts Versus In Vitro Specific IgE Tests*

Antigen	Skin Test, erythema/wheal†	In Vitro Specific IgE
Plum	25 mm/8 mm	Low positive
Peach	24 mm/7 mm	Equivocal
Nectarine	20 mm/8 mm	Equivocal
Saline	Negative	
Histamine	22 mm/8 mm	

* All positive skin reactions were preceded by a strong sensation of itch at the site of the skin prick.

† Erythema and wheal measurements were based on the larger of two perpendicular diameters.

Table 4. RAST Inhibition Studies. Food Antigens as Inhibitors of Patient's IgE Binding to Latex*

Inhibitor	Protein, mg/mL	RAST Inhibition (%)
Avocado	2.65	16 (±5)
Peach	0.45	52 (±8)
Plum	0.45	74 (±2)
Nectarine	0.26	20 (±15)
Reference latex antigen	1.80	100 (±0.4)

* The latex antigen on the solid phase was nonammoniated latex protein (E-5) obtained from the FDA. The results above represent the average of two separate RAST Inhibitions.

RESULTS

The data in Table 1 indicate either an undetectable or low level of specific IgE for the foods implicated in the patient's anaphylaxis history. Since the patient's clinical reactions were so dramatic, allergy prick tests to fresh peaches, nectarines, and plums were then performed (Table 3). These were strongly positive. The skin tests results with the fresh fruits appeared to be more sensitive than the in vitro tests for specific IgE.

Because of the patient's history of reactions to latex, the serum was also tested for the presence of latex-specific IgE. The data in Table 2 clearly document that this patient has been immunologically sensitized to the proteins from natural latex. The three different

laboratory tests all demonstrate extremely high concentrations of latex-specific IgE.

The RAST inhibition data in Table 4 demonstrate that a significant portion of the latex-specific IgE can be inhibited by extracts from these fruits. In these inhibition experiments, the plum extract was the most efficient fruit extract tested. Since the fruit extracts were tested at relatively high doses, the possibility of some nonspecific inhibition cannot be ruled out.

DISCUSSION

This patient presented with a clinical history most compatible with anaphylaxis induced by plum ingestion. Unfortunately, a serum tryptase was not ordered during her hospitalization to

confirm that a systemic mast cell event had produced the symptoms described. To determine the etiology of this patient's apparent food allergy, in vitro specific IgE tests were performed with the implicated foods. The results of these tests for the stone fruits were negative or equivocal and not what one would expect based on the life-threatening nature of her episode. Prick testing with freshly prepared extracts, however, documented a strong reactivity and supported the diagnosis of food-induced anaphylaxis in this patient.

When the patient was hospitalized, it was initially considered that her cross-reactivity was a result of an oral allergy syndrome type of reaction, with cross-reactivity to a pollen. This possibility was made less likely by negative in vitro allergen-specific IgE results, done at a later time to several pollens (birch, maple, oak, and ragweed). It was not until the patient's history of minor latex reactions at the workplace was elicited that we considered that the true mechanism involved was latex sensitivity with significant cross reactivity among the stone fruits.

The inability of commercial RAST materials to demonstrate IgE to the fruits involved in three episodes of anaphylaxis led to skin prick testing using fresh fruits in an attempt to document the suspected high level of sensitivity. The patient showed rapid and impressive skin reactivity to the fresh fruit prick tests. Apparently, most of the active allergenic components of the fruits were degraded in the fruit extract materials used to manufacture the in vitro reagents. The low sensitivity of the in vitro tests for these foods may be attributed to the fact that extensive processing of the fruit antigens preceded the coupling to the solid phase. It would be of interest to couple freshly prepared extracts to the test material to determine whether the sensitivity can be improved.

We investigated the relationship between our patient's latex sensitivity and fruit allergy by RAST inhibition testing. Significant inhibition of the latex binding by the patient's IgE was

observed with the fruit extracts prepared. Additional studies, including immunoblots, to pursue the molecular specificity of this inhibition would be of interest.

In our case, the patient demonstrated mild, minimally problematic clinical symptoms to latex for 4 years before she developed significant, life-threatening cross-reactive fruit reactions. There are cases of latex hypersensitivity in the literature where patients present initially with food reactions.¹¹ It is unlikely that our patient's cross-reactive food allergies preceded her clinical latex sensitivity, as she was having mild clinical problems from latex (contact urticaria from gloves) for several years while eating the implicated fresh fruits without systemic symptoms.

This case illustrates the importance of taking a thorough history in patients with anaphylaxis, especially those considered to be in a high risk group for latex sensitivity. If an occupational history had not been performed on this patient, the knowledge of her latex sensitivity might never have been discovered. This could have resulted in an inaccurate assessment of the patient's clinical status and improper, or at the least, incomplete advice on precautionary measures this patient should take in the future.

This case also demonstrates that in cross-reactive reactions to latex and foods, in vitro testing may not be sensitive enough to give an accurate assessment of the patient's sensitivity. Most physicians, when a patient has a history of severe anaphylaxis, will not perform percutaneous testing to avoid the risk of systemic reactivity. Clearly in this case, the in vitro allergen-specific IgE studies did not accurately reflect this patient's extreme fruit sensitivity. Skin testing with fresh natural food appeared to be more sensitive, as has been reported recently by other investigators.¹² Many allergists who use fresh foods to skin test patients do not dilute the material using the method of skin prick testing described in this paper; studies have generally supported this as a safe procedure.¹³

Though this patient had testing without an untoward event, when investigating foods that are cross-reactive with latex where anaphylaxis is a common presentation, it may be preferable initially to dilute the fresh food material. This recommendation can be changed if later it is shown that there is no greater risk to using undiluted testing material in this group of patients.

The study of the natural history of latex sensitivity in healthcare workers is ongoing.^{14,15} Many health care workers can progress directly from asymptomatic to severe systemic reactions. Others can progress from contact dermatitis, to contact urticaria, to anaphylaxis, or rhinoconjunctivitis and/or bronchospasm. Still others may not have initial contact dermatitis and proceed to contact urticaria then respiratory symptoms.

We believe our patient progressed from latex contact urticaria to latex-allergic rhino-conjunctivitis, to cross-reactive latex food anaphylaxis. Her clinical latex allergies progressed over the 2 years leading up to her most severe anaphylactic event from the plum. Her stone fruit sensitivities appeared to progress during the year preceding her hospitalization, though each worsening reaction was to a different cross-reacting fruit.

There are many areas of incomplete knowledge in latex sensitivity. It is currently unknown whether this patient will start to react to additional cross reactive foods or develop life threatening reactions to latex, if she continues to work in a hospital with further exposure to latex. We know that in vitro cross-reactivity between fruits and latex does not predict clinical sensitivity in patients. It is unknown whether a patient who has sensitivity to fruits that are clinically cross-reactive with latex without known latex sensitivity, should be considered at risk for latex sensitivity. The appropriate studies to address these questions have not been performed.

Another issue that has not been resolved is whether a patient with latex sensitivity who has had a severe anaphylactic reaction to a latex cross-re-

active food should be counseled to avoid all potentially reactive foods. This action might prevent morbidity in latex-allergic patients, but would also cause serious dietary restriction. This patient has been advised to avoid all stone fruits and has been given a list of latex cross-reacting foods. She eats bananas and melons regularly without difficulty at this time. She does not eat avocados. She is avoiding introducing any new cross-reactive foods into her diet, as her initial reaction to the stone fruits was anaphylactic in nature. If this patient desires to consume fresh fruits or vegetables that carry with them a potential risk of latex cross-reactivity, she will be skin prick tested using fresh food material prior to ingestion.

Her work environment has been altered so that all personnel in the neonatal intensive care unit wear nonpowdered gloves and she has been supplied non-latex gloves. She is aware that her condition may progress to involve respiratory symptoms from latex exposure. She has been advised to wear a Medic-Alert bracelet indicating latex and fresh fruit allergy. She carries an Epi-Pen.

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