
Case report

Cross-reactivity between raw mushroom and molds in a patient with oral allergy syndrome

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Background: Oral allergy syndrome, resulting from a cross-reactivity between raw fruits and vegetables and a number of pollens, is well described. However, it has never been associated with mold spore sensitivity and mushrooms. We evaluated a patient with oral allergy symptoms to raw, but not cooked, mushrooms, who also had positive skin testing to molds.

Objective: To identify and characterize antigenic cross-reactivity between mushroom and mold spores.

Methods: The patient underwent skin prick testing to molds and mushroom. Proteins from raw and cooked mushrooms were extracted and immunoblot/inhibition assays were performed to evaluate for cross-reacting immunoglobulin E antibodies between mushroom and mold extracts to which the patient was sensitive.

Results: The patient had a positive skin prick test result to raw mushroom and four types of molds. The immunoblot assay revealed immunoglobulin E antibodies directed against similar molecular weight proteins in the raw mushroom and 3 of the 4 molds: *Alternaria tenuis*, *Fusarium vasinfectum*, and *Hormodendrum cladosporioides*. These protein bands on protein electrophoresis were absent in the cooked mushrooms. Inhibition immunoblot of the raw mushroom with the three molds indicated total inhibition of the 43- and 67-kD protein bands.

Conclusions: We report the first case of cross-reactivity between mushroom and molds in a patient with oral allergy syndrome to raw mushroom and allergic rhinitis secondary to molds.

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INTRODUCTION

Oral food allergy syndrome is a common immunoglobulin (Ig)E-mediated hypersensitivity reaction resulting in symptoms such as lip swelling, pharyngeal itching, and laryngeal edema. Cross-reactivity between a number of pollens and foods has been reported, to include apples, celery, and kiwi with birch and mugwort, banana, carrot, and melon with ragweed. Reports of symptoms after eating mushroom have been described, and it is estimated that up to 1% of the population may be affected.¹ We describe the first case report of cross-reactivity between mushroom and molds in an allergic rhinitis patient with oral allergy syndrome to raw mushroom.

The Case

The patient is a 26-year-old female with history of seasonal and perennial allergic rhinitis on immunotherapy to dust mite, dog, tree, and grasses who complains of immediate lip, palate, and throat itching with the ingestion of raw mushroom since she was a teenager. She has not experienced any associated systemic symptoms, such as body pruritus, rash, shortness of breath, wheezing, or light-headedness. The symptoms

do not occur with cooked or canned mushrooms. She has been able to tolerate all other types of foods without any problems. She states that her immunotherapy is effective, but complains of breakthrough symptoms in the fall, which she believes correlate with elevated mold counts. She has no other significant medical problems and has no drug allergies. Her physical examination is unremarkable. Prick skin testing performed on her back within the past year with commercial extracts revealed a 4+ reaction to *Hormodendrum cladosporioides*, 3+ to *Alternaria tenuis*, *Fusarium vasinfectum*, *Helminthosporium interseminatum*, and 1+ to *Epicoccum nigrum*. Prick skin testing to raw and cooked mushroom on the forearm were 4+ and 0, respectively, with histamine control 4+ and a negative normal saline control (criteria for prick scoring: 1+ is erythema smaller than 21 mm in diameter without wheal, 2+ wheal <3 mm with surrounding erythema, 3+ wheal >3 mm with surrounding erythema, 4+ wheal with pseudopods and surrounding erythema).

METHODS

Preparation of Extracts:

Monterey white mushrooms (*Agaricus bisporus*) were obtained from a local grocery store. After cleaning in water, half of the batch was cooked on a plate covered in aluminum foil in an oven at 350° F for 30 minutes. The patient was skin tested on the forearm to raw and cooked mushroom, along with positive histamine and normal saline controls, using the

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prick method. Raw and cooked mushroom were extracted overnight at 4° C, then filtered, dialyzed, lyophilized, and assayed for protein content.

Sodium Dodecyl Sulfate Polyacrylamide Gel Electrophoresis (SDS-PAGE) and Specific IgE Immunoblot of Molds and Mushrooms

PAGE using raw and cooked mushroom extracts and the four molds to which the patient reacted significantly to on skin testing (*H. cladosporioides*, *A. tenuis*, *F. vasinfectum*, and *H. interseminatum*) was performed. The mushroom and mold proteins were separated by molecular weight using SDS-PAGE.

Three of the molds showed some common bands on SDS-PAGE to those in the raw mushroom (*H. cladosporioides*, *A. tenuis*, and *F. vasinfectum*). These were used to perform specific IgE immunoblotting, which was done as previously described for other antigens.² Separated mushroom and mold proteins were transferred to nitrocellulose membranes that were cut into 4- to 5-mm wide strips and washed, blocked, and incubated overnight at room temperature with the patient's serum neat. The immunoblot membrane was subsequently incubated for 6 hours at room temperature in anti-human IgE monoclonal antibody (Sigma Chemical Company, St. Louis, MO) diluted 1:5,000 in 10% fetal bovine serum (FBS). Membrane strips were then incubated overnight in alkaline phosphatase conjugated goat anti-mouse IgG (Chemicon, Temecula, CA) diluted 1:2,000 in 10% FBS. The membrane strips were then developed and banding patterns compared. Protein-bound IgE was visualized with a mixture of nitroblue tetrazolium and 5-bromo-4-chloro-3-indolyl phosphate reagents, which forms an insoluble chromogenic precipitin.

Amplified Inhibition Immunoblot

To check specificity, an inhibition immunoblot was run. A biotin/avidin immunoblot was performed to amplify the binding signal in the inhibition immunoblot. The patient's serum was preincubated with 1 mg of protein of each of the three molds separately (*H. cladosporioides*, *A. tenuis*, and *F. vasinfectum*). Nonpreincubated serum and cord serums were used as controls. The patient's serum samples were assayed for specific IgE against raw mushroom.

Inhibited patient sera and controls were run next. The first steps of the immunoblot corresponded to that outlined before. After incubation with the monoclonal antibodies, the strips were overlaid overnight with anti-mouse IgG biotinylated diluted 1:3,000 in 10% FBS. A 1-hour incubation with avidin alkaline phosphatase diluted 1:1,000 in 10% FBS followed. The immunoblot was developed with nitroblue tetrazolium and 5-bromo-4-chloro-3-indolyl phosphate. As before, the visualized protein-bound IgE was compared with the pattern obtained in the initial blot.

Mushroom Incubation

To evaluate the possibility that 1 of the 3 molds could have been a contaminant on the mushroom, we incubated two mushrooms on two sets of four different agar plates (Sabouraud [Backson Dixon, MD], Sabouraud with gentamycin,

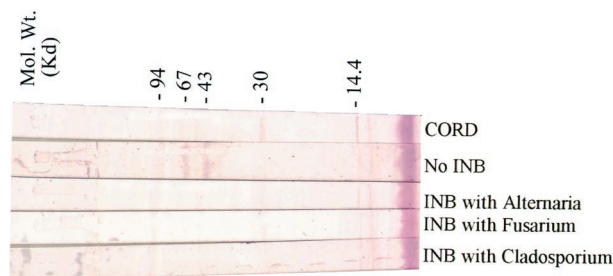


Figure 1. Inhibition immunoblot with *Alternaria*, *Fusarium*, and *Cladosporium*

potato flake agar, and potato flake agar with chloremphenicol and cyclohexamide) for 2 weeks. Each mushroom was from a different Monterey mushroom package.

RESULTS

Specific IgE Immunoblots and Immunoblot Inhibition

Protein bands at the 43- and 67-kD molecular weight range were identified for *A. tenuis*, *F. vasinfectum*, *H. cladosporioides*, and raw mushroom. These were absent in cooked mushroom and the *H. interseminatum* mold. The results of the specific IgE immunoblot with and without inhibition are displayed in Figure 1. As depicted in lanes 1 to 3, these two specific bands were absent with inhibition to the three molds and in the control cord blood sample. One mushroom culture resulted in the growth of a small amount of *Syncephalastrum spp.* The other seven plates did not reveal any growth after a period of 2 weeks.

DISCUSSION

Oral allergy syndrome has been reported to occur in up to 35 to 70% of patients with pollen allergy.² Symptoms develop almost immediately after the mucosa of a sensitized individual comes into contact with certain foods—usually uncooked. It is likely that the hypersensitivity is attributable to the cross-reactivity between pollen and food allergens which is destroyed upon heating. A number of allergens, to include Art v1, Bet v1, profilin, and the nonspecific lipid transfer protein appear to play an important role in oral allergy syndrome.^{3,4} Profilin is a 14-kD molecular weight protein that has been discovered in birch, grasses, mugwort, and a variety of vegetables, such as celery, fennel, coriander, and cumin. For example, cross-reactivity between birch and apple, pear, peach, cherry, kiwi, and celery has been reported. Cross-reactivity has been described between ragweed and melon, watermelon, cantaloupe, and banana as well. The cross-reactivity between latex and bananas, avocados, and kiwi has also been well described in the literature.

Mushrooms are macrofungi with edible fruiting bodies. They belong to the Basidiomycetes class, which also includes puffballs, rusts, smuts, and bracket fungi, whereas molds are classified as fungi imperfecti. It has been suggested that cross-reactivity between the two classes is minimal.⁵ How-

ever, our results suggest that cross-reactivity between the raw mushroom and the molds *H. cladosporioides*, *A. tenuis*, *F. vasinfectum*, and *H. interseminatum* does exist, and may be related to proteins in the 43- and 67-kD molecular weight range. The possibility that cross-contamination with a mold on the mushroom is low, as we grew only a small amount of *Syncephalastrum* from 1 of 8 plates for two mushrooms. A nonspecific inhibition by an aeroallergen other than the mold (ie, dust mite or cat) could possibly have affected our results. Retrospectively, it may have been useful to perform an inhibition immunoblot with an additional aeroallergen, unrelated to the mold family, to rule this out. Radioallergosorbent test inhibition studies could also be performed, but this method is not available in our laboratory at this time.

Our patient describes a long history of allergic rhinitis and symptoms of oral pruritus with raw mushrooms; her skin testing shows significant reactivity to both molds and mushroom. With this in mind, it would be reasonable to assume that immunotherapy could be useful in desensitizing patients with the mushroom allergy syndrome. Kelso et al⁶ reported a case history of a patient with allergic rhinitis to a variety of pollens and oral allergy syndrome to a vast array of fresh fruits and vegetables, who, after having been on immunotherapy to pollens for approximately 1 year, had complete resolution of his symptoms. Asero⁷ showed similar results with a patient with oral hypersensitivity to fresh fennel, cucumber, and melon who was able to eat these without symptoms after immunotherapy to grass, mugwort, and ragweed pollen. We have discussed with the patient the possibility that her symptoms may improve with immunotherapy to the molds, and she has decided to undergo additional immunotherapy to the three selected molds. After 6 weeks of mold immunotherapy, however, the patient became pregnant and asked to stop her

injections. She continues to avoid mushrooms and plans on resuming the treatment after the birth of her baby.

CONCLUSION

We report the first case of oral allergy syndrome with uncooked mushroom in a patient allergic to mold.

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