Clinical Communications

Mushroom allergy: Case series

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Clinical Implications

- To our knowledge, we present the largest mushroom allergy case series. Demonstrated is a high degree of cross-reactivity within the Agaricaceae mushroom family.

TO THE EDITOR:

Mushrooms are the fruiting body of macrofungi mainly belonging to the Basidiomycotina and Ascomycotina divisions. Around 14,000 mushroom species are identified. Mushroom caps release spores, from gills or pores, onto a substrate's surface. Here mycelia, a network of branching hyphae, extract nutrients from the substrate and produce fruiting bodies. Fruiting season and cultivating region vary according to mushroom species. Edible mushrooms are cultivated and consumed, raw and cooked, by many cultures worldwide. Nutritionally, mushrooms contain vitamins and minerals.[1]

Mushrooms are a rare cause of IgE-mediated hypersensitivity reactions. We report 4 cases of IgE-mediated allergy to mushrooms diagnosed in our Allergy Department, one of the largest UK allergy centers, in 2018. Three patients also suffered from other atopic conditions such as asthma, eczema, and/or allergic rhinitis. All patients experienced immediate symptoms on consumption of cooked mushrooms (Table I). One patient (case 4) experienced additional symptoms on cutaneous contact and inhalation (Table I). One patient (case 1) sought emergency treatment. Cofactors including exercise, alcohol, concomitant illness, or analgesia use were not associated with any reactions. All patients described reactions with worsening severity of symptoms after repeated mushroom exposure (Table II). All patients provided convincing histories of multiple, reproducible, and immediate reactions after mushroom allergen exposure and symptom resolution with mushroom allergen avoidance (Table II).

Prick-to-prick testing (PPT) was performed to the raw and cooked caps of 11 mushroom species, except cep and morel, which were rehydrated from dried form by adding boiling water. Using separate kitchenware for each mushroom, cooking was achieved by placing freshly sourced raw mushrooms into boiling water for 10 minutes, with excess water subsequently removed. Skin prick testing (SPT) was also performed to common aeroallergens with commercial extracts (Allergy Therapeutics, Allergopharma GmbH & Co, Reinbek, Germany, and Lofarma, Milan, Italy). Histamine and normal saline were used as positive and negative controls (Allergy Therapeutics), respectively. PPT results to the 11 mushroom species were negative in 4 control volunteers with a history of tolerance to mushrooms. Three of the 4 control volunteers had an atopic background with positive SPT to tree pollen, grass pollen, weed pollen, pet dander, and/or mold.

All patients were positive on PPT to their index species (culpable mushroom species eliciting symptoms), supporting the diagnosis of IgE-mediated mushroom hypersensitivity (Table I). Mushroom challenges were not performed because of ethical and safety concerns considering the high clinical suspicion of mushroom hypersensitivity from clinical history and confirmed mushroom sensitization on skin testing.

In 3 patients, the index mushroom belonged to the Agaricaceae family, the most commonly consumed edible mushroom in Western Europe and North America.[2] These patients cross-reacted to all other Agaricaceae mushrooms tested. This high degree of cross-reactivity suggests the presence of a highly conserved antigen amongst the Agaricaceae family. However, the 3 patients also demonstrated cross-reactivity to mushrooms outside of the Agaricaceae family (Table I). Three patients demonstrated positive PPT results to both the cooked and raw forms of their culpable mushroom species. One patient (case 3) demonstrated a positive PPT result only to the cooked form of their culpable mushroom species. SPT results to fungal aeroallergens were positive in 1 patient (case 1). All patients had positive SPT results to tree pollen, grass pollen, weed pollen, and/or house dust mite (Table I). SPT to 10% and 20% mannitol were negative in all patients.

Hypersensitivity reactions to mushrooms can occur through inhalation, ingestion, and contact. Exercise can act as a cofactor for immediate reactions to mushrooms.[3] Oral allergy syndrome owing to cross-reactivity between mushroom and molds is described.[4] Because of the high mannitol content in mushrooms (2.6 g mannitol per 100 g of mushroom), cross-reactivity between mushrooms and pharmaceutical excipients has been proposed.[5,6] We did not observe cross-reactivity between mushrooms and 10% or 20% mannitol in our described case series. Reactions secondary to mushroom spore exposure including occupational asthma can also occur.[7] Mushroom allergens are poorly characterized, and it is yet to be explored whether the spores, cap, and stalks contain shared or distinctive allergens.

Protein and fiber concentrations in mushrooms are high. Raw mushrooms cooked by being placed in boiling water have been shown to undergo weight reduction and altered concentrations of protein and sugar alcohols such as mannitol.[1] Soaking and cooking is proven to alter mushroom allergen concentrations and may potentially alter mushroom allergen availability. Therefore, in cases with a high suspicion of mushroom hypersensitivity with the negative PPT result to the

TABLE I. Prick-to-prick and skin prick testing results

Patients	Case 1	Case 2	Case 3	Case 4
Age, y	68	36	20	37
Sex	Male	Female	Female	Male
Index species	Shiitake/Chestnut	Chestnut	Button	Shiitake
Route of exposure	Ingestion	Ingestion	Ingestion	Ingestion Inhalation Cutaneous
Clinical symptoms	Angioedema Urticaria Dyspnoea Cough	Abdominal pain Nausea Loose stools Lightheaded	Angioedema Lightheaded Nausea Mouth irritation Throat tightness	Angioedema Throat tightness Eye, lip, and throat irritation Skin irritation

		Division: Basidiomycota Class: Agaricomycetes			
Family, genus	**Species**	**PPT results given in mm wheal diameter (raw form/cooked form)**			
Cantharellaceae, *Cantharellus*	Girolle	0/0	0/4	3/3	0/2
Cantharellaceae, *Craterellus*	Chanterelle	0/0	2/0	0/0	3/0
Boletaceae, *Boletus*	Cep	-/8	-/0	-/0	-/0
Agaricaceae, *Agaricus*	Button	3/6	5/5	0/7	0/2
Agaricaceae, *Agaricus*	Chestnut	3/7	5/7	0/7	2/0
Agaricaceae, *Agaricus*	Flat	3/3	7/3	0/9	0/0
Agaricaceae, *Agaricus*	Portobello	5/4	5/5	0/6	0/0
Marasmiaceae, *Lentinus*	Shiitake	4/7	0/0	3/0	7/10
Tricholomataceae, *Lepista*	Pied bleu	3/8	0/0	0/0	0/0
Pleurotaceae, *Pleurotus*	Oyster	0/0	0/0	0/0	0/4
		Division: Ascomycota Class: Pezizomycetes			
Family, genus	**Species**	**PPT results given in mm wheal diameter (cooked form)**			
Morchellaceae, *Morchella*	Morel	13	0	3	0
Aeroallergen skin prick test results given in mm wheal diameter					
Aspergillus		5	0	0	0
Alternaria		5	0	0	0
Cladosporium		9	0	0	0
Cat dander		0	0	3	0
Dog dander		5	0	0	0
Grass pollen		5	0	5	0
Silver birch		0	0	20	3
Plane pollen		0	3	0	2
Hazel tree		0	2	18	0
Alder tree		0	0	13	0
Mugwort		0	0	0	0
Ambrosia/ragweed		0	0	0	0
Plantain		3	0	5	0
House dust mite		13	2	0	4

PPT, Prick-to-prick testing; -, not performed.

raw culprit mushroom, repeat PPT to soaked and/or cooked mushrooms should be considered. One limitation of our case series is the lack of data on PPT results to soaked uncooked mushrooms in determining the contribution of soaking alone in altering mushroom allergen availability. We were therefore unable to determine whether it is the process of soaking or cooking that appears to increase allergenicity in our case series.

To our knowledge, this is the largest case series of IgE-mediated mushroom allergy. Although there was a high degree of cross-reactivity between the Agaricaceae family, all patients demonstrated cross-reactivity involving additional mushroom families. Patients are required to avoid all mushroom species, unless tolerance is proved. Mushroom allergens would need to be better characterized and *in vitro* investigations performed to better understand patterns of cross-reactivity between mushroom species.

TABLE II. Clinical history related to mushroom exposure

Patients	Case 1	Case 2	Case 3	Case 4
Atopic background	Asthma	Eczema	Allergic rhinitis, eczema	Allergic rhinitis
No. of reproducible reactions on mushroom exposure	3-5 separate reactions on mushroom consumption	5-6 separate reactions on consumption	15-20 separate reactions on mushroom consumption	4-5 separate reactions on mushroom consumption
				Daily to weekly symptoms on inhalation or cutaneous mushroom exposure at work
Symptom progression with repeated mushroom exposure	Initial reactions to mushroom consumption associated with cough	Initial 2 reactions to mushroom consumption associated with gastrointestinal upset occurring within 10-15 min of exposure	Predominately mouth irritation associated with initial 5-10 reactions to mushroom consumption	Mushroom consumption initially associated with lip and throat irritation
	Subsequent reactions associated with cough, dyspnea, and cutaneous symptoms	Subsequent reactions progressed to lightheadedness and palpitations occurring within seconds of exposure requiring smaller amounts of mushroom to elicit symptoms	Subsequent reactions progressed to throat tightness, angioedema, nausea, and lightheadedness	Subsequent reactions associated with angioedema and throat tightness
				Progression on repeated cutaneous and inhalation with more rapid symptom onset and longer time to symptom resolution
				Mushroom inhalation or contact associated with eye and throat itching/irritation
Reaction settings Types of mushroom containing meals associated with reactions Reactions to raw or cooked mushrooms	Home: Home cooked meals including shiitake containing gravy. Reactions to cooked mushrooms only	Restaurants: Mushroom containing Chinese dishes. Work: Mushroom containing soup at work canteen. Reactions to cooked mushrooms only.	Restaurants: Mushroom containing fajitas, sauces, pasta dishes, Thai and oriental dishes, and mixed vegetable dishes Home: Pan fried mushrooms at breakfast, and mushroom containing pizzas. Reactions to cooked and raw mushrooms.	Work: Chef by occupation, since age 14 y, with frequent exposure to mushrooms whole chopped, ground, and minced. Has consumed raw and cooked mushrooms alone and in a variety of dishes at work. Reactions to cooked and raw mushrooms.
Time to symptom onset after mushroom exposure	All reactions occurred within 10-15 min of mushroom exposure	Initial reactions occurred within 10-15 min of mushroom exposure Subsequent reactions occurred within seconds of exposure	All reactions occurred within 5 min of mushroom exposure	Symptomatic within 5 min of mushroom consumption and within seconds/minutes on cutaneous and inhaled exposure
Duration of reactions and medications received	30-45 min	1 to 2 h	30 min to 2 h	30 min to 2 h
	Adrenaline autoinjector and antihistamine	1 h with antihistamine use	30 min with use of adrenaline autoinjector	30 min with antihistamine use

(continued)

TABLE II. *(Continued)*

Patients	Case 1	Case 2	Case 3	Case 4
Mushroom avoidance measures used	Reading food ingredients labeling	Reading food ingredients labeling	Reading food ingredients labeling	Reading food ingredients labeling
	Requests in restaurants for mushrooms to be removed from dishes	Requests in restaurants for mushrooms to be removed from dishes	Requests in restaurants for mushrooms to be removed from dishes	Leaving the kitchen during mushroom cooking
				Handling mushrooms with gloves and masks
				Storing mushrooms in airtight containers
Symptoms and reactions after using mushroom avoidance measures	No further reactions since avoiding mushrooms	No further reactions since avoiding mushrooms	No further reactions since avoiding mushrooms	Fewer symptoms at work with above mushroom avoidance measures put in place at work
		Tolerating the same Chinese restaurant dishes previously eliciting symptoms when mushrooms are removed	Tolerating the same restaurant dishes previously eliciting symptoms when mushrooms are removed	No symptoms when he is on holiday or away from work
Prior tolerance	Tolerated mushroom consumption until 2014	Tolerated mushroom consumption until 2010	Tolerated mushroom consumption until 2009	Tolerated mushroom consumption until 1997
Similar reactions with other foods	No	No	No	No

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No funding was received for this work.

Conflicts of interest: The authors declare that they have no relevant conflicts of interest.

Received for publication April 27, 2019; revised July 29, 2019; accepted for publication August 25, 2019.

Available online ■■

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2213-2198

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https://doi.org/10.1016/j.jaip.2019.08.048

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