







A Case Report of Anaphylaxis Induced by Mushroom (*Hypsizygus marmoreus*) in a Mold-Allergic Patient

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Abstract: Allergic cross-reactivity among different fungal species appears to be widely existing. Fungus-related foods, such as edible mushrooms, mycoprotein, and fermented foods by fungi, can often induce to fungus food allergy syndrome (FFAS) by allergic cross-reactivity with airborne fungi. This article presents a case study of an individual with mold allergy who experienced anaphylaxis after consuming seafood mushrooms. This study indicated that Alt a 1 mediating cross-allergy between *Alternaria alternata* and *Hypsizygus marmoreus*, which has not been documented in the literature concerning the FFAS. Mushrooms tend to induce anaphylaxis in patients with mold-allergy and warrants clinicians' attention.

Keywords: allergens, fungus food allergy syndrome, anaphylaxis

Introduction

Fungi are recognized as a major trigger of type I hypersensitivity reactions, which can lead to severe respiratory and cutaneous allergic diseases.¹ Exposure to fungal allergens may occur through the inhalation of mold spores, direct contact with saprophytic fungi, or ingestion of fungal fruiting bodies (mushrooms).¹ Moreover, Sensitization to fungal allergens via the respiratory tract followed by oral exposure to cross-reactive proteins may lead to diverse food-allergic reactions, potentially resulting in a condition referred to as fungus food allergy syndrome (FFAS).¹

Alternaria alternata is the most prevalent mold allergen.^{2,3} Seafood mushroom (*Hypsizygus marmoreus*) is well known for its nutritional and medicinal properties. It possess a unique sweet and seafood-like flavor with a crunchy texture, making it an increasingly popular culinary ingredient worldwide.⁴ This report describes a case of an individual with mold allergy who developed anaphylaxis after consuming seafood mushrooms.

Case Presentation

A 17-year-old female visited to Department of Allergy, Peking Union Medical College Hospital because of experienced 3 episodes of anaphylaxis within 30 minutes to 1 hour after consuming seafood mushrooms or fried mushrooms (exact type unknown). The clinical syndrome included severe abdominal pain, facial edema, dyspnea, generalized erythema, and occasional vomiting. Additionally, the patient experienced two episodes of facial edema and dyspnea following outdoor exercise while fasting on a rainy day in August of the previous year. Symptoms resolved within 1–3 hours following intravenous corticosteroid and oral antihistamine administration. She had a personal history of cerebral infarction, antiphospholipid syndrome, and right eye blindness with only light perception due to central retinal artery occlusion. Her daily medications included prednisone acetate, aspirin, mycophenolate mofetil, and warfarin.

Prick-by-prick tests with the following eight mushrooms were performed (Figure 1 and Table 1). Serum total IgE and specific IgE levels, determined using the ImmunoCAP technique (Thermo Fisher Scientific Inc., MA, USA), were as follows: total IgE, 54.5 kU/L; m6 (*Alternaria alternata*), 7.94 kUA/L; m3 (*Aspergillus fumigatus*), 1.09 kUA/L; mx2

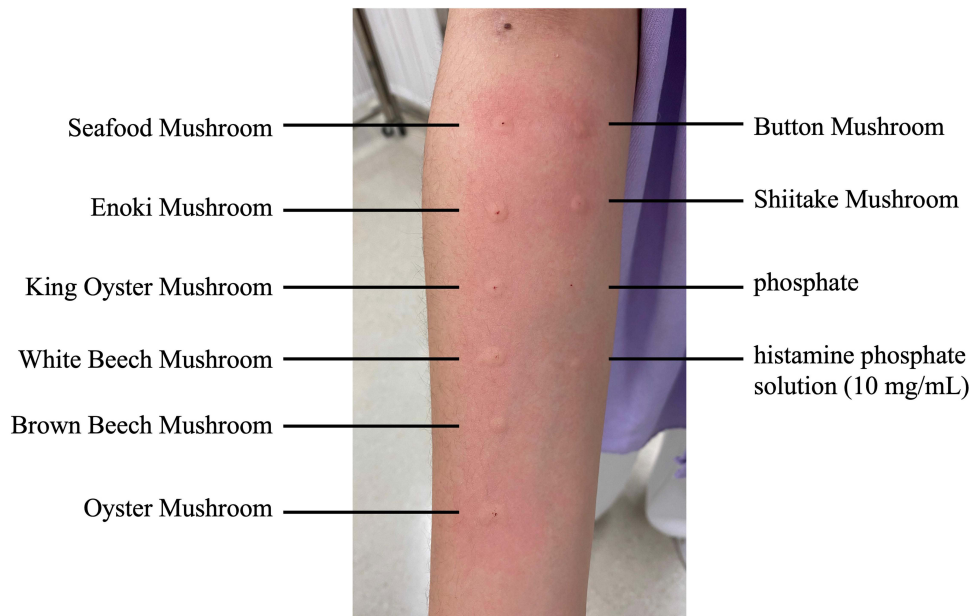


Figure 1 Mushroom Skin Prick Tests.

(m1, m2, m3, m5, m6, m8), 8.81 kUA/L. Additionally, the exhaled nitric oxide (FeNO) level was 20 ppb in January and 54 ppb in August. Based on these findings, a diagnosis of anaphylaxis was established. The patient was advised to avoid consuming mushrooms and to carry an epinephrine auto-injector for potential anaphylaxis recurrence. Over the course of one year, the patient strictly avoided mushroom exposure and experienced no recurrence of symptoms.

To identify allergenic components involved in cross-reactivity between *Alternaria alternata* and mushrooms, the extracts of eight mushrooms were separated using sodium dodecyl sulfate polyacrylamide gel electrophoresis (SDS-PAGE), revealing multiple protein bands with molecular weights ranging from 10 to 180 kDa (Figure 2). Immunoblotting revealed that IgE binding at 12 kDa was observed in *Hypsizygus marmoreus* species (Figure 3A). Additionally, The immunoblot inhibition assay was conducted by pre-incubating the patient’s serum overnight at 4°C with a 100 ug/mL extract of *Alternaria alternata* (Macro-Union Pharmaceutical Ltd., Beijing, China), results shown that *Alternaria alternata* extract markedly inhibited IgE binding to the 12 kDa protein of *Hypsizygus marmoreu* (Figure 3B).

Table 1 The Results of Mushroom Skin Prick Tests

Allergen (Common Name)	Scientific Name	Wheal	Flush
Phosphate		0*0	
Histamine phosphate solution (10 mg/mL)		4*4	15*15
Seafood Mushroom	<i>Hypsizygus marmoreus</i>	5*6	20*25
Enoki Mushroom	<i>Flammulina velutipes</i>	5*5	30*30
King Oyster Mushroom	<i>Pleurotus eryngii</i>	5*4	20*20
White Beech Mushroom	<i>Hypsizygus marmoreus</i>	8*6	20*25
Brown Beech Mushroom	<i>Hypsizygus marmoreus</i>	5*4	20*20
Oyster Mushroom	<i>Pleurotus ostreatus</i>	10*6	30*35
Button Mushroom	<i>Agaricus bisporus</i>	5*4	20*25
Shiitake Mushroom	<i>Lentinula edodes</i>	6*5	30*25

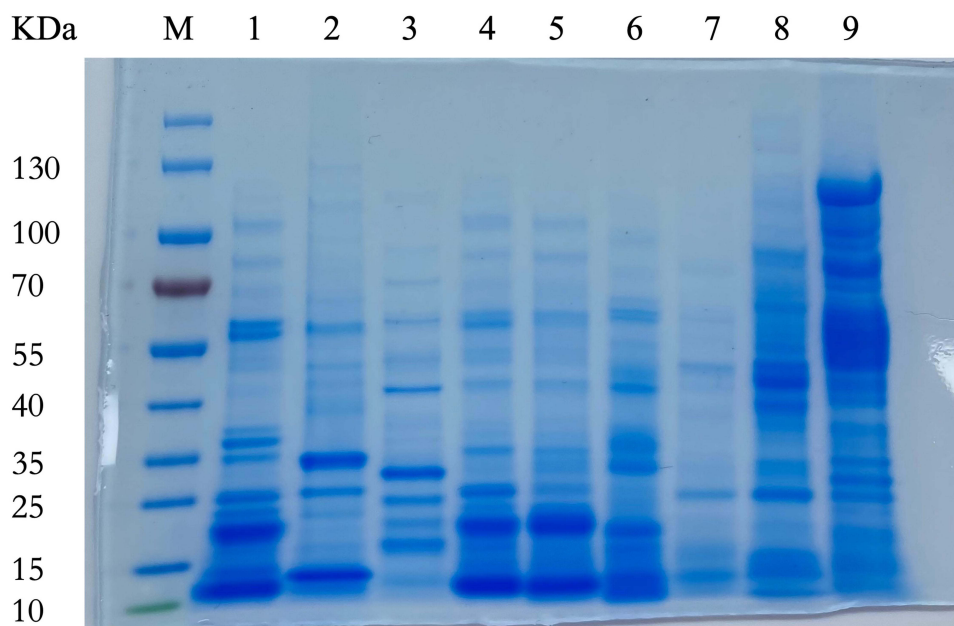


Figure 2 SDS-PAGE results of eight mushroom extracts. M: protein molecular weight marker; line 1–8: Seafood Mushroom, Enoki Mushroom, King Oyster Mushroom, White Beech Mushroom, Brown Beech Mushroom, Oyster Mushroom, Button Mushroom and Shiitake Mushroom; line 9: *Alternaria alternata*.

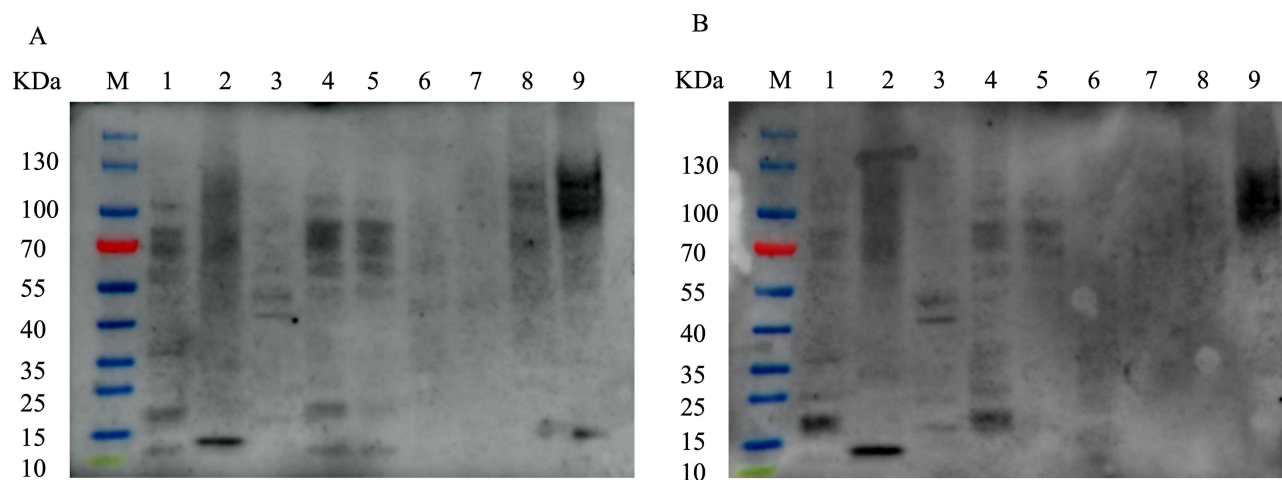


Figure 3 Immunoblot and inhibition analysis of eight mushroom extracts. **(A)** IgE- immunoblotting results of mushroom extracts incubated with the patient's serum. M: molecular weight marker; line 1–8: Seafood Mushroom, Enoki Mushroom, King Oyster Mushroom, White Beech Mushroom, Brown Beech Mushroom, Oyster Mushroom, Button Mushroom and Shiitake Mushroom; line 9: *Alternaria alternata*; **(B)** Immunoblotting inhibition results of the mushroom extract incubated with the patient's serum, which was pre-incubated with *Alternaria alternata* extract. M: molecular weight marker; line 1–8: Seafood Mushroom, Enoki Mushroom, King Oyster Mushroom, White Beech Mushroom, Brown Beech Mushroom, Oyster Mushroom, Button Mushroom and Shiitake Mushroom; line 9: *Alternaria alternata*.

Discussion and Conclusion

In this case, we present a novel finding of a cross-allergy between *Alternaria alternata* and *Hypsizygus marmoreus*. This is the first report of cross-reactivity between mushrooms and the major allergen component Alt a 1 of *Alternaria alternata*. After avoiding mushroom consumption and strenuous activity in humid weather, the patient's symptoms of dyspnea and facial edema did not recur.

Mold spores, hyphae, and/or fungal fruiting bodies can serve as allergens, potentially triggering allergic reactions when they enter the human body through various routes, such as inhalation, ingestion, contact, or injection. *Alternaria alternata* is one of the most significant airborne allergens globally and the most prevalent mold allergen.^{2,3} It contains 17 allergenic components, with the major allergen being Alt a1, which has molecular weights of 15.3 and 16.4 kDa.

Approximately 80% of patients allergic to *Alternaria alternata* are sensitized to Alt a 1.⁵ Allergic reactions following the ingestion of mushrooms are not commonly observed. A limited number of reports indicate that mushroom ingestion can lead to various symptoms, including oral allergy syndrome (OAS), urticaria, abdominal pain, vomiting, dyspnea, and even anaphylaxis.^{6,7} Notably, the severity of such anaphylactic events is further attested to by twenty-seven documented cases or case series, which reported an average Brown grade of 2 (range: 1–3).

Cross-reactivity is an immune-mediated phenomenon in which specific antibodies recognize proteins homologous to the allergen.^{8,9} Generally, the closer the taxonomic relationship between species, the greater the structural and immunological similarity of the allergens, thereby increasing the likelihood of cross-reactivity.¹⁰ Following sensitization to mold allergens via the respiratory tract, cross-reactive proteins may trigger various food allergic reactions, resulting in FFAS.¹ Dauby reported the first case of OAS in a patient allergic to molds after consuming raw mushrooms (*Agaricus bisporus*) identifying heat-sensitive cross-reactive proteins with molecular weights of 43 kDa and 67 kDa.¹¹ While, our findings indicate that cross-reactivity between *Hypsizygus marmoreus* and *Alternaria alternata* may also occur and appears to be associated with Alt a 1. At present, this remains speculative. There is currently no absolute proof, and the precise mechanism remains to be elucidated. What's more, no allergic sensitivity testing was conducted with cooked mushrooms in this patient. The heat stability of the relevant allergens and the effect of cooking on their allergenic potential remain unknown.

In conclusion, patients with mold allergy should be counseled to exercise caution regarding the ingestion of mushrooms. Clinicians should consider it as potential allergens and can utilize the prick-to-prick testing method with the fresh mushroom to confirm suspected allergy.¹

Declaration of Patient Consent

Informed consent for publication was obtained from the patient at the age of 18. The patient understood that her personal information had not been published. Studies involving human participants were reviewed and approved by the Peking Union Medical College Hospital Review Board. The case details are open access and can be browsed without institutional approval.

Author Contributions

All authors contributed significantly to this work through involvement in one or more of the following areas: conception and design, study execution, acquisition of data, analysis and interpretation. Each author participated in drafting the manuscript or critically revising it for intellectual content. All authors provided final approval of the version submitted for publication, agreed upon the target journal, and accept responsibility for all facets of the work.

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Disclosure

The author(s) report no conflicts of interest in this work.

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