

Cross-Reactivity Between Molds and Mushrooms

Helena Ferreira, MD,¹ Marta Alves, MD,¹ Fernando Pineda, PhD,² Cristina Ferreira, MD,¹
Armandina Silva, MD,¹ Alberto Costa, MD,¹ and Águeda Matos, MD¹

Fungi are considered one of the most common allergens responsible for type I allergies. This allergic response can be triggered by inhalation of mold spores, skin contact, or ingestion of mushrooms. There are some case reports in the literature advocating an association between sensitization to mold spores and systemic reactions caused by ingestion of mushrooms. However, this association is scarce and not completely explored. The authors report a case of a 12-year-old girl, with symptoms compatible with allergic rhinitis not previously studied, who developed an anaphylactic reaction after ingestion of mushrooms (*Macrolepiota procera*). The skin prick test revealed sensitivity to *Cladosporium herbarum* and the prick-to-prick test with the *Parasol* mushroom (*M. procera*) was positive, which highlighted the possibility of cross-reactivity between molds and mushrooms, hypothesis that was suggested by Western blot and inhibition test.

Keywords: *Cladosporium herbarum*, cross-reactivity, fungi, *Macrolepiota procera*, molds, mushrooms

Introduction

FOOD ALLERGY, defined as an immune-mediated adverse reaction to food allergens, is an increasing problem in pediatric population, affecting 6% to 8% of children.^{1,2} The most common food allergens in pediatric populations include cow milk, eggs, peanuts, tree nuts, soy, and wheat, although other less common food allergens exist, such as mushrooms.¹

Mushrooms may rarely be responsible for symptoms of food allergy in sensitized patients. Fungal allergens can cause allergic reactions by inhalation of mold spores, skin contact with saprophytic species, or ingestion of mushrooms.³ Although respiratory allergy is induced mainly by mold spores, allergic symptoms after ingestion commonly can also occur through other structures of the mushroom.⁴ There are 1.5 million species of fungi in the world, but the most allergenic species are molds belonging to the genera *Alternaria*, *Aspergillus*, and *Cladosporium*.⁵ The overall extent of allergy of mushrooms is not known, varying from 1% in food allergy to 10% to 30% in pollen and mold allergy.⁶

Previous reports suggest an association between sensitization to mold spores and systemic reactions, namely anaphylaxis, caused by ingestion of mushrooms, although this relationship is not well understood.^{4,7-9}

The authors report a case of an adolescent with sensitivity to molds (*Cladosporium herbarum*) who developed an

anaphylactic reaction after ingestion of *Parasol* mushroom (*Macrolepiota procera*).

Case Report

A 12-year-old girl was referred to the pediatric clinic because of anaphylaxis after ingestion of scrambled eggs with mushrooms. Almost 1 h after the meal, the adolescent suffered an episode of generalized urticaria, tachycardia, dyspnea, and tachypnea, symptoms that motivated admission in the emergency department, where ephinephrine and steroids were administrated with success.

When asked about personal medical background, symptoms compatible with rhinitis were identified, but she was not previously subjected to any allergy diagnostic tests or treatments. No other allergy diseases were identified, namely food allergy or atopic dermatitis. The adolescent denied any previous allergic reaction to the compounds of the meal responsible for the anaphylaxis. No family history of allergy was identified.

The laboratory tests realized in the pediatric clinic revealed an elevation of total immunoglobulin E (IgE) and a positive multiple aeroallergen screen and the specific IgE test was negative for the egg. The skin prick test (SPT) was positive for *Lepidoglyphus destructor* (5 mm), *C. herbarum* (7 mm), *Canis familiaris* (7 mm), nuts (6 mm), and walnuts (5 mm). The prick-to-prick tests to *Psalliota campestris* and

¹Department of Pediatrics, Hospital da Senhora da Oliveira, Guimarães, Portugal.

²Diater Laboratorios, Madrid, Spain.

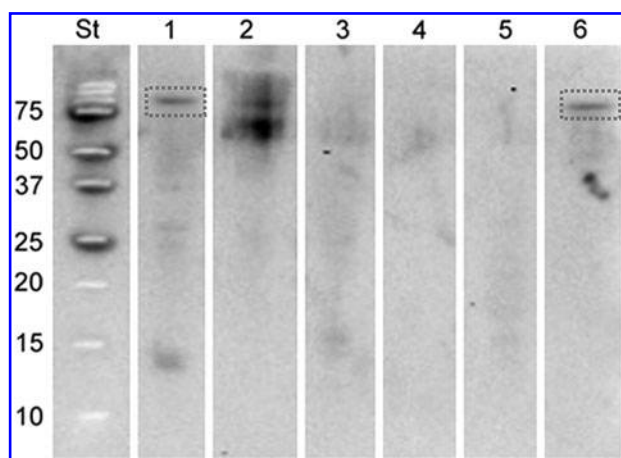


FIG. 1. Western blot test with allergens identified in the skin prick test: 1, mushroom *Macrolepiota procera*; 2, *Canis familiaris*; 3, *Lepidoglyphus destructor*; 4, nuts; 5, walnuts; 6, *Cladosporium herbarum*.

Tricholome equestre mushrooms were negative, but they were positive for different portions of *Parasol* mushroom (*M. procera*), confirming that the anaphylaxis was caused by this type of mushroom.

Because of the suspicion of a cross-reactive mechanism underlying the anaphylaxis, other investigation tests were undertaken to demonstrate a cross-reactivity between the aeroallergen *C. herbarum* and the food allergen *M. procera*. Mushroom extracts and sera from our patient were collected and analyzed by Western blot, which showed a protein with a molecular weight between 80 and 100 kDa in both allergens (Fig. 1). The inhibition assays confirmed that those proteins are related (Fig. 2). There were no similarities between the mushroom and the other allergens identified by the SPT. These results point to an existence of a cross-reactivity allergen between the aeroallergen *C. herbarum* and the food allergen *M. procera*.

The adolescent was encouraged to avoid any contact with the allergens identified, and since then, no other anaphylactic reactions happened.

Discussion

There are about 1.5 million species of fungi in the world, of which only 70,000 have been fully described.¹⁰ Of the 1.5 million species of fungi, it was estimated that 140,000 species produce fruiting bodies of sufficient size and suitable structure to be considered macrofungi, also known as mushrooms.¹¹ The overall extent of mushroom allergy is unknown. Although mold allergy could be as prevalent as 10% to 30% of all allergic population, food allergy is very slight, being responsible for about 1% of all mushroom allergies.⁶ Despite being rare, mushroom allergy is being recognized as a food allergen responsible for severe systemic allergic reactions.^{4,9,11,12} As demonstrated in the reported case, severe allergic reactions can occur even in people who have never had a previous allergic reaction. In fact, our patient had no previous symptoms of food allergy, even when mushrooms were eaten. One possible explanation for this late reaction is her sensitivity to mold spores, namely *C. herbarum*, which predisposed the adolescent to a cross-reaction with the mushroom

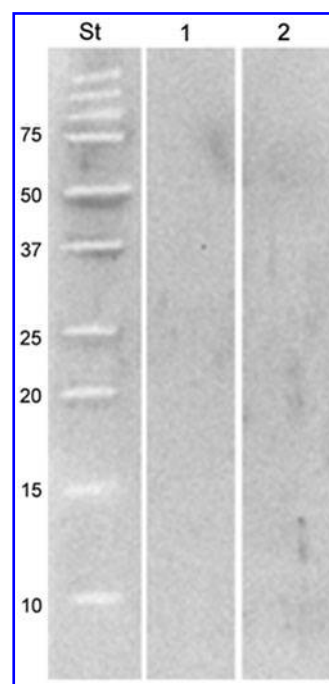


FIG. 2. Inhibition test against *C. herbarum*. 1, mushroom *M. procera*; 2, *C. herbarum*.

M. procera. Actually, although there is increasing evidence of severe allergic reactions to mushrooms, clinical reports defending a cross-reactive mechanism underlying the association between aeroallergens and ingestion of mushroom symptoms are still scarce.^{4,7-9} In fact, knowledge of allergenic proteins that cause cross-reactions between molds and food is limited, which justifies the necessity of reporting this rare case to make possible a better understanding of the underlying immunological mechanisms.

The authors reported a case of an adolescent with respiratory symptoms compatible with allergic rhinitis caused by mold aeroallergens (*C. herbarum*), who suffered an anaphylactic reaction after ingestion of mushrooms (*M. procera*). Suspicion of cross-reaction between the mold aeroallergen and food allergen was confirmed by Western blot and inhibition test. The Western blot test identified a protein with similar weight in both *C. herbarum* and *M. procera*, and the inhibition test with antibodies against *C. herbarum* inhibited both allergens, which confirmed the cross-reactivity between them.

Our findings suggest a cross-reactivity between the aeroallergen *C. herbarum* and the mushroom *M. procera*, which can lead to severe food allergic reaction in mold-sensitized people. This highlights the importance of the recognition and knowledge of this possible relationship between aeroallergens and food allergens, looking for an effective avoidance and prevention of severe systemic reactions.

Consent

The authors state that they have obtained parental permission to publish this case report.

Author Disclosure Statement

No competing financial interests exist.

References

1. Tatachar P, Kumar S. Food-induced anaphylaxis and oral allergy syndrome. *Pediatr Rev* 2008; 29:e23–e27.
2. Sicherer SH, Sampson HA. Food allergy: epidemiology, pathogenesis, diagnosis, and treatment. *J Allergy Clin Immunol* 2014; 133:291–307; quiz 308.
3. Mari A, Schneider P, Wally V, et al. Sensitization to fungi: epidemiology, comparative skin tests, and IgE reactivity of fungal extracts. *Clin Exp Allergy* 2003; 33:1429–1438.
4. Helbling A, Bonadies N, Brander KA, et al. *Boletus edulis*: a digestion-resistant allergen may be relevant for food allergy. *Clin Exp Allergy* 2002; 32:771–775.
5. Crameri R, Weichel M, Fluckiger S, et al. Fungal allergies: a yet unsolved problem. *Chem Immunol Allergy* 2006; 91: 121–133.
6. Koivikko A, Savolainen J. Mushroom allergy. *Allergy* 1988; 43:1–10.
7. Herrera-Mozo I, Ferrer B, Luis Rodriguez-Sanchez J, et al. Description of a novel panallergen of cross-reactivity between moulds and foods. *Immunol Invest* 2006; 35:181–197.
8. Herrera I, Moneo I, Caballero ML, et al. Food allergy to spinach and mushroom. *Allergy* 2002; 57:261–262.
9. Gabriel MF, Gonzalez-Delgado P, Postigo I, et al. From respiratory sensitization to food allergy: anaphylactic reaction after ingestion of mushrooms (*Agaricus bisporus*). *Med Mycol Case Rep* 2015; 8:14–16.
10. Horner WE, Helbling A, Salvaggio JE, et al. Fungal allergens. *Clin Microbiol Rev* 1995; 8:161–179.
11. Torricelli R, Johansson SG, Wuthrich B. Ingestive and inhalative allergy to the mushroom *Boletus edulis*. *Allergy* 1997; 52:747–751.
12. Toda T, Yamaguchi M, Nakase Y., et al. A case of anaphylactic reaction following matsutake mushroom ingestion: demonstration of histamine release reaction of basophils. *Allergol Int* 2010; 59:417–419.

Address correspondence to:

Helena Ferreira, MD

Department of Pediatrics

Hospital da Senhora da Oliveira

Rua dos cutileiros, Creixomil

Guimarães 4835–044

Portugal

E-mail: helena-of@hotmail.com

Received for publication January 24, 2017; accepted after revision April 19, 2017.