



## Rare Ingestive Food Allergy to Mushroom *Boletus badius*

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Food allergy can occasionally be severe and difficult to diagnose, especially in the event of a rare allergen. We describe here a case of severe immediate-type anaphylaxis to bay bolete mushroom, which demonstrates the value of basophil activation testing (BAT) in the diagnosis of rare food allergies in which there is a lack of specific IgE (sIgE) and high risk of oral challenge testing.

### CASE REPORT

A 25-year-old woman experienced a systemic anaphylactic reaction in September 2014 after eating a mushroom omelette made of eggs, bay bolete mushrooms that she had collected, parsley, salt and pepper. Thirty minutes after eating, the patient developed generalized urticaria, pruritus of the oral and nasal mucous membranes, dysphagia, feeling of obstruction in the throat and dyspnoea (anaphylaxis grade 2–3 according to Ring and Messmer's classification). The symptoms ceased after administration of an anti-allergic treatment. Other foods that the patient had consumed that day had been eaten again and tolerated since the incident.

Cofactors, such as infections, alcohol consumption or physical exertion, were not present. The patient had a history of grass-pollen induced allergic rhinoconjunctivitis status post-immunotherapy (sublingual immunotherapy; SLIT for a 3-year course) with only minor symptoms at the time of examination, atopic eczema, allergy to animal hair (horse, cat and dog epithelia), oral allergy syndrome to walnuts, and immediate-type hypersensitivity to ciprofloxacin.

Skin prick test (SPT) to aeroallergens, spices and nutritive allergens, as well as prick-to-prick tests to the mushroom omelette using the same ingredients as the original omelette, bay bolete (*Boletus badius*, Fig. S1a<sup>1</sup>), porcino mushroom (*Boletus edulis*, Fig. S1b<sup>1</sup>), shiitake, portobello, horse, chanterelle and oyster mushrooms were carried out one year after the anaphylactic reaction. Total IgE and sIgE were also performed. Furthermore, a flow cytometric basophil activation test (BAT) measuring CD63 expression (Flow CAST<sup>®</sup>) with bay bolete was carried out. Frozen and pestled *Boletus badius* diluted with stimulation buffer (equally weighted) was used at a 1:25 and 1:100 dilution. Higher concentrations of bay bolete could not be tested, due to the mucous texture of the mushroom and buffer mixture. A healthy control was also tested with the BAT. An immunoblot with the bay bolete extract was performed. Ultimately, unblinded oral challenge tests (OCT) using increasing dosages with the fully cooked omelette seasoned with salt, pepper and parsley (without *Boletus badius*), with chanterelle and brown wood mushrooms as well as *Boletus edulis* was conducted outside of the grass pollen season. Oral challenge with the suspected mushroom as well as the skin test positive mushrooms was omitted due to the severity of the original anaphylactic reaction.

### RESULTS

SPT was positive to pollen from tree mix I and II, hazel, alder, birch, olive, grass mix, herbs, mugwort and ash, other aeroallergens, such as *Cladosporium*, *Aspergillus*, dog, cat, rabbit and guinea pig epithelia, as well as spices, such as garlic, cilantro, curry, and other nutritive allergens, such as hazelnut, apple, walnut, almond, barley flour, and hops. Other perennial and seasonal aeroallergens, spices (native), foods, nuts (native) and flour, brain and yeast types (native) tested negative. Prick-to-prick test was positive to the homemade mushroom omelette, raw bay bolete, shiitake, oyster and portobello mushroom. Egg, parsley, porcino, brown wood and chanterelle mushrooms tested negative in the PPT. Detailed results are shown in **Table I**. Total IgE level was 341 IU/ml and sIgE was positive to timothy (>100 KU/l) and birch tree pollen (11.1 KU/l), cat epithelium (23 KU/l) and hazelnut (1.24 KU/l). sIgE was negative to other food allergens and pollen, including rPhl p7, rPhl p12 and rBet v2, as well as to CCD MUX F3 Bromelain. Flow cytometric BAT showed a positive reaction to bay boletus (bay boletus concentration 1:25 % CD63 91.75%; concentration 1:100 % CD63 86.13%; see Table SI<sup>1</sup>). A healthy control tested negative to the concentrations used. Immunoblotting analysis indicated the specific bands at 25, 35, 50, 60 and 150 kDa (Fig. S2<sup>1</sup>). In the OCT, the homemade omelette without bay bolete, and the sautéed brown wood, chanterelle and porcino mushrooms were tolerated.

Based on the patient's history of a grade 2–3 anaphylaxis according to Ring and Messmer after ingestion of a bay bolete omelette and the findings in the laboratory and skin tests as well as the OCT, we confirmed the

**Table I. Skin prick test results (diameter of wheals) of tested mushroom allergens. Positive result defined as wheal diameter  $\geq 3$  mm (bold)**

| Allergens               | Wheal size, mm |
|-------------------------|----------------|
| Mushrooms (native)      |                |
| Shiitake mushroom       | <b>3</b>       |
| Oyster mushroom         | <b>3</b>       |
| <i>Boletus edulis</i>   | 0              |
| Chanterelle mushroom    | 1              |
| <i>Boletus badius</i>   | <b>7</b>       |
| Brown wood mushroom     | 1              |
| Portobello mushroom     | <b>4</b>       |
| Mixed mushroom omelette | <b>4</b>       |
| Controls                |                |
| Histamine               | <b>6</b>       |
| NaCl 0.9%               | 0              |

<sup>1</sup><https://doi.org/10.2340/00015555-2721>

diagnosis of an immediate-type ingestive allergy to bay bolete mushroom. Furthermore, the patient was diagnosed with a type 1 sensitization to shiitake, oyster and portobello mushrooms. Controls showed negative mushroom SPT.

## DISCUSSION

The bay bolete (*Boletus badius*) is a pored mushroom that is common in spruce and pine forests across Europe and North America and belongs to the Boletaceae family and the Agaricomycetes class. It is a popular edible mushroom in Europe, and is being increasingly eaten in many restaurants and homes. Despite the growing popularity of *Boletus badius* and a small number of cases reported on inhalative, ingestive and contact allergy to various other edible mushrooms, in particular to the related porcino mushroom (*Boletus edulis*) (1–3), so far no case of immediate-type anaphylaxis after ingestion of *Boletus badius* has been reported in the literature.

Inhalative and ingestive food allergy to *Boletus edulis* and its spores causing symptoms, such as oral allergy syndrome, asthma and severe systemic anaphylaxis, were first described by Torricelli et al. (4) in 1997 using skin and serological testing of the mushroom. Our patient tolerated the challenge with *Boletus edulis*. A clinically relevant cross-sensitivity between the Basidiomycetes could not be proven in our patient, but this cannot be generalized for other individual cases.

Furthermore, it has been shown that *Boletus edulis* can cause an IgE-mediated food allergy due to a digestion-resistant protein at 75 kDa (5). Our immunoblot showed no reactivity to a 75 kDa protein, but to proteins at 25, 35, 50, 60 and 150 kDa. Roncarolo et al. (2) first described profilin, a cross-reactive protein as potential cause

in one case of systemic anaphylactic symptoms after ingestion of *Boletus edulis*, but our patient did not have sIgE to rPhl p12 and rBet v2. Proteins responsible for respiratory allergy to *Boletus edulis* also differ from the ones described here (6). Further research is therefore needed to allow for precise allergen characterization of *Boletus badius*.

A number of recent studies have demonstrated flow cytometric BAT to be more accurate and sensitive than SPT and sIgE in the evaluation of various food allergies (7). In our case, with no sIgE available, flow cytometric BAT allowed for identification of *Boletus badius* as a rare allergen source and assessment of the severity of the reaction without risking potentially severe allergic reactions induced by challenge testing.

## REFERENCES

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