

A Pediatric Case of Anaphylaxis Caused by Matsutake Mushroom (*Tricholoma Matsutake*) Ingestion

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ABSTRACT

Background: Anaphylaxis is one of the severest forms of allergic diseases. Some kinds of mushroom are known as causative allergens in food anaphylaxis. Matsutake mushroom (*Tricholoma matsutake*) is a typical edible mushroom available in autumn in Japan. We encountered an 8-year-old Japanese girl who developed anaphylaxis after ingesting matsutake mushrooms.

Methods: We studied the case in detail, by measuring specific IgE antibodies and conducting skin tests, to confirm the diagnosis. We also detected seven cytokines and chemical mediators in the blood in order to study the pathophysiology of the anaphylaxis.

Results: We diagnosed anaphylaxis caused by ingestion of matsutake mushrooms based on the following. A skin prick test showed a positive reaction to matsutake mushroom, and specific IgE antibody for matsutake mushroom extract was detected in the patient's serum by fluorometric ELISA. Blood levels of chemical mediators including histamine, ECP, tryptase and cytokines such as IL-6, IL-5 and IL-10 but not IFN- γ also increased significantly during the allergic episode.

Conclusions: We demonstrated that chemical mediators including histamine, tryptase and ECP as well as several cytokines were involved significantly during the episode of anaphylaxis. In addition, eosinophils as well as mast cells played significant roles in the anaphylaxis. Furthermore, CD4⁺CD25⁺ T regulatory cells that released IL-10 were likely activated during the anaphylaxis. Matsutake mushroom should be considered as a causative allergen in food anaphylaxis.

KEY WORDS

anaphylaxis, chemical mediators, cytokines, IgE, matsutake mushroom

INTRODUCTION

Matsutake mushroom (*Tricholoma matsutake*) is a typical edible mushroom, available in autumn, in Japan. Some kinds of mushroom spores are known as inhalation allergens and contact allergens that cause allergic reactions like bronchial asthma,¹ and contact dermatitis.² There has to date only been a small number of reports describing food anaphylaxis or anaphylactoid reaction caused by mushrooms, in particular by matsutake ingestion.³⁻⁷ In food allergies, it is very important to confirm the causative food in order to prevent relapses.

We report here on a young Japanese girl who de-

veloped anaphylaxis due to matsutake mushroom, which was confirmed by the results of a skin prick test and fluorometric ELISA, and the measuring of a specific IgE antibody for matsutake mushroom. We also detected significant increases in the blood levels of chemical mediators and cytokines during the episode.

CLINICAL SUMMARY

CASE

An 8-year-old Japanese girl was admitted to our hospital because of anaphylaxis, swelling of her face and dyspnea, which set on one hour after having a dinner containing matsutake mushrooms at a Japanese res-

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taurant. She has been suffering from bronchial asthma, atopic dermatitis, and pollinosis to Japanese cedar pollen. In her family her sister has atopic dermatitis, and her father has a peach allergy and Japanese cedar pollen allergy.

One hour after having approximately 14 g of matsutake mushrooms, the patient experienced nausea, swelling of her face and dyspnea. She was therefore transferred to our emergency unit by ambulance. On arrival, she had difficulty breathing and severe stridor. Angioedema of her face, eyelids and fingers, and skin erythema of her extremities were also evident. Based on such a typical clinical course and symptoms, we diagnosed an anaphylactic reaction due to food allergy, most likely matsutake mushroom. The patient was treated with subcutaneous epinephrine at a dose of 0.005 mg/kg, 200 mg of intravenous hydrocortisone, and inhalation therapy of dexamethasone and epinephrine. We also treated her with intravenous prednisolone at a daily dose of 2 mg/kg for two days. With these treatments, her symptoms gradually improved and she was discharged on the fourth hospital day without any sequelae.

Her laboratory data on admission revealed no abnormalities, except for mild elevation of white blood cell count (12,000/ μ L), and serum IgE level (504 IU/mL), (PRIST, Sweden Diagnostic, Uppsala, Sweden). CAP System FEIA RAST (Sweden Diagnostic) data showed positivity against the following environmental and inhaled allergens: house dust mite, class 6, and Japanese cedar pollen, class 3. Further studies were carried out and we diagnosed anaphylaxis due to matsutake mushroom.

None of the allergen extracts, including matsutake mushroom, used in this study were commercially available. Therefore, we prepared our own extracts. Of each mushroom, 14 g of flesh was homogenized. Next, 350 mL of 0.1 M phosphate buffered saline (PBS, pH7.4) containing 700 μ L of protease inhibitor cocktail (Sigma, St. Louis, MI, USA) was added and the resultant substance was homogenized and mixed for 30 minutes at 4°C. The mixture was then centrifuged at 2000 g for 10 minutes. The supernatants were collected, dialyzed and filtered. These were then stored as original allergens at -80°C until used.

Fresh-food prick tests using the prick + prick technique^{8,9} were performed with a matsutake mushroom and other mushrooms. All skin prick tests (SPTs) were performed with steel lancets. Responses were read at 15 minutes and graded according to the standard method recommended by the European Academy of Allergy and Clinical Immunology.¹⁰ Grade + is defined as 25% of the area of wheal induced by the positive histamine control (10 mg/mL). Grade ++ is defined as 50%, Grade +++ as 100% and Grade ++++ as 200%. Grade + or larger is considered positive provided the response to the test solution is also larger than that to the negative control.

The specific IgE antibody levels against each mushroom such as matsutake mushroom in the patient and healthy control sera were measured by the method of fluorometric enzyme-linked immunosorbent assay (ELISA) as previously reported.¹¹ The fluorescence intensity was read as fluorescence units (FU) with a microplate reader (Spectroan FL-2575, Wako Laboratory Co, Tokyo, Japan), whereby 1 FU corresponds to 1 pM 4-MU/well.

We measured the serum levels of seven cytokines using the Cytometric Bead Array (BD PharMingen, San Diego, CA, USA) and Human IL-6 ELISA Ready-SET (eBioscience, San Diego, CA, USA) at different time points (days 1, 2, and 11).¹² We also measured chemical mediators, such as eosinophilic cationic protein (ECP) by Uni-CAP ECP¹² (Sweden Diagnostic, normal range, < 5.0 μ g/L), tryptase by Uni-CAP Tryptase¹³ (Sweden Diagnostic, normal range, 2.1 to 9.0 μ g/L) and plasma histamine by histamine radioimmunoassay kit¹² (Immunotech Ltd., Paris, France, normal range, 0.74 to 1.54 nMol/L).

PATHOLOGICAL FINDINGS

The SPT was performed using a fresh matsutake mushroom and other mushrooms including shiitake (*Lentinus edodes*), shimejidake (*Lyophyllum shimeji*), maitake (*Grifola frondosa*), enokidake (*Flammulina velutipes*), and nameko (*Pholiota nameko*). The results were positive grade ++ with the matsutake mushroom and grade + with enokidake at 15 minutes. However, the result was still positive with matsutake at 30 minutes.

The specific IgE antibody levels against matsutake and other mushrooms in the patient's serum were measured by fluorometric ELISA as FU, which resulted in a score of 2.0 FU against matsutake mushroom and zero against other mushrooms. In healthy control serum we did not detect any IgE antibodies against any mushrooms tested (Fig. 1).

We measured the peripheral blood levels of seven cytokines and chemical mediators including ECP, tryptase and plasma histamine. Histamine, ECP, tryptase, IL-5, IL-6, and IL-10 were significantly higher at the time of anaphylaxis. After treatment with glucocorticoids, these levels went down immediately (Fig. 2). However, the IL-2, IL-4, IFN- γ , and TNF- α levels did not change during the episode. Surprisingly, at day 11, ECP and tryptase levels increased again and the IL-6 level was still high.

The results of SPT and specific IgE antibody testing were definitive in diagnosing this case as anaphylaxis to matsutake mushroom. The patient was therefore instructed to avoid eating matsutake mushrooms in order to prevent recurrence.

DISCUSSION

Food anaphylaxis or anaphylactoid reaction caused by matsutake mushrooms is rare even in Japan, with

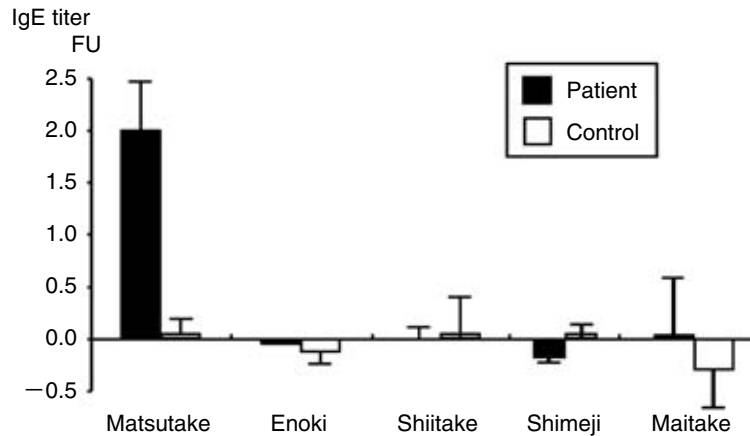


Fig. 1 Specific IgE antibodies for mushrooms in sera by fluorometric ELISA. Bars represent standard deviations of the triplicate data. Solid columns, patient's serum; open columns, negative control serum. 2.0 fluorescent units (FU), as an IgE titer to matsutake antigen, were detected in the patient's serum, but negative to any other kinds of mushrooms or the control serum.

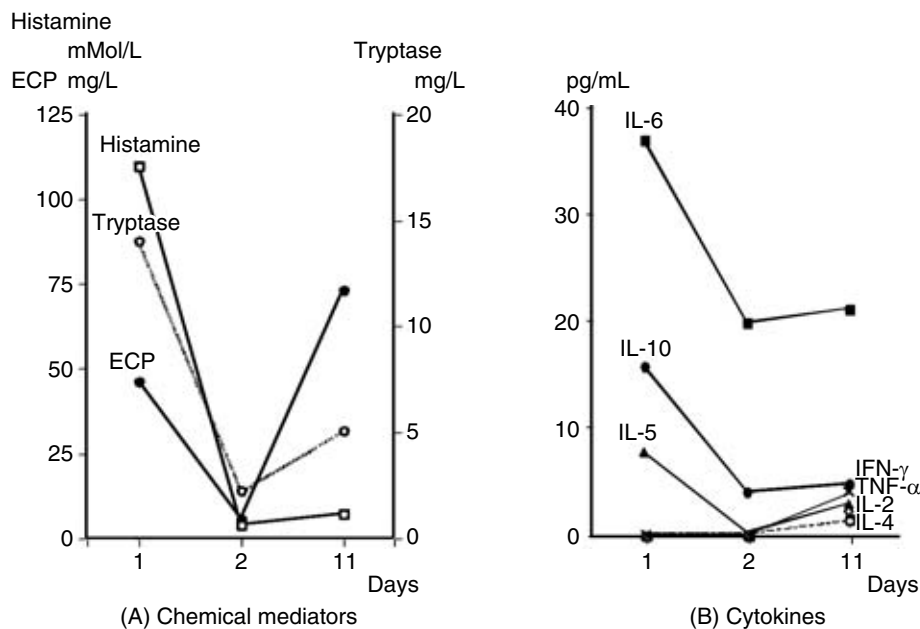


Fig. 2 Blood levels of the chemical mediators in the patient. (A) Histamine in plasma, ECP and tryptase in sera are shown. (B) IFN- γ , TNF- α , IL-2, IL-4, IL-5, IL-6, IL-10 in sera are shown. Day 1 represents the day of the anaphylaxis episode. The normal ranges of all seven cytokines in the serum are <0.1 pg/mL.

few studies published about food anaphylactic reaction caused by the mushroom.³⁻⁷ With food allergies, especially anaphylactic reactions, it is important to confirm the causative food or the component of food to prevent recurrence.

There have to date been five case reports about

anaphylactic reactions caused by matsutake mushrooms.³⁻⁷ Three cases were anaphylaxis, one case was anaphylactoid reaction after matsutake mushroom ingestion, and one case was food-dependent exercise-induced anaphylaxis due to matsutake mushroom ingestion followed by exercise. In four of

the five cases, positive reactions to skin tests or provocation tests were obtained, but the specific IgE antibody for matsutake mushroom was not detected in any case.

In the present case, the diagnosis of anaphylactic reaction was not difficult, because of its typical clinical course and symptoms. Based on the dinner menu of the patient before the episode, we suspected matsutake mushroom as a causative allergen. Therefore, the patient was screened and tested for all food allergens in the menu, and showed a positive reaction to matsutake mushroom on the SPT. The patient's serum specific IgE antibody levels against matsutake mushroom extract, measured by fluorometric ELISA, strongly suggested that her anaphylaxis was caused by matsutake mushroom.

The skin prick + prick test was thus useful to confirm the food allergen of the anaphylaxis. We considered a positive reaction against enokidake in SPT to be a non-specific reaction in our case because the patient had already eaten enokidake without any problems, and specific IgE antibody to enokidake was not detected. However, we could not rule out completely the possibility of cross-reactive epitopes between matsutake and enokidake. Measuring the specific IgE antibody by fluorometric ELISA was also useful to determine the causative food allergens, in comparison with CAP-RAST as reported previously.³⁻⁷

Furthermore, in our case higher blood levels of chemical mediators and cytokines including histamine, tryptase, ECP, IL-5, and IL-6¹⁴ suggested that the immune balance tended to be T helper 2 (Th2) dominant and mast cells and eosinophils were activated at the time of the anaphylaxis. A similar finding was observed in patients with acute allergic reactions in an emergency study.¹⁵ Interestingly, immunosuppressive/regulatory cytokine IL-10¹⁶ also increased during the episode in our case. It is now known that CD4⁺CD25⁺ T regulatory cells release IL-10.¹⁷ Our data suggest that T regulatory cells¹⁶ are also activated to maintain an immunological balance such as between Th2 to Th1 cells and to inhibit inflammation during anaphylaxis. These responses were immediately suppressed by the administration of glucocorticoids. In addition, re-elevation of ECP and tryptase were shown on day 11. This might not be explained simply by a rebound phenomenon. Rather, the activations of eosinophils and mast cells might persist longer during anaphylaxis than first thought. Further studies are necessary to clarify this.

In conclusion, an SPT and specific IgE antibody testing using fluorometric ELISA were useful methods to determine that the causative food in a school girl who developed anaphylaxis was matsutake mushroom. We also demonstrated that many kinds of chemical mediators and cytokines were involved in the anaphylaxis. We believe that this case has shed further light on the understanding of the pathophysiology of food anaphylaxis.

ology of food anaphylaxis.

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