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CASE REPORT

A Case of Anaphylaxis Caused by Major Royal Jelly Protein 3 of Royal Jelly and Its Cross-Reactivity with Honeycomb

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Purpose: Royal jelly and honeycomb are commonly consumed in China, and anaphylaxis caused by ingestion of royal jelly is rare. To date, there is no report of anaphylaxis after ingestion of royal jelly in China. Its cross-reactivity with honeycomb is still unclear.

Case Report: A 56-year-old Chinese female experienced two episodes of anaphylaxis within 1 hour after ingestion of royal jelly within one month. After avoiding royal jelly and other bee products, no anaphylactic reaction occurred again. The skin prick test and basophil activation test showed positive reactivity to royal jelly and honeycomb. In immunoblotting and immunoblotting inhibition tests, a 60 kDa protein was recognized in royal jelly and cross-reactivity with honeycomb. The mass spectrometry data revealed that the 62kDa protein belongs to major royal jelly protein 3.

Conclusion: Our data suggest that major royal jelly protein 3 of royal jelly is a main allergen that induces anaphylaxis and cross-reactivity with honeycomb. Therefore, the patient was allergic to royal jelly to avoid other bee products.

Keywords: royal jelly, honeycomb, major royal jelly protein 3, anaphylaxis

Introduction

Royal jelly is secretions from the hypopharyngeal and mandibular glands of worker bees.[1,2] Honeycombs are dwelling places where honeybees live and breed. It is thought to improve health status and promote immune function, so it is widely consumed in China as a health tonic or alternative medicine. Although a few cases[3–5] of anaphylaxis due to royal jelly were reported in Japan, this is the first Chinese report of royal jelly-induced anaphylaxis. Many proteins contained in royal jelly can induce anaphylaxis. We identified 62 kDa major royal protein 3 which was the main allergen in our cases and cross-reactivity with honeycomb by several experiments.

Case Presentation

A 56-year-old Chinese female visited the Department of Allergy, Peking Union Medical College Hospital because he experienced two episodes of anaphylaxis within 1 hour after ingestion of food within one month. The clinical syndrome included urticaria, pruritus, laryngeal edema, chest tightness, hypotension, and collapse.

Skin prick tests were performed with crude extracts of royal jelly, honey, and honeycomb from our laboratory. Skin prick tests revealed that royal jelly (4 mmx4

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mm wheal and 37 mm x 16 mm erythematous area) and honeycomb (3 mmx3 mm wheal and 36 mmx 20mm erythematous area) positive, honey was negative. The total IgE was 438kU/L, specific IgE antibodies to i1 (0.19kUA/L), i3 (0.03kUA/L), i208 (0.01kUA/L) and i209 (0.01kUA/L) were below 0.35kUA/L by ImmunoCAP (Thermofisher, USA).

The basophil activation test was analysed by the Flow CAST kit (BÜHLMANN, Schönenbuch, Switzerland), as shown in Figure 1. According to the manufacturer' s protocol, coincubation with whole peripheral blood and crude extract of royal jelly and honeycomb respectively (0.25 μg /mL, 0.5 μg /mL and 1 μg /mL), CCR3+CD63+cells were defined as activated basophils that were determined by flow cytometry (Partec, Germany) according to the manufacturer's protocol. For the crude extract of RJ, 4.53%, 6.9%, and 9.58% of activated basophils were detected, 0.64%, 1.18%, and 2.81% of activated basophils were detected when the crude extract of honeycomb as a stimulant.

The proteins of bee venom, royal jelly and honeycomb were separated by sodium dodecyl sulfate-polyacrylamide gel electrophoresis and immunoblotting analysis of royal jelly extract (Figure 2) revealed serum IgE antibodies reacting only 60 kDa protein. For honeycomb extract, serum IgE antibodies bound to 70 kDa protein and 60 kDa protein. No immunoreactive bands were detected in bee venom extract. In the immunoblotting inhibition test, honeycomb extract showed complete inhibition of IgE, which can bind to royal jelly 60 kDa protein, and the same inhibition occurred when royal jelly extract was an inhibitor.

We extracted 60 kDa and 70 kDa proteins from polyacrylamide gels and analyzed them by high-performance liquid chromatography–mass spectrometry (HPLC–MS) method. According to the mass spectrometry data, 60 kDa protein had 18 unique peptide and 34 unique spectrum of 62kDa major royal jelly protein 3, 70 kDa protein had 4 unique peptide and 4 unique spectrum of 70kDa major royal jelly protein 5.

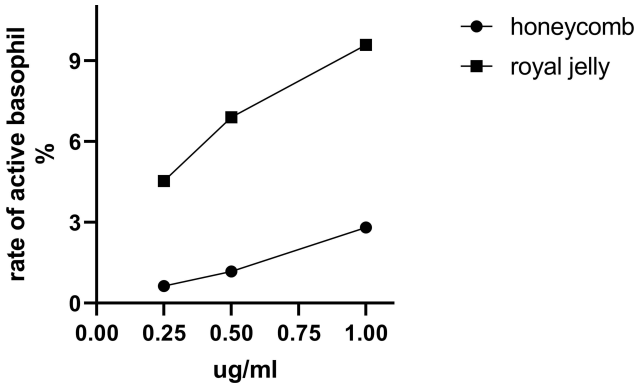

Figure 1 The results of basophil activation test.

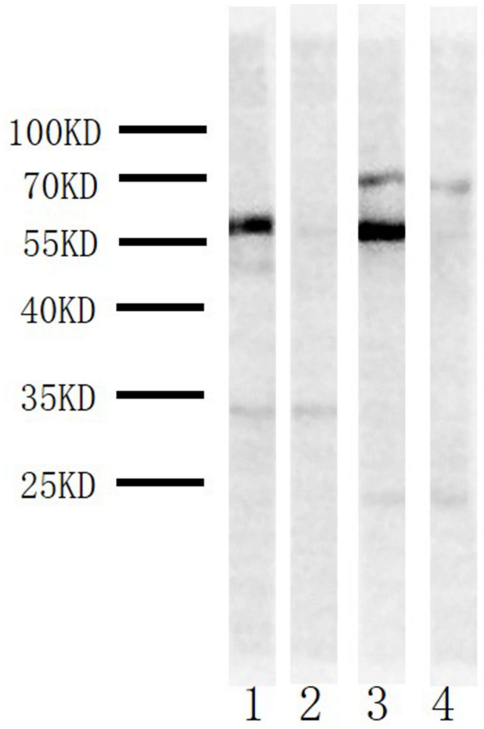

Figure 2 Immunoblot and inhibition analysis. The serum-specific IgE bind to royal jelly and honeycomb. Line 1: royal jelly, serum; Line 2: royal jelly, serum co-incubated with honeycomb; Line 3: honeycomb, serum; Line 4: honeycomb, serum co-incubated with royal jelly.

Discussion and Conclusion

In our study, we identified that the culprit protein of royal jelly is 62 kDa-major royal jelly protein 3 and showed cross-reactivity with other bee product honeycombs. The skin prick test and basophil activation test confirmed allergens in vitro and in vivo, respectively, and basophils showed higher reactivity to royal jelly extract than honeycomb. Serum IgE antibody specific binding to 60 kDa protein was simultaneously discovered in royal jelly and honeycomb, band of 70 kDa protein only shown in honeycomb which is weaker than band of 60 kDa protein. In the immunoblotting inhibition test, serum IgE-binding to 60 kDa protein was inhibited by both extractions, which suggested that there were some similar proteins in royal jelly and honeycomb. According to mass spectrometry data, there was a very higher protein identification

probability to identify 62 kDa MRJP 3 and 70 kDa MRJP 5,[7] and to have more than 60% similarity amino acid sequences through alignment.

Bee products are favored by customers because of their health benefits in China. Food-induced anaphylaxis caused by ingestion of royal jelly is rare, and a few cases[6,8] have been reported overseas, most in Japan. This is the first case of anaphylaxis reported in China. In 2011, Mizutani et al[4] reported a case of anaphylaxis caused by ingestion of royal jelly and deduced that major royal jelly protein3[7] is a possible allergen. Our study proved that various bee product could induce anaphylaxis and that it has nothing to do with bee venom, allergenic cross-reactivity between royal jelly and honeycomb was found. Therefore, patients who are allergic to royal jelly should avoid other bee products.

Declaration of Patient Consent

The authors obtained informed consent for publication from the patient. The patient understands her personal information will not be published. The case required institutional approval to publish the case details and was reviewed and approved by the Ethical Committee of Peking Union Medical College.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors report no conflicts of interest in this work.

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