

学位論文の要旨

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学位論文名 Tropomyosin Is a Minor but Distinct Allergen in Patients with Shrimp Allergies in Japan

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論文内容の要旨

INTRODUCTION

Shellfish including crustaceans are the most frequent causes of IgE-mediated allergic reactions to food, which range from mild oral allergy syndrome (OAS) to systemic anaphylaxis. Food allergies caused by crustaceans are known to cross-react among the crustacean species, such as shrimp and crab.

The first major allergen identified in crustaceans is tropomyosin, a muscle protein of shrimp (Pen a 1). Following studies have demonstrated that more than 70% of the patients with shrimp allergy have IgE to tropomyosin. Tropomyosin was identified as a major allergen in other crustaceans such as lobster *Homarus americanus* (Hom a 1), crab *Charybdis feriatus* (Cha f 1), and mollusks such as squid *Todarodes pacificus* (Tod p 1), oyster *Crassostrea gigas* (Cra g1) and snail *Turbo cornutus* (Tur c 1). In addition, many reports present tropomyosin to be an important component of immune and allergic reactions in other invertebrates such as house dust mites *Dermatophagoides farinae* (Der f 10), and *Dermatophagoides pteronyssinus* (Der p 10). Tropomyosins from house dust mites have a high sequence homology to shellfish tropomyosins, and cross-reactivity between tropomyosins from shellfish and house dust mites has also been well documented. These findings provided evidence for cross-reactivity in allergen-specific IgE test among crustaceans, mollusks, insects, arachnids and even nematodes.

Allergen-specific IgE test is widely used in the diagnosis of immediate-type food allergies because this test can be performed with ease for identifying causative allergens in patients with food allergies. It is noteworthy that the *in vitro* immunoassay system usually employs crude extracts of foodstuffs to detect the food-specific IgE; thus, the sensitivity and specificity of the test is not always satisfactory in identifying patients with true food allergies. The purpose of this study was to evaluate the specificity and sensitivity of tropomyosin-specific IgE test in the diagnosis of shrimp allergies in Japan.

MATERIALS AND METHODS

We enrolled 27 patients with shrimp allergy, whose diagnosis had been given according to the history of immediate allergic symptoms after ingesting shrimp and a positive reaction in the skin prick test using shrimp extract. The patients were classified into 3 groups according to their clinical symptoms: group I, 11 patients with OAS after ingesting shrimp; group II, 13 patients with urticaria without OAS; and group III, 3 patients with other symptoms without OAS and urticaria. 5 patients with atopic dermatitis who showed positive shrimp-specific IgE test but had no allergic history after shrimp ingestion were enrolled as controls. Serum allergen-specific IgE (shrimp, crab, squid, tropomyosin, Der p 1 and Der p 10) were detected by the CAP-fluorescent-enzyme immunoassays. Values greater than 0.35 Ua/ml were considered to be detectable and those greater than 0.70 Ua/ml were considered to be positive. Tropomyosin-specific IgE was confirmed by IgE immunoblotting and involvement of carbohydrate moieties in the IgE-binding was examined by periodate treatment. The levels of allergen-specific IgE were compared using Pearson correlation test and *P*-value with < 0.05 was considered to be significant.

This study protocol was approved by the Research Ethics Committee of Shimane University and written informed consent was obtained from all subjects.

RESULTS AND DISCUSSION

Tropomyosin-specific IgE was detected in 13 (48.1%) and positive in 10 (37%) of the 27 patients with shrimp allergy, whereas shrimp-specific IgE was detected in 21 (77.8%) and positive in 20 (74%) of these 27 patients. Out of the 13 patients with detectable levels of tropomyosin-specific IgE, 7 were confirmed to have tropomyosin-specific IgE by immunoblotting analysis, whereas no IgE-binding was seen in the 5 patients with atopic dermatitis, indicating high specificity of the tropomyosin-specific IgE test. Tropomyosin-specific IgE was positive in 54.5% in group I, 23% in group II, and 33.3% in group III, suggesting that tropomyosin-specific

IgE is well associated with OAS. Cross-reactivity between crustaceans and mollusks is also clearly explained by the sensitization to tropomyosin because the 9 patients with positive tropomyosin-specific test showed positive IgE against crab and squid. Level of tropomyosin-specific IgE was well correlated with that of Der p 10-specific IgE but not with that of Der p 1-specific IgE indicating that shrimp tropomyosin-specific IgE strongly cross-reacts to Der p 10. The positivity rate of tropomyosin-specific IgE test in the present study (37%) was far lower than those obtained in the previous studies: Positivity rates of 57% in the USA, 89% in Spain, and 71.4% in Brazil, respectively. In other studies, involving more than 100 Italian adult patients with shrimp allergy and 38 Singaporean patients with shrimp allergy, only 41% and 15.8%, respectively, were found to be tropomyosin-reactive when investigated by immunoblot analysis and tropomyosin-specific IgE measurements. These findings indicate that sensitization to tropomyosin may be dependent on the geographic area, and low sensitization rates are observed in the areas located near the sea, such as Japan, Italy and Singapore.

CONCLUSION

In this study, we demonstrated that tropomyosin is a minor but distinct allergen in the patients with shrimp allergy in Japan, because, in spite of its low sensitivity (37%), the specificity of the tropomyosin-specific IgE test (80%) was much higher than that of the shrimp-specific IgE test (0%). In addition, the findings via immunoblotting were well compatible with the results of tropomyosin-specific IgE tests, supporting that tropomyosin is a highly specific allergen for shrimp allergy.