

Five cases of food allergy to vegetable worm (*Cordyceps sinensis*) showing cross-reactivity with silkworm pupae

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Vegetable worm (caterpillar fungus, *Cordyceps sinensis*) is a traditional medicine in East Asia including China, Korea and Japan. It has recently enjoyed popularity as a food, with health benefits including respiratory-

Vegetable worm can induce food allergy, which is mediated by both IgE and non-IgE mechanisms, and cross react with silkworm pupae.

system protection, improved kidney function and enhanced immunity (1, 2). Despite reports of various allergic reactions to silkworm pupae, the hosts of the vegetable worm (3, 4), allergic reactions to vegetable worm are unknown. Here, we report five cases in which allergic symptoms developed following vegetable worm ingestion.

The three women and two men had clinical histories of recurrent and immediate-onset allergic symptoms after consuming vegetable worm. All had associated allergic diseases such as respiratory allergy, chronic urticaria and food allergy. Generalized urticaria was the most common symptom. Conjunctivitis, rhinorrhoea, nasal obstruction, cough and dyspnea symptoms were presented in one patient. Symptoms developed 30–120 min after vegetable worm ingestion. All patients had been orally exposed to the suspected allergen, e.g. by drinking tea containing vegetable worm, rather than by skin contact or inhalation. Furthermore, after ingesting silkworm pupae, all experienced allergic symptoms similar to those produced by the vegetable worm (Table 1).

Based on their clinical histories, the patients were diagnosed as being allergic

to vegetable worm and silkworm pupae. Cross-reactivity between the two was concluded because of antigenic components likely shared during growth of the vegetable worm on silkworm pupae. The patients refused food-challenge testing using the suspected allergens because they had already demonstrated recurrent allergic symptoms after ingesting either one. For immunological studies, vegetable worm and silkworm pupa extracts were prepared in our laboratory as described previously (5), and skin prick tests that was performed using them showed positive responses. Serum-specific IgE antibodies to both extracts were detected by enzyme-linked immunosorbent assay (ELISA). The positive cut-off value for high level of serum-specific IgE antibody was defined as the mean $\pm$ 3 standard deviation of the absorbance value from 32 nonatopic healthy controls. Accordingly, four of the five patients showed high levels of a serum-specific IgE to vegetable worm and silkworm pupa extracts (Fig. 1A). Competitive ELISA inhibition tests to evaluate cross-reactivity between the vegetable worm and silkworm pupae showed significant dose-dependent inhibitions in response to either antigen

Table 1 Clinical features of the study subjects

Patient	Sex	Age (years)	Associated allergic disease	Total IgE (IU/ml)	Evoked symptoms to		Skin prick test	
					Vegetable worm	Pupa	Vegetable worm	Pupa
P1	F	22	AR	76	Rhinitis, conjunctivitis, angio-oedema	Rhinitis, conjunctivitis, asthma	3+	3+
P2	M	40	AR	821	Urticaria	Urticaria	NA	2+
P3	F	33	CU	89	Urticaria	Urticaria	NA	3+
P4	M	39	BA, AR	760	Pruritus	Urticaria	NA	3+
P5	F	24	AR, FA (seafood)	105	Urticaria	Urticaria, angio-oedema	3+	3+

Skin prick test results presented as the wheal size ratio of the allergen to histamine (1 mg/ml).

M, male; F, female; BA, bronchial asthma; AR, allergic rhinitis; CU, chronic urticaria; FA, food allergy; NA, not available.

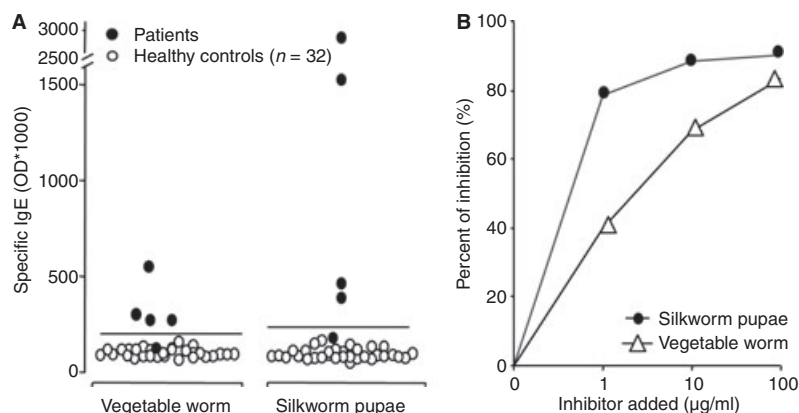


Figure 1 (A) Specific IgE bindings to vegetable worm and silkworm pupae as measured by ELISA using sera from patients (●) or healthy controls (○). Horizontal bars indicate the positive cut-off value determined from the mean $\pm$ 3 SD of the absorbance values of normal controls. (B) IgE-ELISA inhibition result of silkworm pupa-coated wells with serial additions of silkworm pupae (●) and vegetable worm (Δ) extracts. Four of the five patients had high serum-specific IgE. ELISA inhibition test using sera of these four patients showed significant inhibitions following the addition of vegetable worm or silkworm pupae extract in a dose-dependent manner.

(Fig. 1B), suggesting that each was capable of inducing IgE-mediated food allergies in exposed adults. Concurrent symptoms were because of cross-reactivity between the two allergens in sensitized subjects. A non-IgE-mediated mechanism was also noted in one patient.

With increasing interest in health care, vegetable worm is widely used in the preparation of tea or food as well as in traditional drugs in the Asian countries. Silkworm pupae are nutrient-rich with a high protein content, but they are known to cause food allergies, sometimes inducing severe anaphylactic reactions (4). Nevertheless, there has been

no report of food allergy to vegetable worm. We first demonstrated five cases developed IgE- and non-IgE-mediated allergic reactions after ingesting vegetable worm. Moreover, cross-allergenicity with silkworm pupae was confirmed in all cases. These findings highlight the need for caution in the consumption of vegetable worm by individuals with known allergies to silkworm pupae.

In conclusion, we report five cases of food allergy caused by vegetable worm ingestion, which exhibits cross-reactivity with silkworm pupae and is mediated by both IgE and non-IgE mechanisms.

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