Case Series

Late Onset of Acute Urticaria after Bee Stings

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Abstract
Here we report the cases of five patients with a late onset of acute urticaria after a bee sting. The ages of the five Japanese patients ranged from 33 to 86 years (median: 61). All patients had no history of an allergic reaction to bee stings. The onset of urticaria was 6–14 days (median: 10) after a bee sting. Although four of the patients did not describe experiencing a bee sting at their presentation, the subsequent examination detected anti-bee-specific IgE antibodies. So, we think a history of a bee sting should thus be part of the medical interview sheet for patients with acute urticaria, and an examination of IgE for bees may help prevent a severe bee-related anaphylactic reaction in the future.

Introduction
Acute urticaria is caused by various factors including foods, chemical agents, infections, and insect bites [1]. When a clinician is trying to determine the cause of a patient’s urticaria,
it is important to ask about the patient’s food intake, possible chemical agent exposure, and symptoms that may indicate an infection. Here, we report the cases of five patients with acute urticaria. Although four of the patients did not describe experiencing a bee sting at their presentation, the subsequent examination detected anti-bee-specific IgE antibodies.

Case Presentation

The ages of the five Japanese patients ranged from 33 to 86 years (median: 61). Three were male and two were female (table 1). All patients had no history of an allergic reaction to bee stings. The onset of urticaria was 6–14 days (median: 10) after a bee sting. All five patients presented at our hospital in the 3-month period from July to September. The patients had no symptoms suggesting general anaphylaxes other than skin eruption. Only one patient had a local skin reaction at the sting site, 2 days before the onset of urticaria.

The type of bee involved was paper wasp in three cases and yellow jacket in two cases. The number of sting sites was one in all cases. Venom-specific IgEs for paper wasp, yellow jacket and honeybee were examined in four cases. The three patients stung by a paper wasp were positive for paper wasp and yellow jacket but not for honeybee. One patient stung by a yellow jacket was positive for only yellow jacket. The urticaria was well controlled by a type 2 antihistamine antagonist in three patients; the other two patients required oral prednisone. Urticaria did not recur after the withdrawal of medications.

Discussion

Although most anaphylactic reactions caused by insect stings occur shortly after the sting, they occasionally have a delayed onset [1]. In the study by the American Academy of Allergy and Immunology Committee, there were only three patients in whom the reaction started more than 48 h after the sting in the recorded 2,219 patients with allergic reaction by insect sting [2]. So, it may be difficult to suspect bee sting as cause of allergic reaction if it shows a delayed onset. Four of our five patients took no notice of a relationship between their acute urticaria and their bee sting history. Importantly, an examination detected IgE antibodies for bees in all four examined cases with a cross-reactivity between paper wasp and yellow jacket in three of them. A history of a bee sting should thus be part of the medical interview sheet for patients with acute urticaria, especially in the summer to early autumn. If a patient has incurred a bee sting within 2 weeks prior to his or her presentation, an examination of IgE for bees may help prevent a severe bee-related anaphylactic reaction in the future. Moreover, individuals who are stung by a bee should be advised that their antibodies for bees should be examined if a general or local eruption with pruritus occurs within approximately 2 weeks after the sting.

A question is raised regarding the mechanism of late onset of acute urticaria in our cases. Reisman and Livingston [1] reported 10 patients with allergic reactions 1–2 weeks after bee stings. Four of them had serum sickness-type reactions with joint swelling, arthralgia and urticaria, three had only generalized urticaria, two had severe symptoms of anaphylaxis with urticaria and the remaining one had a large local swelling. All patients had venom-
specific IgE and four had serum venom-specific IgG which relates to serum sickness reaction. However, sickness-type reactions were observed only in one of four patients with venom-specific IgG. Reisman and Livingston [1] suggested that the late reaction ranges from typical anaphylaxis to serum sickness, probably related to simulation of IgE antibodies and subsequent reaction with persisting venom antigen. Although the mechanism of late onset of acute urticaria without rapid reaction is unclear, our cases might show delayed urticaria caused by a reaction of the bee antigen-specific IgE antibody to the antigens remaining in the body, after the first sensitization. It suggests that bee antigens can remain for 1–2 weeks in the body after a bee sting, because the bee antigen-specific IgE antibody cannot react without bee antigens. Further examination is required to clarify the late-onset reaction by bee stings.

**Statement of Ethics**

The patient gave written informed consent.

**Disclosure Statement**

The authors declare no conflicts of interest.

**References**

1. Reisman RE, Livingston A: Late-onset allergic reactions, including serum sickness, after insect stings. J Allergy Clin Immunol 1989;84:331–337.
2. Lockey RF, Turkeltaub PC, Baird-Warren IA, et al: The Hymenoptera venom study I, 1979–1982: demographics and history-sting data. J Allergy Clin Immunol 1988;82:370–381.

**Table 1. The five cases**

| Case | Age, years | Sex | Time of onset after sting, days | Type of bee | Venom-specific IgE, class |
|------|------------|-----|---------------------------------|-------------|--------------------------|
| 1    | 33         | F   | 12                              | YJ          | 3 (YJ)                   |
| 2    | 61         | M   | 14                              | PW          | 2 (PW), 1 (YJ)           |
| 3    | 62         | M   | 13                              | YJ          | not examined             |
| 4    | 49         | F   | 6                               | PW          | 5 (PW), 2 (YJ)           |
| 5    | 86         | M   | 10                              | PW          | 3 (PW), 2 (YJ)           |

PW = Paper wasp; YJ = yellow jacket. IgE class levels: <0.34 U/ml = 0; 0.35–0.69 = 1; 0.70–3.49 = 2; 3.50–17.49 = 4; 50.0–99.9 = 5; ≥100 = 6.