Ladybug Hypersensitivity: Report of a Case and Review of Literature

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ABSTRACT

For years, allergists have known that inhalant allergens arise from insects such as flies, beetles, moths, cockroaches, and mites. Now, it is becoming evident that the Asian ladybeetle Harmonia axyridis *possibly should be added to this list. Several cases have been reported recently in the literature describing patients suffering from allergic respiratory symptoms including rhinitis, conjunctivitis, and asthma related to exposure to ladybugs. These patients reveal positive skin-prick testing with ladybug extract and immunoglobulin E immunoblotting with the sera showing at least two distinct allergenic proteins. This species infests homes in very large numbers in the fall and winter months and stay there in a hibernation-like state until the warm weather arrives with early spring. We discuss avoidance measures, which are the key to successful treatment.* (Allergy and Asthma Proc 25:133–136, 2004)

CASE PRESENTATION

A 36-year-old woman with a history of perennial allergic rhinitis and asthma presented with worsening symptoms of rhinitis and asthma over the past 1–2 years. She had a long history of allergies and received immunotherapy as a child. She had been taking loratadine, 10-mg tablets, and an albuterol sulfate metered-dose inhaler for years with reasonable control of her symptoms. About 2 months before presenting to this office, she was placed on triamcinolone acetonide and salmeterol xinafoate inhalers for worsening shortness of breath and chest tightness. These measures were very helpful but not completely successful in relieving the patient's symptoms. She stated that over the past 2–3 years, her home had been infested with "thousands" of ladybugs. She also stated that her symptoms began to worsen over the past 2 years and had peaked in the winter season, while her home was infested with ladybugs. She tended to do better in the warm-weather months when the ladybugs had left her home.

Physical exam revealed the nasal mucosa to be pale with clear drainage visible with significant edema of the nasal turbinates. The rest of her exam was unremarkable, including a normal chest exam with good air movement.

Skin-prick testing to common inhalant allergens revealed the patient to be atopic with positive reactions to many allergens, including trees, grasses, and animal dander. She also had a strong reaction to ladybug whole-body extract and to an extract made from washate made by washing the surface of large numbers of ladybugs with buffered saline.

Pulmonary functions were done on two occasions 8 months apart. In both instances, the patient already was maintained on triamcinolone acetonide and salmeterol xinafoate inhalers and the results were interpreted as being within normal range. The forced expiratory volume in 1 second equaled 89 and 94% of predicted, respectively, forced expiratory volume in 1 second /forced vital capacity equaled 91% in both instances, and forced expiratory flow rate of 25–75% of the forced vital capacity equaled 69% in both instances.

Because of these findings, she was instructed on routine allergen avoidance and also specific measures of reducing ladybug exposure. She was started on immunotherapy for the aforementioned common allergens to which she had a positive skin test. She was treated with mometasone furoate monohydrate nasal spray, triamcinolone acetonide and salmeterol xinafoate inhalers, and loratadine tablets on a regular basis, and she used the albuterol inhaler as a rescue medication. She improved significantly, particularly during the winter months, although she was still having trouble with ladybug infestation. Avoidance procedures did reduce the degree of infestation, and her symptoms became easier to control.

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MATERIALS AND METHODS

The patient was skin tested by prick technique using "derma-pick" from Greer Laboratories (Lenoir, NC). Ladybug whole-body extract was prepared courtesy of Dr. Robert Esch, Ph.D. (Greer Laboratories), using standard methods yielding a preparation containing 6 mg/mL of protein in whole-body extract. A similar extract was prepared by washing the insect body surfaces with phosphate-buffered saline, yielding a preparation containing 3 mg/mL of protein extract. The ladybugs used for preparation were actually collected from the home of another patient. The patient had positive skin-prick tests to both ladybug extracts with a wheal size of >3 mm and a large red flare. Both prick tests were significantly larger than the histamine control containing 1 mg/mL of histamine base. Seven controls were tested to the same extracts and they were all negative and had positive histamine control reactions.

BACKGROUND

Respiratory allergy due to insects is well documented.[2] There are many different species of ladybugs in the United States. However, there appears to be one species that has been causing most of the allergy problems. Since their introduction into this country in the late 1970s, the ladybug *Harmonia axyridis* has grown to be somewhat of a nuisance. Other names for this species include: Asian ladybeetle, Japanese ladybeetle, multicolor Asian ladybeetle, Halloween ladybeetle, and other variations. They were brought into this country from Japan for feeding on aphids, scale insects, and other soft-bodied insects, which are a threat to many commercial farming crops. They feed on insects that often are pests for ornamental roses, plum, peach, apple, magnolia, and other plants. As their population grows, so do the number of complaints to local pest control agencies. These complaints arise from the unique overwintering habits. During the winter months in Japan, ladybugs overwinter on mountainside rocks, caves, cliffs, and trees. In the United States, they have shown a tendency to congregate inside buildings and homes. Typically, they are attracted to the sun-exposed, southwest side of lighter-colored homes. In the late fall, they find their way indoors through tiny crevices or cracks in the wall or around doors and windows. While the ladybug is overwintering, it will not eat or move much until the weather warms again in early spring. At this time, they again become active and begin looking for ways to get outside and feed.

As suggested by its name, the multicolor Asian ladybeetle comes in a variety of color patterns. Most commonly, they are orange with multiple black spots, but they also can be black or yellow with many spots or no spots at all. The most common identifying characteristic is a black "M" inscribed on their thorax, just above the wing covers. Typically, the larvae are black, white, and yellow (Figs. 1 and 2).[2]

Figure 1. *This photograph shows examples of various ladybug colors and patterns. (Courtesy of Robert L. Pienkowski, Emeritus Professor of Entomology, Virginia Tech, 1202 Highland Circle, Blacksburg, Virginia.)*

Figure 2. *This photograph shows a close-up view of a single adult ladybug. (Courtesy of ARS Photograph Unit, Scott Bauer, USDA Photographer, 5601 Sunnyside Avenue, Beltsville, Maryland.)*

LITERATURE REVIEW

In addition to the aforementioned case, there have been other documented cases of allergy symptoms related to exposure to ladybugs. Yarbrough *et al.* reported two different patients in whom both appeared to have ladybug-related symptoms.[3] Both of these patients tested positive to skin testing with ladybug extract prepared from whole bodies. Immunoglobulin E (IgE) immunoblotting was performed on the serum of each patient to identify potential allergens. The first patient's serum revealed a single band at 16.6 kDa, and the second patient's serum revealed a band at 16.6 kDa and a second band at 30 kDa. Glass *et al.* described three patients in whom new onset allergy and asthma symptoms were found to be attributable to ladybug exposure.[4] Two of the patients were a married couple who both began experi-

TABLE I

Clinical Features of the Nine Cases

Patient	Source	Age (yr)	Sex	Exposure	Symptoms	IgE Immunoblot	Other Allergies
1	Ref. 3	48	M	Home	Rhinitis, conjunctivitis	16.6 kDa	None
2	Ref. 3	56	F	Home	Rhinitis	16.6 and 30 kDa	Rhinitis
3	Ref. 5	40	M	Home	Rhinitis, asthma, conjunctivitis	14 and 31 kDa	Rhinitis
4	Ref. 6	40	F	Home	Asthma, rhinitis, conjunctivitis	14 and 30 kDa	Unknown
5	Ref. 4	46	M	Home	Rhinitis, asthma	NR	Rhinitis
6	Ref. 4	42	F	Home	Rhinitis	NR	None
7	Ref. 4	22	F	Work	Rhinitis, conjunctivitis	NR	Rhinitis
8	Ref. 7	67	M	Work	Asthma	16.6 and 30 kDa, others	Unknown
9	This paper	36	F	Home	Asthma, rhinitis	NR	Rhinitis, asthma

Summary:
Ages: 22–67 yr
Sex: Four men and five women
Exposure: Seven patients at home and two patients at work
Symptoms: Nine patients with rhinitis, five patients with asthma, and four patients with eye symptoms
IgE Immunoblot: 14, 16.6, and 30 kDa
Other allergy: Two patients were negative and six patients were positive
NR = Not done.

encing symptoms ~2 years after their home was infested with ladybugs. Both of them showed positive skin-prick test to ladybug whole-body extract. The third patient was an employee at a garden shop who would develop acute onset of ocular and nasal itching and nasal congestion within minutes of handling ladybugs. This indicates that ladybug hypersensitivity can affect people both at home and at work and that it does not necessarily require large numbers of ladybugs to elicit an allergic response. Pence *et al.* also described a patient with new onset of asthma and worsening allergic rhinitis secondary to ladybug exposure.[5] This patient's serum also showed two different types of IgE banding at 14 and 31 kDa. This patient had new onset asthma symptoms related to ladybug exposure and improved greatly when the ladybugs left his home in the warm-weather months. Kagen *et al.* described a patient who had worsening asthma, rhinitis, and angioedema.[6] History revealed that her home became infested with ladybugs and that touching her eye after contact with a ladybug caused acute angioedema of the eyelids. Like the sera of the patients described before, her serum showed two major IgE immunoblotting bands at 14 and 30 kDa. Magnan *et al.* reported a 67-year-old man who developed severe persistent asthma while working in an area infested with ladybeetles. He had positive skin tests to the whole-body extract of the insect, IgE binding at 16.6 and 30 kDa, and other proteins between 40 and 80 kDa.[7] Muthiah and Kagen recently sequenced the amino acid structure of the 14-kDa protein and a "BLAST" search failed to reveal any other proteins identified with a similar amino acid sequence.[8]

Table I summarizes the clinical features of the nine reported cases. The age range was 23–67 years with five women and four men. Seven patients had exposure at home, and two patients were exposed at work. They all had symptoms of rhinitis or conjunctivitis, and five patients had asthma. Of interest is the fact that two of the patients had no background history of allergy at all and only developed symptoms when exposed to ladybug beetles. In most cases in which IgE immunoblotting was done, the most common bands were at 16.6, 14, or 30 kDa. Magnan *et al.* reported other bands between 40 and 80 kDa, indicating there may be other potential allergens. It also is important from these figures to note that work exposure is a possibility, although it is far more common for patients to have symptoms at home after their home has been infested with ladybugs.

DISCUSSION

When ladybugs have infested a home, there is no easy way to eliminate them. Insecticides generally are not effective in ridding the creatures once inside the home. Dead ladybugs tend to attract other insects to the home and can cause additional problems. Typically, it is considered beneficial to allow the ladybugs to live so that they can

leave in the spring or they may be collected and removed physically from the home by vacuuming or sweeping.

The source of the allergens from *H. axyridis* is not clear. They could come from the surface proteins, as shown by positive skin testing to extracts prepared from washing the whole bodies. Waste products, emissions, or "bleeding" that occurs from the joints are all potential sources of allergen. The fact that the saline washings of the external surfaces contain strong allergens suggests a high concentration on the body surfaces. They are known to "bleed" from the femoral tibial joints when distressed.

Insecticides such as cipermethrin or other synthetic pyrethroids may help prevent ladybugs from entering the home if used outside the home before they enter. They can be applied to entry points such as external borders of windows and doors, overhangs, eaves, openings around plumbing, vents, or any other crevices or cracks that allow entry. Because ladybugs enter the home through tiny cracks or crevices in the walls, roofs, windows, and doors, properly sealing the home from the outside is extremely important. Adequate caulking to seal cracks and crevices in the walls, as well as repairing damage to windows and roofing, also helps keep them out of the home. Caulking can be done with quality silicone or silicone-latex caulk (R. Bessin, University of Kentucky, College of Agriculture, personal communication, 2002).

CONCLUSION

Currently, there are nine cases in the literature that have described patients sensitive to ladybugs. The source of the allergen is not clear, but it appears to be in high concentration on the body surface. One possibility is that body surface antigens are emitted into the air. This idea is supported in our case in which the patient had a strong reaction to ladybug washings. Another possibility could be that the allergens arise from the joints during the bleeding process or from waste products. To date, there is no standardized ladybug allergy extract that can be purchased. Development of such an extract certainly would lead to better diagnosing and treatment of patients with this condition. Hopefully, increasing awareness of ladybug allergy will lead to additional investigations and increasing recognition. The Asian ladybeetle continues to spread throughout the United States and it has been described in the southeast, midwest, New England, as far north as Wisconsin, and as far west as Oregon and Washington (R. Bessin, University of Kentucky, College of Agriculture, personal communication, 2002).[2,6] It is very likely that this new allergy will continue to be a problem in the future and should be considered in anyone with fall and winter seasonal allergies.

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