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Seventeen-year-old girl hospitalized for localized swelling, pruritus, tenderness, and lymphatic streaking with eosinophilia

Joshua L. Kennedy, MD^a, Susanne K. Jeffus, MD^b, Thomas A. E. Platts-Mills, MD, PhD, FRS^a, Anubha Tripathi, MD^a, Adnan Divjan, BA^c, Matthew S. Perzanowski, PhD^c, and Peter W. Heymann, MD^d

^aAsthma and Allergic Disease Clinical Research Center, Carter Immunology Center, University of Virginia, Charlottesville, Va

^bDepartment of Pathology, University of Virginia, Charlottesville, Va

^cDepartment of Environmental Health Sciences, Mailman School of Public Health, Columbia University, New York, NY

^dDepartment of Pediatrics, Asthma and Allergic Disease Clinical Research Center, University of Virginia, Charlottesville, Va

TO THE EDITOR:

We report about a 17-year-old female who came to our clinic after admission to the hospital for suspected cellulitis. Her skin symptoms began as an area of localized swelling on her left elbow, which increased in size over the subsequent 3 days. On the day of hospital admission, her primary care physician started trimethoprim/sulfamethoxazole for presumed cellulitis. However, the swelling worsened and spread to a second area on her left hand. Both areas of swelling were edematous, pruritic, and painful. There were also 3 to 4 punctate lesions on her arm that were proximal to the hand swelling (Figure 1, A). She also had lymphatic involvement with erythematous streaking that extended upward. She was afebrile and had no other systemic signs or symptoms. During the hospitalization, she was treated with intravenous clindamycin. She was found to be eosinophilic (absolute eosinophil count, $1.5 \times 10^9/L$). Her total IgE (4027 IU/mL) was elevated as well as allergen-specific IgE levels to white oak (54.3 IU/mL), Bermuda grass (76.4 IU/mL), and timothy grass (123.5 IU/mL), consistent with her symptoms of rhinitis and conjunctivitis in the spring. A punch biopsy from her left elbow showed an intraepidermal vesicopustule accompanied by localized spongiosis, acanthosis, and parakeratosis. The dense superficial and deep dermal inflammatory infiltrate was mixed and consisted of numerous eosinophils. Although an eosinophilic cellulitis was considered,¹ a hypersensitivity response to an arthropod bite was favored (Figure 1, B and C).

EVALUATION AFTER HOSPITALIZATION

During follow-up in the clinic, she reported previous reactions that were similar, but less extensive, 3 times over the past 6 months. In January, she had right-sided facial swelling and swelling of her left elbow, which required hospitalization for 3 days, secondary to presumed cellulitis. During that hospitalization, she was evaluated by orthopedics for compartment syndrome that involved her left elbow, secondary to the extent of swelling. Subsequently, she developed a pruritic rash with swelling on her forearm, which resolved over 2 to 3 days with no interventions. The third episode led to her hospitalization as detailed above.

On further questioning, the patient reported previous problems with bedbugs in her apartment. However, she had not seen any in her bedding or apartment (which had been sprayed for bedbugs) for >6 months. She shared a bed with her infant. The infant had not experienced any skin symptoms. The patient had no history of asthma or atopic dermatitis, but she did report symptoms of springtime rhinoconjunctivitis. Examination of her skin showed 4 annular lesions on her left hand and forearm, again with erythematous, nontender (lymphatic) streaking that extended upward. She had no palpable lymphadenopathy. No other abnormalities were observed on examination.

FURTHER EVALUATION AND FOLLOW-UP

Skin prick testing showed wheal and flare reactions to both species of dust mites (7-mm wheals to *Dermatophagoides pteronyssinus* and *Dermatophagoides farinae*), cat (7 mm), eastern tree mix (7 mm), red oak (10 mm), grass mix (10 mm), Bermuda grass (10 mm), cockroach mix (3 mm) (Greer, Lenoir, NC), and AP dog (4 mm) (Hollister-Stier, Spokane, Wash). Negative tests were observed for *Alternaria*, *Aspergillus*, *Cladosporium*, *Penicillium*, *Candida*, *Trichophyton*, and short ragweed. Total and specific IgE antibodies were measured by ImmunoCAP (Phadia US, Portage, Mich) or a modification of the assay with streptavidin on solid phase (Galactose- α -1,3-galactose,² ladybug,³ and nitrophorin [cNP] protein⁴) (Table I). The ladybug and galactose- α -1,3-galactose assays were performed as controls.

After her clinic visit, the patient called because she found a bedbug in her home, which she provided during a home visit. The identity was confirmed as *Cimex lectularius* (bedbug). Unfortunately, although we were awaiting the blood test results, the patient had another episode of swelling with lymphatic streaking again on her left elbow and arm, which led to a visit to the emergency department (ED) for presumed cellulitis. She had no systemic symptoms of sepsis, although she did again have significant eosinophilia. Blood eosinophil counts obtained during and after her hospital and ED visits are shown in Figure 1, D. Serum from the patient was tested for IgE antibody to cNP found in the saliva of *C lectularius*.⁴ Her result (735 IU/mL) is the highest value of IgE antibody to this allergen reported to our knowledge.

DISCUSSION

Both hospital admissions and the ED visit for our patient were associated with localized swellings, edema, pruritus, tenderness, and lymphatic streaking. It is important to note that,

unlike with mosquitos, fleas, or ticks, the risk of transmitting infectious diseases via bedbugs is almost nonexistent.^{5,6} The extent of her blood eosinophilia correlated with her hospitalizations and treatments with oral steroids (20 mg twice daily for 5 days) (Figure 1, D). This treatment was associated with symptom improvement, although treatment for bedbug bites has not been well established, and some reports suggest that antihistamines and local/systemic corticoids may be ineffective.⁷ Her hypersensitivity reactions were striking and were associated with marked tissue and blood eosinophilia in keeping with her high titers of IgE antibody to the cNP salivary protein from *C lectularius*. The major IgE binding proteins from biting insects are apyrase from bloodfeeding arthropods, a Vespidae Group 5 homologue, and a nitrophorin found in saliva from *Triatoma* and *C lectularius* species.⁸ cNP is also associated with salivary nitric oxide, an important vasodilator and inhibitor of platelet aggregation.⁹ The triatomines and *C lectularius* are from different families of *Hemiptera* (*Reduviidae* and *Cimicidae*, respectively), and their nitric oxide/nitrophorin salivary proteins have different structures and origins with the same job, assisting with hematophagy.¹⁰

Several cases of *Triatoma* anaphylaxis are known, particularly in the southwestern United States,¹¹ yet anaphylaxis to bedbug is rare,¹² possibly because of the differences in protein structure between the species. The *Triatoma* nitrophorin is a procalin, whereas the cNP in *C lectularius* is derived from the enzyme inositol polyphosphate 5-phosphatase. In addition, the amount of allergen injected by bedbug into the skin is likely much less than *Triatoma*, which might lead to an increased risk of anaphylaxis simply as a function of exposure.

Information about the epidemiology of hypersensitivity reactions to bites from *C lectularius* is limited. Evidence is available of specific IgE to whole-body bedbug extract in 17 subjects in New York, 9 of whom showed specific IgE responses to cNP. The whole-body bedbug extract showed cross-reactivity with cockroach and dust mite species to which our patient was also sensitized, whereas her high IgE antibody level to cNP is specific for *C lectularius*.⁴

Despite reports of insecticide resistance, difficulties with pesticides reaching bedbug hiding places, and the health concerns of placing pesticides on mattresses,⁵ additional spraying to eradicate bedbugs from our patient's apartment dwelling was recommended by the health department, and she has not experienced subsequent reactions as of this report. Her hospitalizations and high titers of IgE to cNP are of interest because *C lectularius* infestations are increasing across the eastern seaboard, particularly in large cities, and are being reported more frequently in central Virginia.

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Clinical Implication

- A variety of skin disorders are referred to allergists, especially when they are associated with other atopic symptoms and/or blood eosinophilia. Although urticaria and atopic dermatitis are the most common skin manifestations of allergic disease in children and adults, the clinician must maintain a high degree of suspicion with regards to other potential sources of IgE, including biting insects, in a patient with these symptoms.

FIGURE 1.

Reactions at presentation. **A**, *Yellow arrows* mark the sites of bites, and *black arrows* mark the lymphangitic spread. **B**, Lowpower image of epidermis (H&E stain; original magnification, ×40). **C**, Dermal infiltrate centered on vessels comprised predominantly of eosinophils (H&E stain; original magnification, ×400). **D**, Absolute eosinophil count over six months. *Steroids were administered at each hospital admission of ED visit as listed.

TABLE I

Specific serum IgE responses

Allergen	IgE level (IU/mL)
Indoor allergens	
<i>Dermatophagoides pteronyssinus</i>	5.57
<i>Dermatophagoides farinae</i>	4.16
<i>Blattella germanica</i>	4.1
<i>Periplaneta americanum</i>	3.09
Cat	3.1
Dog	3.04
Aeroallergens	
Oak	54.3
Timothy grass	123.5
Bermuda grass	76.4
Insects	
Ladybug	<0.35
<i>C lectularius</i> cNP	735
Other	
Galactose- α 1,3-galactose	<0.35
Total IgE	4027