



Letter to the Editor

Allergic reaction to *Hyperlasion Schmitz* (Diptera: Sciaridae)

Dear Editor,

Sciarid fly (Shizuoka-kurobane-kinoko-bae in Japanese) infestations have been reported in Gifu, Shizuoka, and Aichi prefectures in Japan since 2011.¹ Sueyoshi *et al.* recently discovered the sciarid fly as a new species in the genus *Hyperlasion* Schmitz and named it *Hyperlasion breviantenna* (HB) based on its morphological features and the results of genetic analyses.¹ HB is recognized as a pest and its infestations occur during the rainy season (June to July). With a body length as small as 1.4–1.8 mm, more than 100 HB can enter a building in half an hour, even through the mesh of a screen door. Most HBs are female and are assumed to inhabit forests and forest edges; however, the details of their habits are currently unknown. Therefore, it is difficult to develop control measures against this insect.

Some patients in Tajimi City, Gifu prefecture reported to our institution with complaints of rhinitis and conjunctivitis with itching immediately after being touched or surrounded by HB. Their symptoms were similar to those of allergic rhinitis (AR) and allergic conjunctivitis. Herein, we report the symptoms of these patients and the results of assays performed confirm whether their symptoms were induced by IgE-mediated immediate allergic reactions.

This study was approved by the research ethics board of Aichi Children's Hospital (approval number: 2,022,017) and the Ethics Review Committee, Fujita Health University (approval number: HM22-269). Informed consent was obtained from all the participants.

We enrolled eight patients into this study between July 2021 and August 2021 (Table 1, Supplementary Table 1, 2). All the patients experienced nasal symptoms, whereas six had conjunctival symptoms. Patient (Pa) 1 and Pa2 had respiratory symptoms. However, Pa1 had bronchial asthma (BA), whereas Pa2 did not (Supplementary Table 1). Pa4 and Pa6 experienced mild skin symptoms after they were directly touched by HB. Administration of antihistamines was effective for the treatment of all nasal, conjunctival, and cutaneous symptoms. Some of the symptoms were severe and required additional treatment using eyedrops and nasal sprays. Inhalation of bronchodilators was effective for treating respiratory symptoms (Table 1).

To determine whether the patients' symptoms were IgE-mediated, we performed immunological assays using slightly modified previously described methods (Supplementary Methods).^{2,3} First, proteins were extracted from HB as described in the Supplementary Methods, confirmed using electrophoresis (Supplementary Fig. 1), and used for ELISA, skin prick test (SPT), and basophil activation test (BAT).

We confirmed the presence of IgE antibodies that uniquely recognize antigens of HB extracts using ELISA (Fig. 1). We detected relatively high optical densities in seven of the eight patients. In addition, we performed an ELISA inhibition test using HB extracts and confirmed the inhibitory effect in these seven patients. Although the inhibitory effect was relatively weak in Pa1, the results suggested that the binding of IgE antibodies to HB extracts was HB antigen-specific.

We performed SPT and BAT to confirm whether HB caused an IgE-mediated allergic reaction in four of the eight patients (Table 1, Supplementary Table 1). Although Pa8, whose symptoms were the weakest, showed flare reactions without wheals, three of four patients had positive results in both tests, and the reactions were concentration-dependent. Considering these immunological test results and the effectiveness of the anti-allergic treatment administered, it seems reasonable that HB contains antigens recognized by the IgE of sensitized patients and induces IgE-mediated allergic reactions.

Insects (Class, *Insecta*), such as cockroaches, moths, chironomids, and booklice, have been identified as important causes of respiratory allergies, including asthma and allergic rhinitis.⁴ Among Diptera (Order, *Diptera*), champignon flies⁵ and fruit flies⁶ are reported to be occupational insect allergens, whereas chironomid⁴ and houseflies⁷ are non-occupational insect allergens. The prevalence of sensitization to insect allergens in non-occupational settings is considerably high among patients with asthma and/or AR.⁴ In Japan, chironomid antigens were detected in airborne dust collected using an air sampler.⁸ In addition, a higher sensitization rate to chironomids was documented among patients with asthma living around Lake Suwa, which has a massive adult chironomid population, than among those living far from the lake.⁹ In the present study, all patients except Pa4 had comorbidities, such as asthma or AR. It is reasonable to consider that exposure to HB and a history of AR and BA could be a risk factor for HB sensitization. All the patients experienced HB infestations that occurred several years ago in their areas of residence, and the onset of most of their allergic symptoms was during the HB infestation of the 2021 season.

It is possible that the positive immunological results in this study are attributable to cross-reactivity with other arthropods. Arthropods, including insects, contain various cross-reactive IgE allergens, such as tropomyosin and arginine kinase.¹⁰ Although seven of the eight patients were sensitized to *Dermatophagoides pteronyssinus*, five of them were not sensitized to insects, suggesting that cross-reactivity between *D. pteronyssinus* and insects is limited (Supplementary Table 2). We confirmed that control subjects sensitized to *D. pteronyssinus* (Pa9–13, Supplementary Table 2), as well as unsensitized control subjects (Pa14–17), did not have IgE antibodies that bound to HB (Fig. 1). Moreover, we

Table 1
Clinical data of the patients.

No	Sex	Age (year)	Symptoms	Medications				SPT (mm)	BAT (%)
				Oral	Inhalant	Eyedrop	Nasal spray		
1	Male	6	Wheezing, coughing, mild sneezing, nasal discharge, mild nasal congestion, eyelid swelling, conjunctival hyperemia, itchy eyes	Olopatadine, Montelukast	Procaterol	Epinastrine 0.1%, Fluorometholone 0.02%	Beclomethasone 25 µg	15 × 15	92.5
2	Female	7	Wheezing, coughing, sneezing, nasal discharge, mild nasal congestion, eyelid swelling, conjunctival hyperemia, itchy eyes	Fexofenadine	Procaterol	Epinastrine 0.1%, Fluorometholone 0.02%		15 × 15	66.6
3	Female	10	Sneezing, nasal discharge, nasal congestion, eyelid swelling, itchy eyes	Fexofenadine		Epinastrine 0.1%, Fluorometholone 0.02%		Not tested	
4	Male	13	Sneezing, nasal discharge, mild nasal congestion, eyelid swelling, itchy eyes, erythema and itching when the area is touched	Olopatadine				Not tested	
5	Male	8	Sneezing, nasal discharge, nasal congestion, conjunctival hyperemia, and itchy eyes	Olopatadine, Pranlukast		Epinastrine 0.1%, Fluorometholone 0.02%	Beclomethasone 25 µg	Not tested	
6	Female	13	Sneezing, nasal discharge, nasal congestion, erythema and itching when the area is touched	Olopatadine, Pranlukast				Not tested	
7	Female	7	Mild nasal discharge, itchy eyes	Olopatadine, Montelukast		Epinastrine 0.1%, Fluorometholone 0.02%		7 × 7	15.2
8	Female	5	Mild nasal discharge	Olopatadine				0 × 0	1.9

SPT (mm) means the diameter (longest × shortest) of a wheal caused by the extract from *Hyperlasion brevantenna*.

Of each concentration of the extract, only the one with the maximum reaction is listed.

BAT (%) means the maximum activated percentage of basophils stimulated by the extract.

SPT, skin prick test; BAT, basophil activation test.

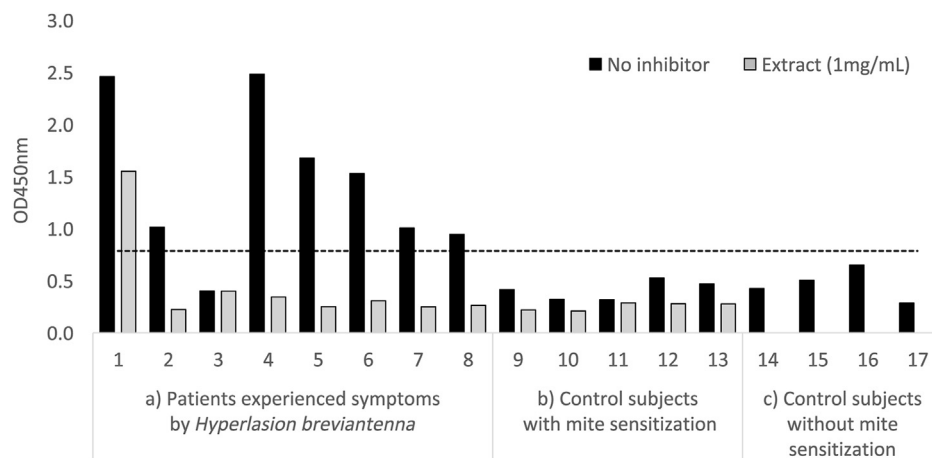


Fig. 1. ELISA and inhibition assay using extracts from *Hyperlasion brevantenna*. This figure shows the results of the ELISA and inhibition assays of (a) patients who experienced symptoms caused by *H. brevantenna*, (b) control subjects with mite sensitization, and (c) control subjects without mite sensitization. The black columns indicate the optical density observed after the ELISA performed without the inhibitor, whereas the gray columns indicate the optical density after inhibition treatment using *H. brevantenna* extract. The dotted line indicates the average number of the control subjects (No. 9–17 + 3 SD). The optical densities of the control group with and without mite sensitization were low, and all patients, except No. 3, showed higher optical densities than the control group and were confirmed to be inhibited by the *H. brevantenna* extract.

confirmed specific sensitization to HB extracts in Pa4, who was not sensitized to any arthropod allergen. These findings support the hypothesis that patients who showed allergic reactions to HB were directly sensitized to HB, but not through cross-reactions with *D. pteronyssinus*.

To our knowledge, this is the first case series of children who experienced symptoms caused by HB. However, this study had some limitations. First, Pa8 showed negative SPT and BAT results. However, this patient's symptoms were the weakest and the

patient showed concentration-dependent flare reactions. Second, although three out of four patients showed concentration-dependent reactions in both SPT and BAT, we did not perform SPT or BAT on negative controls who did not experience symptoms upon exposure to HB for ethical reasons. Third, the sample size of this study is too small. Thus, further studies with larger sample sizes are needed to identify the major allergen components of HB and elucidate their cross-reactivity with house dust mites and other insect allergens.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.alit.2023.03.004>.

Conflict of interest

KM is an endowed chair at Hoya Co., Ltd. and received research funding from Hoya. NS, TK, and MN are employees of Hoya. The rest of the authors have no conflict of interest.

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