

# Immune response profiles after caterpillar exposure: a case report

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**Rationale:** The role of the immune response to caterpillar exposure is not well described. This case study is the first to report a patient who presented with an allergic reaction after exposure to the larvae of the sycamore tussock moth, *Halysidota harrisii* Walsh, 1864.

**Methods:** Blood was collected from an allergic asthmatic adult (m/42 y/o) at 2 hrs – 2 wks after contact urticaria with associated dyspnea after exposure to the larvae of the sycamore tussock moth, *Halysidota harrisii* Walsh, 1864. Distributions of blood lymphocytes (CD4<sup>+</sup>, CD8<sup>+</sup>, CD8<sup>+</sup>CD60<sup>+</sup>, CD19<sup>+</sup>, CD23<sup>+</sup>, CD16/56<sup>+</sup>, CD25, CD45RA<sup>+</sup>, CD45RO<sup>+</sup>), monocytes (CD1d<sup>+</sup>), levels of serum immunoglobulins (IgM, IgG, IgA, IgE), and cytokines (IFN- $\gamma$ , IL-4, TNF- $\alpha$ ) were studied (flow cytometry, nephelometry, UniCAP Total IgE Fluoroenzymeimmunoassay, cytokine ELISA, clinical toxicology).

**Results:** Numbers of CD4<sup>+</sup> T cells, CD25<sup>+</sup> cells, CD19<sup>+</sup> B cells, and CD1d<sup>+</sup> monocytes decreased (22, 27, 33, 20%, respectively) one week post reaction, CD45RA<sup>+</sup> naïve T cells decreased at 36 hours (21%), while CD8<sup>+</sup>CD60<sup>+</sup> T cells and CD23<sup>+</sup> cells decreased 48 hrs (33, 74%, respectively) post reaction. In contrast, numbers of CD16/56<sup>+</sup> NK precursor cells increased (60%) 12 hrs, then decreased (65%) 48 hrs post reaction; other lymphocyte subsets were unaffected. Serum IgM, IgG and IgA were within normal range; however, serum IgE demonstrated a bimodal elevation at 2 hrs (15%) and one week post reaction. Levels of IFN- $\gamma$ , IL-4, and TNF- $\alpha$  were not detected in serum pre-exposure (<1.0–4.0 pg/mL). However, high levels of IFN- $\gamma$  (187–319 pg/mL) and TNF- $\alpha$  (549–749 pg/mL) were detected in serum 24–36 hrs and 3.5–24 hrs post reaction, respectively. In contrast, levels of IL-4 were undetected (<1.0 pg/mL) in serum at all time points.

**Conclusions:** Exposure to the larvae of the sycamore tussock moth, *Halysidota harrisii* Walsh, 1864 may result in increased cytokine levels and blood CD16/56<sup>+</sup> NK precursor cells.

**Keywords:** caterpillar exposure, *Halysidota harrisii* Walsh, 1864, serum IgE

## Introduction

It has been reported that caterpillar exposure results in symptoms including: local effects (dermatitis),<sup>1,2–5</sup> local pain,<sup>1,6</sup> and systemic effects, including anaphylaxis, depending on the species.<sup>1,6–9</sup> Caterpillar dermatitis or lepidopterism is a toxic irritant whose reaction is triggered by the release of histamine thaumetopoein and other kinins from the hairs of caterpillars and butterflies.<sup>10</sup> In central Europe, the two main causes of caterpillar dermatitis are the oak and pine processionary caterpillar.<sup>10</sup> It has been observed that patients may develop cutaneous reactions, conjunctivitis, bronchitis and in some instances, anaphylactic reactions.<sup>10</sup> With the exception of bee and wasp venom allergies, immediate-type allergic reactions to mosquitoes, flies, ticks, bed bugs, moths, caterpillars and spiders are rare.<sup>11</sup>

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Other studies have reported gypsy moth caterpillar dermatitis after direct contact with the first instar larva of the gypsy moth (*Lymantria dispar*).<sup>12</sup> The pathogenesis of this dermatitis most likely involves histamine release by the caterpillar and a delayed hypersensitivity reaction in its host.<sup>12</sup>

Exposure to hairs from 'itchy' caterpillars are usually nonvenomous, but a contact reaction may produce mechanical irritation<sup>1,13</sup> and dermatitis.<sup>1,3,5,14</sup> Studies of Vega et al have reported allergic reactions to allergens from the pine processionary caterpillar *Thaumetopoea pityocampa*, which induces dermatitis by a toxic-irritative mechanism;<sup>15</sup> these reactions were confirmed by positive skin prick tests and specific IgE determination (immunoblot) using crude larval extracts.<sup>15</sup> However, a specific low molecular weight 15-kDa IgE-binding protein, *Tha p 1*, was later identified as a major caterpillar allergen.<sup>16</sup> Patients with suspected contact urticaria from pine processionary caterpillars displayed allergic reactions/symptoms that included angioedema, conjunctivitis, and anaphylaxis.<sup>15</sup> The wheals were localized mainly on the neck and forearms.<sup>15</sup> Cutaneous reactions to pine processionary caterpillar have also been reported in children.<sup>17</sup> However, these cases are frequent in pinery zones, and only in some cases, due to an IgE-mediated allergic mechanism caused by pine processionary caterpillar proteins.<sup>17,18</sup> Systemic allergic reactions to the larvae of the sycamore tussock moth, *Halysidota harrisii* Walsh, 1864 in humans have not been reported.

In the current study, we are the first to describe the clinical and immunological responses following contact with the larvae of the sycamore tussock moth, *Halysidota harrisii* Walsh, 1864, in Brooklyn, NY. Even though reactions to Lepidoptera (moths, butterflies, and caterpillars) are usually mild and self-limited, reactions in sensitive individuals and to specific species can be severe.<sup>19</sup>

Because the reported responses to caterpillar exposure are variable and the habitat of *Halysidota harrisii* Walsh, 1864 is prevalent in eastern parts of the United States as well as southeast regions of Canada,<sup>20</sup> the potential importance of cells and cytokines post exposure in atopic individuals may be underrepresented. As such this case demonstrates the complexity of immune reactions to caterpillar exposure. Awareness and further understanding of caterpillar exposure may be important for atopic individuals with caterpillar sensitivity.

## Materials and methods

### Patient history

A 42-year-old man presented to his private doctor's office (Brooklyn, NY) with a severe allergic reaction from contact

with a caterpillar which fell on his arm, when he was entering his car which was parked under a tree in front of his house (Brooklyn, NY). A more detailed description of the patient's symptoms is listed in the Results section.

In order to further characterize the systemic immune response to the caterpillar, informed consent was obtained, and blood and serum samples were drawn at various time points after diagnosis (eg, 2, 3.5, 12, 24, 36, 48 hrs; 1, 2 wks).

### Caterpillar identification

The caterpillar observed at the time of the exposure was obtained from the patient for identification. Identification was performed at the Dept of Entomology, Cornell University (Geneva, NY) according to standard clinical taxonomic methodology.

### Immunoglobulin determination

Blood was collected and immunoglobulin (Ig) levels (IgG, IgM, IgA) were detected in serum (Quest Diagnostics, Teterboro, NJ). All serum IgE determinations were carried out in the Clinical Diagnostic Laboratory at SUNY Downstate Medical Center (UniCAP Total IgE fluoroenzymeimmunoassay, Pharmacia and Upjohn Diagnostics, Kalamazoo, MD) which was performed according to manufacturer's recommendation.

### Flow cytometry

For flow cytometry studies, blood was collected into ethylenediaminetetraacetic Monoject tubes (Sherwood Medical Company, St. Louis MO) (EDTA) and retained for up to 2 hr at room temperature.

### Antibodies

Mouse antihuman monoclonal antibodies directly conjugated to fluorescein isothiocyanate (FITC) (IgG<sub>1</sub> anti-CD45RA, CD25, CD23; IgM anti-CD60); phycoerythrin (PE) (IgG<sub>1</sub> anti-CD4, CD8, CD1d; IgG<sub>2a</sub> anti-CD45RO), Simultest (FITC/PE-conjugated) reagents (CD3/CD4, CD3/CD8, CD3/CD19, CD3/CD16<sup>+</sup>CD56), and appropriately matched isotype control monoclonal antibodies (FITC-conjugated IgG<sub>1</sub>, PE-conjugated IgG<sub>1</sub> and IgG<sub>2a</sub>, Simultest control  $\gamma_1/\gamma_{2a}$ , FITC-conjugated IgM). All antibodies were purchased from BD Biosciences (San Jose, CA), except IgM anti-CD60 which was purchased from Ancell, (Bayport, MN); and IgG<sub>1</sub> anti-CD1d, which was purchased from BD Pharmingen (San Diego, CA). All were used according to manufacturers' recommendation.

## Assay

For labeling studies, conjugated antibodies (10  $\mu\text{L}$ ) (or 80  $\mu\text{L}$  of titrated anti-CD60) directed against 1–3 markers, were added to blood (100  $\mu\text{L}$ ) in 12  $\times$  75 mm (5 mL) tubes (Fisher Scientific, Springfield, NJ) and incubated for 10 mins at room temperature, after which erythrocytes were lysed with whole blood lysing reagent (Immunoprep; Beckman Coulter, Hialeah, FL), and the cells counted. Lymphocyte distributions were determined with a Coulter Epics XL/MCL Flow Cytometer with System II software (Coulter), and CytoComp (Coulter) QC Windows (Flow Cytometry Systems, San Juan, Puerto Rico) used to ensure consistent instrument settings. Absolute lymphocyte numbers are calculated from the total lymphocytes. Data are expressed as total lymphocytes per cubic millimeter ( $\text{mm}^3$ ) or mean percentage (%) of positive cells.

## Cytokine determination

Serum cytokines (interferon gamma [IFN- $\gamma$ ], interleukin-4 [IL-4], Interleukin-12 [IL-12], Tumor necrosis factor-alpha [TNF- $\alpha$ ]) were determined by sandwich ELISA (Biosource; Camarillo, CA) according to the manufacturer's protocol.

## Results

### Patient symptoms

Patient symptoms began immediately after exposure to caterpillar larvae; the local effects included redness, swelling, pain, and severe itchiness with medium size urticaria (3–5 mm with flare) on his left forearm (Figure 1), which spread to his upper chest and neck area. He complained about breathing difficulty with shortness of breath. The patient had a history of moderate asthmatic episodes (mild-intermittent) and atopy (environmental and food), with high serum IgE levels (208 IU/mL). He had no known drug allergies; his social history was unremarkable. Treatment was initiated immediately (doctor's office) (within 10–15 min) with the antihistamine diphenhydramine HCl (75 mg po), and albuterol (mdi, 2 puffs, po). Patient's symptoms resolved uneventfully, contact urticaria and itchiness resolved 48 hrs later while breathing difficulty resolved within 1–2 hrs. No persistent symptoms were observed over the next couple of days.

### Taxonomic evaluation

The caterpillar was identified as the larvae of the sycamore tussock moth, *Halysidota harrisii* Walsh, 1864 (Figure 2).



**Figure 1** Appearance of contact exposure reaction in an allergic asthmatic patient to the larvae of the sycamore tussock moth, *Halysidota harrisii* Walsh, 1864. Inflammation and induration are evident in the antecubital fossa (site of caterpillar exposure) with proximal and distal radiation.

### Serum immunoglobulins Total IgM, IgG, IgA, and IgE

Serum IgM, IgG, IgA were within normal range (see materials and methods), while serum IgE levels were high. Even though no differences were observed between any of the Igs, serum IgE levels demonstrated a slight bimodal elevation at 2 hrs and one week post reaction (Table 1).

### Distributions of blood lymphocyte subpopulations

Distributions of blood lymphocytes (CD4<sup>+</sup>, CD8<sup>+</sup>, CD8<sup>+</sup>CD60<sup>+</sup>, CD19<sup>+</sup>, CD23<sup>+</sup>, CD16/56<sup>+</sup>, CD25, CD45RA<sup>+</sup>, CD45RO<sup>+</sup>) and monocytes (CD1d<sup>+</sup>) were studied in peripheral blood. Absolute numbers of CD4<sup>+</sup> T cells, CD25<sup>+</sup> cells, CD19<sup>+</sup> B cells, and CD1d<sup>+</sup> monocytes decreased (22, 27, 33, 20%, respectively) one week post reaction, while CD8<sup>+</sup>CD60<sup>+</sup> T cells and CD23<sup>+</sup> cells decreased 48 hrs (33, 74%, respectively) post reaction and CD45RA<sup>+</sup> naïve T cells decreased (21%) 36 hours post



**Figure 2** Picture of the larvae of the sycamore tussock moth, *Halysidota harrisii* Walsh, 1864.

**Table 1** Immunoglobulin levels in serum of a patient with an allergic response to caterpillar exposure

Time	Immunoglobulin			
	IgM (mg/dL)	IgG (mg/dL)	IgA (mg/dL)	IgE (IU/mL)
Pre	54	725	322	181
2 hrs	47	815	339	208
3.5 hrs	52	753	317	182
12 hrs	52	760	324	193
24 hrs	69	817	337	184
36 hrs	55	805	349	198
48 hrs	55	755	323	188
1 wk	54	798	337	202
2 wks	55	760	318	191

**Notes:** Immunoglobulin levels in a serum IgE<sup>+</sup> allergic asthmatic adult, before (pre) and after (2, 3.5, 12, 24, 36, 48 hrs and 1–2 wks) an allergic response to caterpillar hair (from the larva of the sycamore tussock moth, *Halysidota harrisii* Walsh, 1864), as determined by Quest Diagnostics (Nephelometry, ELISA). Data are expressed as either mg/dL or IU/mL. Quest Diagnostics reference range for healthy adult serum: IgM: 47–367 mg/dL; IgG: 648–2045 mg/dL; IgA: 55–375 mg/dL; IgE: 20–100 IU/mL.

reaction (Tables 2, 3). In contrast absolute numbers of CD16/56<sup>+</sup> NK precursor cells increased (60%) 12 hrs, then decreased (65%) 48 hrs post reaction; other lymphocyte subsets were unaffected.

### Cytokines in serum

Levels of IFN- $\gamma$ , IL-4, and TNF- $\alpha$  were not detected in serum pre-exposure (<1.0–4.0 pg/mL). However, high levels of IFN- $\gamma$  (187–319 pg/mL) and TNF- $\alpha$  (549–749 pg/mL) were detected in serum 24–36 hrs and 3.5–24 hrs post reaction, respectively (Figure 3). In contrast, levels of IL-4 were undetected (<1.0 pg/mL) in serum at all time points. All cytokines returned to baseline levels one year post reaction (Figure 3).

## Discussion

This is the first study of an allergic reaction resulting from caterpillar exposure that demonstrates that contact/exposure

to the larvae of the *Halysidota harrisii* Walsh, 1864. The sycamore tussock moth (*Halysidota harrisii*) is a species of moth of the Arctiidae family, which is found in south-eastern Canada and the eastern parts of the United States.<sup>20</sup> Depending on its location, the moth flies either from May to June or from July to August,<sup>20</sup> the latter which was reported in our study. Larvae are typically very hairy,<sup>20</sup> as observed (Figure 2). Systemic allergic responses to contact reactions with the larvae of *Halysidota harrisii* have not been previously described.

Studies of Maier et al have reported dermatitis in children who came in contact with the urticating hairs (setae) of oak processionary caterpillars, the larvae of *Thaumetopoea processionea* L., in a suburb of Vienna.<sup>21</sup> An increase in the number of cases of reported lepidopterism, an airborne disease caused by the setae of the oak processionary caterpillar, has caused public health concerns.<sup>22</sup> Studies of Jans and Franssen<sup>23</sup> described direct animal exposure to the urticating hairs of the oak processionary caterpillar due to ingestion and inhalation; symptoms included labial angioedema, ptialism, sloughing, tongue swelling, stomatitis, conjunctivitis and respiratory distress.<sup>23</sup>

Other caterpillars, including the pine processionary caterpillar, which is responsible for dermatitis, contact urticaria, and, rarely, respiratory and anaphylactic reactions through IgE-mediated or non-IgE-mediated mechanisms,<sup>24</sup> can also cause significant local reactions and airway swelling if ingested.<sup>24</sup> Accidents with the caterpillar *Lonomia obliqua* have been described, which are associated with a coagulation disorder and hemorrhagic syndrome in humans, caused by envenomation with this caterpillar.<sup>25</sup> Antivenin is available in the case of potentially fatal *Lonomia* envenomation.<sup>19</sup>

In general, lepidopterism outbreaks are rare.<sup>26</sup> However, Redd et al<sup>26</sup> investigated a lepidopterism outbreak associated

**Table 2** Distributions of lymphocyte subpopulations in peripheral blood of a patient with an allergic response to caterpillar hair

Time	CD3 <sup>+</sup> CD4 <sup>+</sup>		CD3 <sup>+</sup> CD8 <sup>+</sup>		CD8 <sup>+</sup> CD60 <sup>+</sup>		CD16 <sup>+</sup> 56 <sup>+</sup>		CD19 <sup>+</sup>		CD23 <sup>+</sup>	
	(%)	mm <sup>3</sup>	(%)	mm <sup>3</sup>	(%)	mm <sup>3</sup>	(%)	mm <sup>3</sup>	(%)	Mm <sup>3</sup>	(%)	mm <sup>3</sup>
2hrs	51	1049	28	575	6.0	130	3.0	58	12	250	2.0	38
3.5 hrs	51	1049	29	594	7.0	140	3.0	51	12	254	1.0	23
12 hrs	48	975	29	588	6.0	114	7.0	146	10	200	1.0	19
24 hrs	54	1096	27	547	6.0	122	3.0	71	11	215	1.0	20
36 hrs	48	979	29	586	7.0	139	6.0	114	11	223	1.0	13
48 hrs	54	1106	26	541	4.0	86	3.0	51	14	289	0.5	10
1 wk	48	818	32	553	9.0	162	4.0	76	10	170	1.0	23
2 wks	46	950	31	639	8.0	160	4.0	77	11	233	0.4	9.0

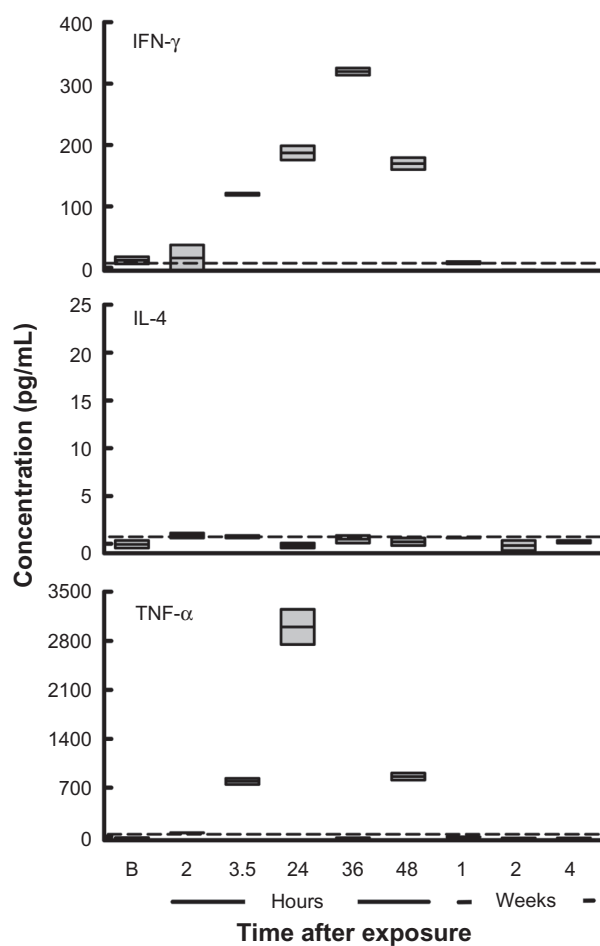
**Notes:** The distributions of lymphocyte subpopulations in peripheral blood of a serum IgE<sup>+</sup> allergic asthmatic adult after (2, 3.5, 12, 24, 36, 48 hrs and 1–2 wks) an allergic response to caterpillar hair (from the larva of the sycamore tussock moth, *Halysidota harrisii* Walsh, 1864). Data are expressed as mean total cells/mm<sup>3</sup> or mean percentage (%) of positive cells.

**Table 3** Distributions of lymphocyte subpopulations in peripheral blood of a patient with an allergic response to caterpillar exposure

Time	CD25 <sup>+</sup>		CD4 <sup>+</sup> CD25 <sup>+</sup>		CD45 RA <sup>+</sup>		CD45RO <sup>+</sup>		CD1d <sup>+</sup> monocytes)	
	(%)	mm <sup>3</sup>	(%)	mm <sup>3</sup>	(%)	mm <sup>3</sup>	(%)	mm <sup>3</sup>	(%)	mm <sup>3</sup>
2hrs	5.0	112	0	0	37	750	66	1343	90	1835
3.5 hrs	6.0	127	0	0	36	730	65	1339	92	1892
12 hrs	5.0	97	0	0	37	764	64	1307	88	1808
24 hrs	6.0	124	0	0	35	713	69	1409	92	1886
36 hrs	4.0	86	0	0	23	479	67	1366	85	1745
48 hrs	7.0	136	0	0	35	713	66	1349	85	1746
1 wk	5.0	82	0	0	35	595	70	1203	85	1461
2 wks	5.0	104	0	0	33	676	68	1395	86	1767

**Notes:** The distributions of lymphocyte subpopulations (activation and memory markers) in peripheral blood of a serum IgE<sup>+</sup> allergic asthmatic adult after (2, 3.5, 12, 24, 36, 48 hrs and 1–2 wks) an allergic response to caterpillar hair (from the larva of the sycamore tussock moth, *Halysidota harrisii* Walsh, 1864). Data are expressed as mean total cells/mm<sup>3</sup> or mean percentage (%) of positive cells.

with caterpillars of the Douglas-fir tussock moth (*Orgyia pseudotsugata*) at a Boy Scout summer camp in New Mexico. Contact exposure included symptoms of itch, rash, or hives.<sup>26</sup> The authors concluded that avoiding areas of heavy infestation can reduce illness risk, as well as modifying behaviors



**Figure 3** Serum levels (pg/mL) of cytokines (IFN- $\gamma$ , IL-4, TNF- $\alpha$ ) determined by ELISA in patient after immune response to caterpillar exposure (2–48 hrs, 1–4 weeks post exposure). Dashed line indicates the assay detection threshold based on calibration curves.

associated with lepidopterism.<sup>26</sup> Allergic reactions to Lepidoptera can be treated with removal of offending hairs, followed by topical steroids, and oral antihistamines.<sup>19</sup>

In the present study, our patient suffered a severe allergic reaction when he came in contact with the larva from the *Halysidota harrisii* Walsh. While we did not obtain serum tryptase levels in order to confirm anaphylaxis, the rapid development of contact urticaria and acute asthma are consistent with a systemic type 1 allergic response.

Our subject, an allergic asthmatic who had elevated serum IgE (>100 IU/mL), had normal immunoglobulin levels (IgG, IgM, IgA). However, his serum IgE levels slightly increased (15%), 2 hrs and then again one week post exposure. Numbers of blood CD16/56<sup>+</sup> NK precursor cells increased (60%) 12 hrs post exposure, and then decreased (65%) 48 hrs post reaction. Further, the observed decreases in absolute numbers of T and B cell subsets at one week with yet earlier decreases (48 hours post reaction) occurring for CD8<sup>+</sup>CD60<sup>+</sup> T cells and CD23<sup>+</sup> cells may relate to a cellular interplay pertaining to IgE modulation. Earlier work in our laboratory has demonstrated the presence of CD8<sup>+</sup>CD60<sup>+</sup> T cells in the placenta of twins with a family history of asthma and atopy.<sup>27</sup> Others have shown that CD23<sup>+</sup> cells, which express the low affinity receptor for IgE (Fc $\epsilon$ R2), can be activated by IgE sensitization and potentiate TNF $\alpha$  and MIP-1 $\alpha$  cytokine expression.<sup>28</sup> The stoichiometric relationship between changes in immune cell subsets, IgE/antigen specific IgE and clinical severity after caterpillar exposure remains to be determined.

Serum IFN- $\gamma$  levels were high, but IL-4 was not detected, postulating a non-IL-4-mediated allergic response. It is well known that IgE can survive without allergen contact for long periods bound to Fc receptors of mast cells or basophilic granulocytes.<sup>29</sup> It could be that our patient was presensitized to caterpillar antigen, and that exposure induced mast cell

degranulation and induction of massive IFN- $\gamma$  levels but total serum IL-4 and IgE levels remained basically low or unchanged, due to cross linking, not induction. The levels of TNF- $\alpha$  observed may result from mast cell degranulation, maybe in the early phase and late phase reactions but may also be in response to direct sensitization of IgE.<sup>28</sup> It could be that our patient demonstrated an allergic reaction to the larva, either by direct contact with hair or other proteinaceous components, which was induced by a non IgE-dependent mechanism that had a mast-cell dependent mechanism. However, the molecular mechanisms underlying the inflammatory effect of caterpillar antigen(s) remain to be elucidated.

As a case study of a single subject, this study has other limitations including the lack of confirmation of anaphylaxis as tryptase levels were not obtained, possible affects of antihistamine therapy on the immune response, and the lack of confirmation of IgE anti-larvae by classical methods (ELISA, Western blot). Finally, the lack of standardized caterpillar extract for skin testing and for the determination of specific IgE.<sup>11</sup> Nonetheless, since severe responses to caterpillar exposure are infrequent and vary based on species, continued awareness is critical to further the understanding of such responses.

In summary, our descriptive data provides detailed information on the immune response to the larvae of the sycamore tussock moth, *Halysidota harrisii* Walsh, 1864. Even though these exposures may be uncommon, it is important to recognize the potential clinical sequelae, including anaphylaxis, of contact with these larvae. Further, since the habitat of *Halysidota harrisii* Walsh, 1864 comprises eastern regions of the United States and southeastern Canada, the paucity of reports could be due to under-representation. Although our findings are based on one patient and extrapolation of the immunological findings to other patients or to other species of caterpillar would be premature, increased awareness of caterpillar exposure in atopic individuals may prove useful in identifying caterpillar sensitivities and clinical sequelae related to such exposure.

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## Disclosure

The authors declare no competing financial interest.

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