

Anaphylaxis after horsefly sting: a strange case of wasp-horsefly syndrome

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Horseflies belong to the *Diptera* order and encompass several families such as *Tabanidae*. They are hematophagous insects that can also bite humans. Their bite is painful and may provoke a local wheal and flare reaction. Systemic reactions till anaphylaxis are also described in the literature [1–3].

The so-called wasp-mosquito syndrome has already been investigated, and hyaluronidase was shown to be the cross-reactive allergen between *Hymenoptera* venom and mosquito saliva [4, 5].

We describe the case of a 45-year-old man who experienced an anaphylactic reaction (general malaise, unconsciousness, and loss of sphincter control) immediately after 3 horsefly bites on the trunk. He was immediately treated with intramuscular epinephrine 0.5 mg and betamethasone 8 mg by emergency medical personnel and then transported to the emergency department of our hospital. Here he underwent a head computed tomography (CT) scan with a negative result and was then discharged in good clinical conditions. Serum tryptase was not measured after the acute event.

After 2 months, the patient was referred to our allergy unit. He underwent intradermal tests with *Apis mellifera* (Aquagen, ALK-Abelló), *Vespula* spp. (Aquagen, ALK-Abelló), and *Polistes dominula* (Pharmalgen, ALK-Abelló) venoms. Basal tryptase as well as total and specific IgE to whole venoms (horsefly, *Polistes dominula*, *Vespula* spp., *Vespa crabro*) and to molecular components (Ves v 5, Pol d 5, Ves v 1) were assessed (Thermo Fisher Scientific, Waltham, USA).

Intradermal tests were positive for *Vespula* and *Polistes* venoms at a concentration of 100 USQ/ml and 0.01 µg/ml, respectively.

Basal tryptase was within the normal range (9.3 µg/l) while specific IgEs were positive for all the venoms tested (Table 1).

The patient was then provided an emergency action plan, including auto-injectable epinephrine. Specific immunotherapy with wasp venom was not taken in consideration because the patient had been stung by wasps several times with no systemic reactions. We also took in consideration the possibility of a systemic mastocytosis (REMA score = +3), but the patient refused to undergo a bone marrow biopsy.

Horseflies are hematophagous biting insects. Their saliva contains a wide range of molecules active on blood and immune systems, but the relevant allergens are not well characterized.

In the literature several reports describe systemic reactions to *Diptera* bites in patients with a clinical history of systemic reactions to *Hymenoptera* stings.

Some authors showed the relevant allergen of horsefly is a 69 kD salivary gland protein that can bind IgE. These authors also stated that this protein could not cross-react with relevant *Hymenoptera* allergens because of its higher molecular weight [1].

Other authors identified and characterized 2 IgE-binding proteins from the salivary glands of the horsefly *Tabanus yao*, called Tab y 1 and Tab y 2, with molecular weight of 26 and 35 kDa, respectively. Tab y 1 is an Ag 5-like protein that is the major allergen of *Vespidae*, and Tab y 2 is a hyaluronidase with a 60% sequence similarity to *Vespid* hyaluronidase (Ves v 2). These findings provide support for the presence of the wasp-horsefly syndrome [6].

Tab y 1, a 70-kDa apyrase, was identified as a new major horsefly allergen [7]. This protein is able to inhibit platelet aggregation and have antithrombotic activity. Tab y 1 may also induce basophil activation. Tab y 1 does not cross-react with other *Hymenoptera* venoms, which might explain the primary sensitizations to *Diptera* bites as previously reported [1].

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Table 1. Laboratory test results

Allergen	Result [U/ml]
Horsefly, i204	4.17
Vespula spp. (yellow jacket), i3	9.87
Vespa crabro, i75	6.17
Polistes dominula (paper wasp), i77	80.5
Ves v 1, i211	0.18
Ves v 5, i209	7.41
Pol d 5, i77	50.0

Our patient showed a primary sensitization to *Hymenoptera* venoms (Table 1) with a clinical history of local reactions, and so we think cross-reactive allergens might be involved.

No specific treatment is available for these patients, and specific immunotherapy with Vespidae venoms seem not to be effective. In fact, some patients with systemic reactions to *Diptera* bites were under immunotherapy with Vespidae venoms and the treatment was not protective. Moreover, we must take in consideration that Tab y 1 sensitization may also occur, and this is a unique *Diptera* allergen [2, 3].

So, in the case of systemic reactions to *Diptera* bites, the patient should be provided with an emergency action plan and trained to use an epinephrine auto-injector.

Further studies are needed to identify other relevant allergens of *Diptera* saliva and to improve the diagnostic tools.

Conflict of interest

The authors declare no conflict of interest.

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