

# Epidemiology, Diagnosis, and Treatment of *Hymenoptera* Venom Allergy in Mastocytosis Patients

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## KEYWORDS

- Hymenoptera venom allergy • Venom immunotherapy • Immunoglobulin E serology
- Mastocytosis

## KEY POINTS

- Hymenoptera venom allergy (HVA) is a typical immunoglobulin E (IgE)-mediated reaction caused by sensitization to 1 or more allergens of the venom, and accounts for 1.5% to 34% of all cases of anaphylaxis.
- Patients suffering from mastocytosis are more susceptible for the anaphylactic reactions to an insect sting.
- Total avoidance of Hymenoptera is not feasible, and there is no preventive pharmacologic treatment available. HVA patients should carry an emergency kit with autoinjectable epinephrine.
- Venom immunotherapy (VIT) represents a safe and effective treatment decreasing the risk of subsequent systemic reactions.
- In addition to the regular workup for mastocytosis, specific diagnostic examinations for insect venom allergy include specific IgE measurements, such as serologic IgE (sIgE) measurement and skin test with standardized allergen concentrations.
- Skin tests in mastocytosis can be complicated by systemic allergic reactions. Specific IgE might be more often negative in comparison with the insect venom allergic population with no mastocytosis.
- If standard tests are negative, basophil activation test or recombinant sIgE assessment might be helpful in making a correct diagnosis, which was studied in the general population of patients with insect venom allergy (IVA).

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- The only treatment that is able to reduce the risk of systemic reactions to IVA is allergen immunotherapy.
- Lifelong treatment is recommended in subjects with diagnosed mastocytosis and mast-cell activation syndrome.

**INTRODUCTION**

Hymenoptera venom allergy (HVA) is a typical immunoglobulin E (IgE)-mediated reaction caused by sensitization to 1 or more allergens of the venom, and accounts for 1.5% to 34% of all cases of anaphylaxis.<sup>1</sup> The severity can vary from large local reactions (a swelling >10 cm lasting up to 24 hours) to systemic anaphylaxis. Systemic reactions are classified with 4° of increasing severity according to Mueller.<sup>2</sup> The diagnostic procedures, which are mandatory for a correct prescription of venom immunotherapy (VIT), include skin-prick or intradermal tests, and serum-specific IgE assays.

The culprit insects of allergic reactions are Hymenoptera belonging to the suborder Aculeate, which includes the families Apidae, Vespidae, and Formicidae. The Apidae family comprises *Apis mellifera* and *Bombus*. The Vespidae family includes the Vespinae subfamilies (*Vespula* and *Dolichovespula* species, and *Vespa crabro*) and Polistinae subfamilies (*Polistes* species).<sup>3,4</sup> The Formicidae family is represented in the United States by the imported fire ants (*Solenopsis* species).

Total avoidance of Hymenoptera is not feasible, and there is no preventive pharmacologic treatment available.<sup>4</sup> HVA patients should carry an emergency kit with autoinjectable epinephrine in addition to antihistamines and oral corticosteroid, although the effect of the latter 2 in acute anaphylaxis is doubtful. VIT represents a safe and effective treatment that decreases the risk of subsequent systemic reactions<sup>4</sup> and improves the quality of life.<sup>5</sup> VIT is prescribed to all subjects with a clear history of systemic reaction and positive skin test or venom-specific IgE in serum.

Over the preceding years, by studying those patients with anaphylaxis, it was progressively realized that there is a preferential association between HVA and mastocytosis, a group of clonal disorders of the mast-cell lineage.<sup>6–13</sup> In addition, the risk of anaphylaxis increased with increasing levels of tryptase.<sup>13</sup> Whereas in the general population the prevalence of HVA is lower than 2%,<sup>8</sup> in patients with mastocytosis the prevalence of IVA is about 25%.<sup>7</sup> Anaphylactic reactions to an insect sting affect a substantial percentage of patients with systemic mastocytosis.<sup>6</sup> The study by van Anrooij and colleagues<sup>7</sup> shows in patients with mastocytosis that the prevalence of HVA differs according to the specific form of mastocytosis and basal tryptase level. The highest prevalence was found in patients with a tryptase level of 20.4 to 29.9 µg/L, in whom prevalence reaches 50%. On the other hand, the prevalence among patients with levels below 6.1 µg/L and above 191 µg/L is lower than 10%.<sup>7</sup> Nevertheless it is higher than the prevalence in the general population, which is lower than 2%.<sup>8</sup> The expected life expectancy of patients with the cutaneous and indolent forms of mastocytosis is similar to that of the general population.<sup>9</sup> Anaphylactic reactions (the most common being to an insect sting) and osteoporotic fractures are the most important risk factors among mastocytosis patients.<sup>9</sup> This article aims to answer the most important clinical questions raised by the diagnosis and treatment of IVA in mastocytosis patients.

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