Hymenoptera Anaphylaxis as a Clonal Mast Cell Disorder

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KEYWORDS

• Systemic mastocytosis • Monoclonal mast cell activation syndrome
• Hymenoptera venom allergy • Anaphylaxis • Tryptase • Clonal mast cell disease

KEY POINTS

- Up to 7% of adult patients with Hymenoptera venom allergy may simultaneously suffer from a clonal mast cell disease.
- Patients with clonal mast cell disease and Hymenoptera venom anaphylaxis are commonly males, without skin lesions, and anaphylaxis is characterized by hypotension and syncope in the absence of urticaria and angioedema.
- A normal value of tryptase ($\leq$11.4 ng/mL) in these patients does not exclude a mastocytosis.
- The diagnosis of a mast cell disease leads to several therapeutic consequences concerning the treatment of Hymenoptera venom allergy.
- These patients have to undergo long-life venom immunotherapy to prevent further, potentially fatal severe reactions.

INTRODUCTION

Mastocytosis is a clonal mast cell disorder (CMD) that encompasses a heterogeneous group of clonal disorders characterized by the proliferation and accumulation of mast cells (MC) in different tissues, with a preferential localization in the bone marrow (BM) and skin.[1] Subjects with mastocytosis can experience symptoms owing to a massive MC activation and release of mediators.

Systemic symptoms may include hypotension and anaphylactic shock, flushing, headache, itching, abdominal pain, dyspepsia, diarrhea, and bone and soft tissue pain.[2]

CMD includes cases not fulfilling sufficient criteria for systemic mastocytosis (SM) but showing MC clonality markers by expression CD25/CD2 on immunophenotyping

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and/or a KIT mutation at codon 816 on molecular analysis. These latter patients may have a limited, prediagnostic form of SM, also indicated as monoclonal MC activation syndrome (MMAS), but their risk of developing severe life-threatening anaphylaxis is similar to patients with SM.[2–4]

The prevalence of anaphylaxis in patients with mastocytosis is much higher than the 0.05% to 2.00% estimated frequency of anaphylaxis in the general population[5,6] and has been reported to be between 22% and 49% in adults[7–9] and between 6% and 9% in children[7,8]; discrepancies between different studies might be a result of the heterogeneity of patient cohorts, the definition of anaphylaxis, and the sensitivity of diagnostic techniques.

A wide variety of stimuli (venom, drug, or food) can trigger anaphylaxis in patients with mastocytosis, but for certain patients no eliciting factors can be identified despite a comprehensive allergy workup and, therefore, we use the term idiopathic anaphylaxis. All epidemiologic studies have shown that Hymenoptera stings represent the most common trigger of anaphylaxis in subjects with mastocytosis.[7–10]

Hymenoptera Venom Allergy

Hymenoptera venom allergy (HVA) is a typical immunoglobulin (Ig)E-mediated disease, whose clinical manifestations are the result of the MC degranulation, which is triggered by the binding of the venom allergens to specific IgE (sIgE). Severity can vary from large local reactions to systemic anaphylaxis. The reactions are classified according to Mueller's scale with 4° of increasing severity.[11] Diagnostic procedures include skin prick and intradermal tests and serum-sIgE essays.

The insects responsible for allergic reactions are Hymenoptera belonging to the suborder Aculeate, which includes the Apidae, Vespidae, and Formicidae families (Fig. 1). The Apidae family includes *Apis mellifera* and *bombus*. The Vespidae family takes in the Vespinae subfamilies (*Vespula* species and *Vespa crabro*) and Polistinae subfamilies (*Polistes* species), among which *Polistes dominulus* is widespread especially in the Mediterranean area.[12] There is no preventive pharmacologic treatment

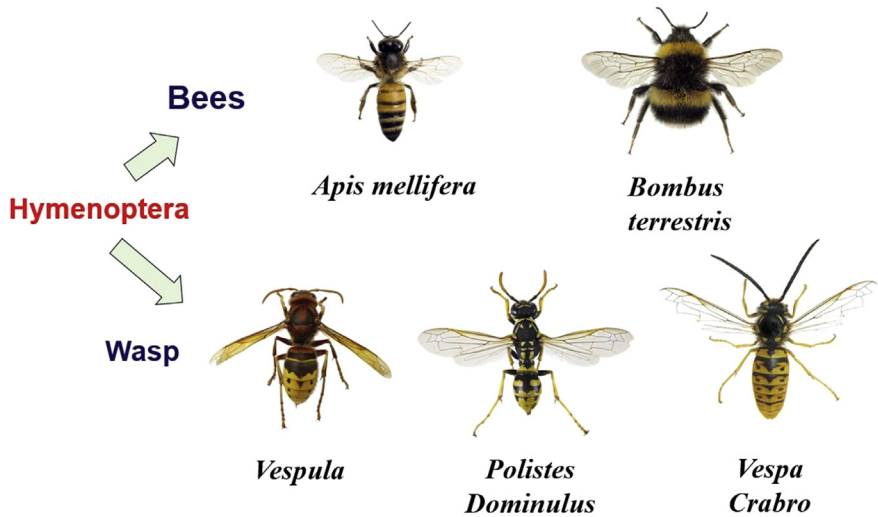

Fig. 1. Hymenoptera venom allergy and clonal mast cell disorders (CMD). (*Courtesy of* Anallergo, Scarperia e San Piero FI, Italy.)