Prevalence of Clonal Mast Cell Disorders in Patients Presenting With Hymenoptera Venom Anaphylaxis Might Be Higher Than Expected

Vázquez-Revuelta P1,*, González-de-Olano D1
1Allergy Department, Hospital Universitario Ramón y Cajal,
Madrid, Spain
*Both authors contributed equally to this manuscript and should be considered first authors

doi: 10.18176/jiaci.0233

Key words: Clonal mast cell activation syndromes. Hymenoptera venom anaphylaxis. Mastocytosis. Prevalence.


Anaphylactic reactions after hymenoptera stings are probably the leading cause of anaphylaxis in patients with mast cell disorders, especially indolent systemic mastocytosis without skin involvement (ISMs–) or with clonal mast cell activation syndrome (c-MCAS) [1,2]. According to published data, mastocytosis accounts for 1%-7% of all cases of hymenoptera venom anaphylaxis (HVA) [3]. In most patients, the anaphylactic reaction after exposure to hymenoptera venom might be the sole manifestation of their disease [2,4]. Although the confirmed diagnosis of mastocytosis requires a complete bone marrow study, the European Competence Network on Mastocytosis recommends using the so-called REMA score (Red Española de Mastocitosis [Spanish Mastocytosis Network]) as a useful screening tool for predicting the presence of clonal mast cells before the bone marrow examination is performed [5]. The REMA score analyzes 4 independent factors, namely, gender, cardiovascular symptoms, absence of pruritus/urticaria/angioedema, and baseline serum tryptase level. A score ≥2 predicts clonality with high values of specificity in patients in the absence of skin lesions of mastocytosis. This score is even more sensitive for patients with HVA [6]. Therefore, the REMA score can facilitate the diagnosis of clonal mast cell disorders [7,8].

In an effort to discover the prevalence of possible clonal mast cell disorders among patients presenting with HVA according to the REMA score, we retrospectively analyzed data from all patients who had experienced anaphylactic reactions after hymenoptera stings and were referred to the allergy department of our hospital, which is located in an urban area in the center of Spain, where the frequency of hymenoptera stings is low. During April 2017, we queried all electronic medical records of patients who had been evaluated at our department since electronic medical records were available (June 1999) until the date of the search. We used the current Boolean search software (Excalibur, Retrieval Ware/Convera, Inc.) and introduced the terms honeybee, wasp, and hymenoptera. We obtained a total of 1924 results that were carefully analyzed. Symptoms following the hymenoptera sting were recorded, and only 174 patients with hymenoptera venom anaphylaxis according to accepted criteria [9] were selected. At the time the search was made, 9 patients (6.4%) had already been diagnosed with mastocytosis after a bone marrow study. In 32 patients, clinical and analytical variables were not registered and, thus, the REMA score could not be calculated. The score was applied to the remaining patients with HVA, who were divided into 2 groups according to the result. Both groups were subsequently analyzed (Table). Our study is limited by its retrospective design.

Confirmation of the diagnosis of mast cell disorder requires a complete bone marrow study and fulfilment of diagnostic criteria for cytology, histology, and flow cytometry immunophenotyping using specific gating strategies for the detection of bone marrow mast cells that are present at low frequencies, as well as the study of the KIT mutation in purified mast cells [10]. Mast cells are infrequent in patients with ISMs– or c-MCAS, in whom HVA is, by far, the most frequent trigger of anaphylaxis [2,11]. Therefore, specialized centers with more sensitive techniques are needed to reach the final diagnosis in most cases. On this basis, the REMA score has become an extremely helpful tool that easily predicts clonality in a subset of patients who will require further specific management. In the present study, 23.2% of patients with HVA had a positive REMA score. Clinical features and gender distribution were similar to those of the mastocytosis group,

Table. Baseline Characteristics of the Population

<table>
<thead>
<tr>
<th></th>
<th>Mastocytosis (n=9b)</th>
<th>P value</th>
<th>Score ≥2 (n=33)</th>
<th>P Value</th>
<th>Score &lt;2 (n=100)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>7/9 (78)</td>
<td>NS</td>
<td>23/33 (70)</td>
<td>.03</td>
<td>49/100 (49)</td>
</tr>
<tr>
<td>Age</td>
<td>55 (30-71)</td>
<td>NS</td>
<td>47 (13-87)</td>
<td>NS</td>
<td>49 (10-78)</td>
</tr>
<tr>
<td>Total IgE, kU/L</td>
<td>73.7 (16-202)</td>
<td>NS</td>
<td>109* (0-330)</td>
<td>NS</td>
<td>191 (2-2001)</td>
</tr>
<tr>
<td>Baseline tryptase, μg/L</td>
<td>12.1 (1-17.9)</td>
<td>0.01</td>
<td>5.7 (1-10)</td>
<td>NS</td>
<td>5.2 (1-21)</td>
</tr>
</tbody>
</table>

Abbreviation: REMA, Red Española de Mastocitosis (Spanish Mastocytosis Network).

Results expressed as number of patients/total patients studied (percentage) for categorical variables and median (range) for continuous variables.

7/8 had a REMA score ≥ 2. The remaining patient had cutaneous mastocytosis.

Only 28/33 patients had total IgE determination available.
References