Venom Allergy and Mastocytosis
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Hymenoptera venom allergy (HVA) is a typical IgE-mediated disease, which clinical manifestations are the result of the degranulation of mast cells, triggered by the binding of the venom allergens to specific IgE. The symptoms of HVA range from local reactions at the site of the sting to near fatal or fatal systemic anaphylaxis. During the last decade, by studying those patients with anaphylaxis or skin disorders, it was progressively realized that there is a preferential association between HVA and mastocytosis, a group of clonal disorders of the mast cell lineage.

Mastocytosis is a heterogeneous disorder characterized by the proliferation and accumulation of MCs in the skin, BM and other tissues. These accumulation of MCs is caused by mutations in the c-kit gene (the receptor for stem cell factor, or c-Kit ligand, which is a growth factor for MCs), resulting in ligand independent activation of the c-Kit receptor and proliferation of MCs.

The data on prevalence of mastocytosis in the general population are scanty, but less than 1:100000. According to the World Health Organization, SM can also be subdivided into clinical variants: indolent SM (ISM) that represent the majority of cases; SM with an associated clonal, hematologic, non-MC lineage disease (SM-AHNMD); aggressive SM (ASM) and MC leukaemia, mast cell sarcoma, and extracutaneous mastocytoma.

Severe anaphylactic reactions after hymenoptera stings were initially described in case reports or a small series of patients with CM or SM. Of note, increased sBT is associated with a history of more severe sting reactions also in patients without SM.

Two large studies reported 19% and 5% of patients who experienced anaphylactic reaction to HV among 74 and 163 adult mastocytosis, mostly systemic demonstrating an higher incidence of HVA in MC disease. Assessment of sBT is widely considered a useful screening test for mastocytosis in patients with systemic reaction after hymenoptera, although some cases of SM and several patients with CM may present normal value (<11.4ng/mL), and an elevated sBT may be found also in other conditions (chronic urticaria, chronic renal failure, onchocerciasis or haematologic diseases not associated with the MC lineage).

The frequency of CMD in screened subjects with HVA ranged from 1% to 7.9%, higher than that in general population.

Mastocytosis and venom immunotherapy

The treatment of choice in patients with HVA is VIT. Nonetheless, the use of VIT in patients with mastocytosis remained a matter of discussion for years. In fact, some authors have suggested that anaphylactic reactions in mastocytosis are more frequently non IgE-mediated and, therefore, VIT would not be of benefit. In addition, several reports suggested an increased occurrence of side effects during VIT in patients with mastocytosis. Indeed, the most recent studies, involving large numbers of subjects, demonstrated that VIT is well tolerated and efficiently protect against further anaphylactic sting reactions.

Although most subjects well tolerate VIT, some patients may develop severe and recurrent VIT induced reactions, making difficult to reach the maintenance dose of 100 mcg. The overall incidence of side effects in patients with mastocytosis is not different from that reported in unselected patients undergoing VIT. When an adverse reaction occurs, it is recommended to repeat the last dose without further increase and to use a premedication with antiH1. A recent report described successful prophylactic treatment with omalizumab in a patient who was than able to reach maintenance dose without further side effects.

In patients with mastocytosis and HVA it is recommended that all injections are performed under medical supervision, with trained personnel and with an emergency equipment immediately available. Even if patients with mastocytosis are undergoing immunotherapy, they should always have an emergency medication set that includes EPIPEN®.
Three to 5 years of VIT induces long-term protection in most HVA patients, but in patients with mastocytosis and venom induced anaphylaxis, all the reported fatalities occurred after VIT discontinuation. Since there are no studies formally assessing the risk of discontinuing VIT in patients with severe anaphylaxis and mastocytosis, it is generally recommended that the treatment is prosecuted life-long.

Although most patients with mastocytosis are protected by VIT, a minority may develop systemic allergic symptoms after re-exposure. Usually, when a HVA patient is not efficiently protected by the 100 mcg maintenance, the dose is increased to 200 mcg or more. The same applies to patients with mastocytosis, as reported in some studies.

Some aspects of VIT treatment in patients with mastocytosis are still unclear or not sufficiently investigated. For instance, in those subjects with mastocytosis and venom positive test, but without reactions after stings, there is currently no indication on the opportunity to start a VIT course. As mentioned before, there is a subset of patients with mastocytosis and hymenoptera-induced systemic reactions, but with negative allergy tests. In these cases, it is very difficult to decide whether start immunotherapy or not, and there are very few data to support a protective effect of VIT in such a situation. Finally, it is not clear if patients allergic to one venom have an increased risk of systemic reactions to other venoms, and the natural history of HVA in mastocytosis is not known.

REFERENCES