ABSTRACT BOOK

Oral presentation session 1
Thursday, 19 September 2024

Submission number: 000017
Prefix: OA1

HYMENOPTERA VENOM ALLERGY IN PATIENTS WITH SYSTEMIC MASTOCYTOSIS: THE IMPORTANCE OF SPECIFIC IGE ASSOCIATED WITH SKIN TESTS

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BACKGROUND

In patients reporting a severe systemic allergic reaction (SAR) subsequent to a Hymenoptera sting, it is essential to make a correct diagnosis of Hymenoptera venom allergy (HVA) and to perform basal serum tryptase (BST) and further exams in case of suspicion of systemic mastocytosis (SM). HVA is indeed the most common cause of anaphylaxis in patients with clonal mast cell disorders. Current guidelines for HVA diagnosis include an accurate anamnesis, skin tests and dosing serum-specific IgE (sIgE) to Hymenoptera venoms. However sIgE levels in patients with mastocytosis could be particularly low, making the diagnosis more challenging.

METHOD

Longitudinal observational study involving a cohort of 380 patients: Group A including 97 patients with HVA and a subsequent diagnosis of SM, and Group B including 283 patients with HVA but without SM. Statistical analyses were conducted to identify significant differences between the two groups, focusing on demographic, clinical and laboratory parameters.

RESULTS

The whole study population was 73% male with a median age of 48 years old at the first SAR. A statistically significant difference between the two groups was observed regarding median BST (11.80 µg/L vs 4.50 µg/L, p <0.001) and the severity of initial reaction (3.7 vs 2.7, p <0.001). Moreover, total IgE were significantly lower in Group A (58 kUA/l vs 97 kUA/l, p=0.005). Our analysis especially focused on levels of sIgE: as expected, the values were generally lower in Group A, specifically a statistically significant difference was observed in case of sIgE for Vespula spp venom (2.30 kU/l vs 0.90 kUA/l, p=0.001) and Polistes dominulus (2.29 vs 1.03 kUA/L, p=0.025). In addition, in 5 patients of Group A with undetectable or nearly detectable levels of sIgE, skin tests resulted clearly positive helping the choice of a specific venom to perform immunotherapy.

CONCLUSION

Our data confirm that patients with SM have a greater risk of HVA and have more severe SAR. We demonstrated that HVA patients with SM have lower levels of total IgE and sIgE than HVA patients without SM (despite this being predictable, there are no data in literature). For this reason skin tests are essential in order to choose the correct venom for immunotherapy. In suspected cases of SM, in addition to REMA score, law values of sIgE could encourage the clinician to ask for further investigation. More studies are needed to establish a cut off value of total IgE below which SM is more likely.

	Group A	**Group B**	
	(N = 97)	(N = 283)	***p-value***
Sex			
0 Male	78 (80.4%)	198 (70.5%)	/
1 Female	19 (19.6%)	83 (29.5%)	/
***Age**	50 (44-61)	46 (29-57)	/
Grade of index reaction (Mueller)			
I	4 (4.1%)	62 (21.9%)	/
II	3 (3.1%)	55 (19.4%)	/
III	8 (8.2%)	65 (23.0%)	/
IV	82 (84.5%)	101 (35.7%)	/
***Basal serum tryptase ug/l**	11.80 (8.60-25.10)	4.50 (3.30-5.89)	**<0.001**
***tIgE kUA/l**	57.90 (26.40-107.50)	97.10 (43.10-260.00)	**0.005**
***sIgE Ape**	1.88 (0.30-9.00)	7.20 (0.30-9.00)	0.121
***sIgE Bombo**	0.74 (0.30-0.90)	0.90 (0.30-0.90)	0.084
***sIgE Vespula spp**	0.90 (0.45-2.52)	2.30 (0.85-7.44)	**0.001**
***sIgE Vespa crabro**	0.59 (0.30-0.90)	0.89 (0.30-1.59)	0.247
***sIgE Polistes dominulus**	1.03 (0.42-4.74)	2.29 (0.73-9.22)	**0.025**

*Median (I-III quartile)

Demographic, clinical and serological parameters of Group A and Group B.

CONFLICTS OF INTEREST

The authors did not specify any links of interest.

Submission number: 000015
Prefix: OA2

PROSPECTIVE COMPARISON OF THE EFFICACY OF 3 MONTH EXTENDED VENOM IMMUNOTHERAPY (VIT) ADMINISTRATION IN PATIENTS WITH MASTOCYTOSIS VERSUS CONVENTIONAL TREATMENT

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BACKGROUND

Hymenoptera venom allergy (HVA) is a potentially life-threatening condition. One of the major risk factors for severe hymenoptera sting reactions is mastocytosis, the only therapy that prevents severe reactions in HVA patients is VIT. In accordance with the position paper of the EAACI, following the induction phase a maintenance dose of 100 mcg every four weeks is given for the first year, from the second year the interval may be extended to 6 weeks, after the third year it may be extended to 8 weeks. Currently, there is a lack of data on the optimal duration therapy in subjects with mastocytosis, in this patients, VIT should be prolonged indefinitely. Consequently in these patients adherence to VIT is significantly diminished, therefore we conducted this study to evaluate the efficacy of extending the timing of administration.

METHOD

Multicentric prospective observational study of patients with a diagnosis of systemic mastocytosis (SM) and HVA undergoing VIT. The efficacy of maintenance dose administered every 12 weeks (group A) versus 4-5 weeks (group B) was evaluated by comparing the risk of systemic reactions after repuncture between the two groups.

RESULTS

The study population included 191 patients with SM who started VIT between 1992 and 2014. 104 patients belongs to group A, with a maintenance interval of 4 weeks for the first year, 6 weeks from the second year, 8 weeks after the third year than 12 weeks from the end of the fifth year. Whereas, a total of 87 patients in group B with maintenance dose interval every 4-5 weeks. After the fifth year of VIT, 51 patients of group A were re-stung: 47 had no reaction, 2 RLE, and 1 severe reaction (Muller 4). In group B, 29 patients were re-stung: 17 had no reaction, 6 RLE and 4 severe reactions (Muller 4). There is no statistical difference in the VIT efficacy between the two groups of patients.

CONCLUSION

VIT has changed the medical history of patients with HVA and mastocytosis. Our data demonstrate the efficacy and safety of prolonging the interval between venom doses , this improves adherence to therapy in patients with mastocytosis, who to date continue VIT for life.

CONFLICTS OF INTEREST

The authors did not specify any links of interest.

Submission number: 000020
Prefix: OA3

SELECTION OF THE BEST COMMERCIAL IMMUNOTHERAPY THROUGH CAP INHIBITION IN PATIENTS WITH ANAPHYLAXIS DUE TO VESPA VELUTINA

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BACKGROUND

The *Vespa velutina nigrithorax* is an invasive wasp species in Western Europe and Spain, prevalent along the northern coast of Spain and Catalonia. Stings from *Vespa velutina* are a significant cause of hymenoptera venom-induced anaphylaxis in this geographical area. Nevertheless, diagnosing hypersensitivity to *Vespa velutina* is challenging due to the limited availability of specific skin test extracts and the low prevalence compared to other species.

Objective: To optimize immunotherapy in patients with anaphylaxis due to Vespa velutina among the commercially available options using the CAP inhibition technique.

METHOD

Materials and Methods: The allergic sensitization profile was studied *in vitro* [total IgE, specific IgE (sIgE) to complete extracts, molecular components including CCDs, specific IgG4 (sIgG4), and CAP inhibition] in patients diagnosed with anaphylaxis due to *V. velutina* venom allergy and studied in the Allergy Department of Hospital Vall d'Hebron between 2021-2024. A total of 41 patients from Galicia, Catalonia, Asturias, the Basque Country, and Navarra were included.

RESULTS

A total of 43 patients (36 men/5 women) diagnosed with anaphylaxis due to *Vespa velutina* stings were included. Most patients, 39/41 (95%), presented with a Müller grade III-IV / 3 EAACI reaction. Based on the in vitro tests, the recommendation for hymenoptera venom immunotherapy was as follows: 20 (46.51%) patients with a single *Vespula* venom immunotherapy, 5 (11.63%) patients with a single *Polistes dominula* venom immunotherapy, 8 (18.60%) patients with double immunotherapy [*Vespula* associated with *Polistes dominula*], 5 (11.63%) patients with a single *Vespa velutina* venom immunotherapy, and 4 (9.30%) patients with single immunotherapy that could be either *Vespula* or *Velutina venom*, and finally, 1 patient (2.33%) with an *Apis mellifera* immunotherapy.

CONCLUSION

The in vitro study allows for the best commercially available immunotherapy treatment for Vespa velutina venom allergic patients.

CONFLICTS OF INTEREST

The authors did not specify any links of interest.

Oral Presentation Session 2
Saturday, 21 September 2024

Submission number: 000027
Prefix: OA4

STUDY OF THE IMMUNE SYSTEM CHANGES DURING BEE VENOM IMMUNOTHERAPY

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BACKGROUND

Currently, the only reliable method to assess the effectiveness of bee-venom immunotherapy (BVIT) is the sting challenge. Our objective was the identification of possible immunological and cellular biomarkers of tolerance.

METHOD

Blood samples were drawn from 17 patients prior to the start of BVIT (T0) and after 1 (T1), 3 (T3) and 5 (T5) years, when sting challenges were performed. We analysed specific immunoglobulins E and G4 against *Apis mellifera* venom and its components and kynurenine levels. A basophil activation test with bee-venom extract at 0.1 and 1 µg/mL and an analysis of T-regulatory subpopulations were performed.

RESULTS

The study population included 13 (76%) men and 4 (24%) women (mean age 50±13).

A reduction in sIgE levels accompanied by an increase in sIgG4 levels was observed throughout the BVIT course with statistically significant differences: *Apis mellifera* venom (sIgE, $p < 0.001$; sIgG4, $p < 0.001$), Api m 1 (sIgE, $p = 0.016$; sIgG4, $p < 0.001$), Api m 2 (sIgE, $p = 0.005$; sIgG4, $p = 0.002$), Api m 3 (sIgG4, $p = 0.003$), Api m 5 (sIgG4, $p = 0.035$) and Api m 10 (sIgE, $p = 0.011$). Kynurenine levels increased significantly at T1 (T0 vs T1, $p < 0.001$), but subsequently decreased.

The percentage of degranulating basophils (CD63+) was significantly reduced over the course of BVIT (T0: 53.3%; T1 22.1%; T3: 8.7% and T5: 10.2%; p = 0.001). Regarding T-regulatory cells, the population of Helios- cells increased in T1 (T0 vs T1, p = 0.039); the Ki67+ population suffered a significant increase from T3 (T0 vs T3, p < 0.001); and the CD39+ population increased in T3 although they subsequently decreased. No statistically significant differences were found in the proportion of total T-regulatory and CTLA-4+ cells. All the patients tolerated the sting challenges.

CONCLUSION

BVIT causes a desensitization of basophils and a series of changes in the immune system which may constitute possible candidates for immunotolerance biomarkers. More studies are needed to clarify the relationships between them.

CONFLICTS OF INTEREST

The authors did not specify any links of interest.

Submission number: 000011
Prefix: OA5

EVALUATION OF THE NEGATIVE PREDICTIVE VALUE OF THE STING CHALLENGE TEST

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BACKGROUND

The sting challenge test (SCT) is considered the most reliable method for evaluating the effectiveness of venom immunotherapy (VIT). However, there has been controversy surrounding its negative predictive value (NPV). The objective of this study is to evaluate the NPV of the SCT.

METHOD

A retrospective observational study was conducted on patients who underwent SCT, gathering data on patient filiation, diagnosis, immunotherapy, SCT outcomes, and tolerance to field sting (FS).

RESULTS

A total of 261 patients were included, and 372 SCT were recorded. The majority of the patients (75.1%) were men and 20% beekeepers. The degree of the sting reaction was severe in 33.4%, and 7.7% were diagnosed with mastocytosis. The results of the complementary tests are presented in Table 1. The culprit insect of the reaction was *Apis mellifera* in 48.7%, *Polistes dominula* in 36.8%, *Vespula spp*. in 2.7%, and *Polistes dominula* plus *Vespula spp*. in 10,7%. SCT were performed with *Apis* in 61.6% of the overall tests, *Polistes* in 34.1% and *Vespula* in 4.3%. The majority (95.7%) of the SCT were negative. On the other hand, 146 patients (56.2%) experienced 306 field

stings and 95.1% were negative. Among these patients, 137 had a negative SCT and 130 of them had a negative FS, resulting in a 94.9% of NPV of the test. Of the patients who experienced FS, 9 had a positive SCT and only 3 of them had a positive FS, resulting in a positive predictive value of 33,3%. Risk factors for a positive SCT were also analysed finding that the severity of the initial reaction, bee venom and a lower age were associated with a positive SCT. However, a high ratio of Api m 10 at diagnosis or the diagnosis of mastocytosis were not risk factors for a positive SCT in our study.

CONCLUSION

SCT is a safe procedure, and its high negative predictive value reinforces the usefulness of this test in evaluating the effectiveness of VIT.

Laboratory values at diagnosis (Median (IQR))	
Total IgE (U/mL)	61 (30-203)
Tryptase (mcg/L)	4.91 (3.69-6.79)
Apis mellifera allergic patients (n=127)	
sIgE *Apis mellifera* (kU/L)	10.1 (3.54-27.4)
sIgE Api m 1 (kU/L)	2.7 (0.94-15)
sIgE Api m 2 (kU/L)	0.02 (0.01-0.11)
sIgE Api m 3 (kU/L)	0.13 (0.01-0.27)
sIgE Api m 5 (kU/L)	0.1 (0.02-1.26)
sIgE Api m 10 (kU/L)	1.28 (0.1-13.27)
Polistes dominula allergic patients (n=96)	
sIgE *Polistes dominula* (kU/L)	7.02 (3.38-21.07)
sIgE Pol d 5 (kU/L)	0.39 (0.08-3.2)
Vespula spp. plus *Polistes dominula* allergic patients (n=35)	
sIgE *Vespula* spp. (kU/L)	5.61 (1.78-10.23)
sIgE Ves v 1 (kU/L)	0.3 (0.1-4.77)
sIgE Ves v 5 (kU/L)	2.3 (0.98-9.9)

Table 1. Laboratory values at diagnosis.

Table 1. Laboratory values at diagnosis

CONFLICTS OF INTEREST

The authors did not specify any links of interest.

Submission number: 000066
Prefix: OA6

VESPA CRABRO VENOM: ACCURACY OF COMMON DIAGNOSTIC TESTS

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BACKGROUND

The diagnosis of European hornet (*Vespa crabro*, VC) allergy is challenging because patients who report stings are rarely able to identify the species; however, accurate identification is important for correct immunotherapy. Diagnostic work-up includes skin testing (ST) with VC extract and *in vitro* tests such as specific IgE (sIgE) and basophil activation tests (BAT). This study compares ST, sIgE and BAT for VC venom in patients with suspected hymenoptera allergy.

METHOD

We analyzed data from patients who underwent ST, BAT and sIgE for VC venom in our center between March 2019-March 2024. We performed prick tests (PT) at 100 mcg/ml, followed by intradermal tests (ID) at 0.1 mcg/ml and, if negative, at 1 mcg/ml. Sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) of BAT and sIgE relative to ST was calculated. McNemar's test was used to assess differences in agreement rates between BAT vs. sIgE in relation to ST.

RESULTS

A total of 60 patients were included. Twenty-nine (48.3%) had a positive skin test, of these 22 had positive BAT and 28 had positive sIgE. The remaining 31 patients (51.7%) had negative ST, of which 30 had negative BAT and 20 had negative sIgE. Overall agreement between BAT and ST vs. sIgE and ST was not significantly different (86.7% vs. 80%, p=0.327). However, negative BAT showed higher agreement vs. negative sIgE for negative ST (96.77% vs 64.52%, p=0.0094). Conversely, positive sIgE showed higher agreement vs. positive BAT for positive ST, but this difference did not reach statistical significance (96.55% vs 75.86%, p=0.077). Sensitivity, specificity, PPV, and NPV of BAT and sIgE relative to ST are shown in Table 1.

Of 22 patients with positive ST and positive BAT, 8 had positive PT, 9 had negative PT but positive ID at 0.1 mcg/mL and 5 had positive ID at 1 mcg/mL. Median BAT in these three groups progressively decreased (79.2%, 51.6% and 26.6%, respectively). Overall median BAT in patients with positive ST was 60.2 (IQR 29.3 – 85.9); median sIgE in patients with positive ST was 0.97 (IQR 0.44 – 1.35).

CONCLUSION

According to preliminary data, both BAT and sIgE showed high concordance with ST for VC in patients with suspected hymenoptera allergy. BAT had higher specificity and PPV, implying that it is of more value in confirming positive results on ST, whereas sIgE was more sensitive and had a higher NPV, suggesting greater utility in confirming negative ST. The low reactivity of sIgE even in the presence of clear skin test positivity may be due to underrepresentation of major allergens in VC extracts, and advances in molecular allergology may improve diagnostic accuracy. Further studies are warranted to corroborate these results.

Test	Sensitivity	Specificity	PPV	NPV
BAT	75.86% (22/29)	96.77% (30/31)	95.65% (22/23)	81.08% (30/37)
sIgE	96.55% (28/29)	64.52% (20/31)	71.79% (28/39)	95.24% (20/21)

Table 1: Sensitivity, specificity, PPV, and NPV of BAT and sIgE relative to ST

Table 1: Sensitivity, specificity, PPV, and NPV of BAT and sIgE relative to ST

CONFLICTS OF INTEREST

The authors did not specify any links of interest.

Poster discussion Session - Group 1 – Topic: Diagnosis of Hymenoptera venom allergy
Friday, 20 September 2024

Submission number: 000064
Prefix: P01

THE ROLE OF API M 5 IN THE COMPONENT RESOLVED DIAGNOSIS FOR HYMENOPTERA VENOM ALLERGY

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BACKGROUND

Hymenoptera venom-allergic patients can develop severe or even fatal anaphylaxis after a single sting and venom-specific immunotherapy (VIT) is the only treatment capable of protecting them. Since it, a proper prescription of VIT is mandatory and this is possible mainly thanks to component resolved diagnosis (CRD). Particularly, honeybee venom (HBV) and yellow jacket venom (YJV) share several homologous allergens, so CRD is useful in distinguishing primary and double sensitization in HBV and YJV sensitized patients. Although, some aspects of CRD remain to be solved, especially the identification of reliable markers and of particular interest is the role of Api m 5. Sensitization to Api m 5 was found in 16-70% of HBV-allergic patients but Api m 5 shares sequence identity of 53-54% to Ves v 3 and Pol d 3 resulting in high cross-reactivity. These considerations prevent the use of Api m 5 as a marker allergen and the aim of this study is to support this hypothesis with our data.

METHOD

Retrospective observational study in a cohort of 76 double-sensitized (DS) to HBV and YJV patients who underwent VIT only to one of the venoms. Data regarding laboratory exams, skin tests and clinical history were collected from medical records.

RESULTS

76 patients showed DS to the whole venom of HB and YJ (positive cut-off > 0.35 kU/L). 49 of them underwent VIT with YJV (group A), while 27 with HBV (group B). In the group A, 42 patients (85.7%) tested positive both to Api m 5 and Ves v 5 with an average concentration respectively of 7.49 kU/L and 39.27 kU/L. Two (4,08%) patients were positive to Api m 5 and negative to Ves V 5 and underwent VIT with YJV relying on skin test and identification of the culprit insect and resulted protected to subsequent stings. In the group B, 16 patients resulted

positive to Api m 5 and Ves v 5 with an average concentration respectively of 6.85 kU/L and 0.70 kU/L. Two patients came out negative to Api m 5 and positive to Ves v 5 but started VIT with HBV relying on skin test and identification of the culprit insect.

CONCLUSION

We verify that Api m 5 can not be considered a reliable marker to confirm neither to rule out primary sensitization to HBV. Thus, the prescription of the correct VIT in double sensitized patients should not be based on Api m 5.

CONFLICTS OF INTEREST

The authors did not specify any links of interest.

Submission number: 000045
Prefix: P02

INVESTIGATION OF THE INHIBITORY EFFECT OF HIGH ALLERGEN DOSES ON BASOPHILS DEGRANULATION IN PATIENTS ALLERGIC TO HYMENOPTERA VENOM

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*Presenting author: A. Starosz

BACKGROUND

Allergy to Hymenoptera venom (bee and wasp predominantly) affects up to 7.5% of the European population. Basophils activation is an effective diagnostic parameter in determining hyperreactivity of patients to specific allergens. However, based on our own experience a specific range of allergen concentrations is required to achieve reliable sensitivity of the assay. Interestingly, application of doses used subcutaneously in venom immunotherapy (VIT) inhibited blood basophils reactivity, creating false negative results. To date, there is no data on such phenomenon or its underlying mechanism. Here, we aimed to evaluate of the blood basophils' response to high allergen concentrations used in ultra-rush protocol of bee/wasp venom allergic patients' immunotherapy.

METHOD

Peripheral blood from 40 bee/wasp venom-allergic patients were collected. BAT (basophil activation test) was used to assess basophils' reactivity to specific allergens. Degranulation and activation of basophils based on the CD63 and CD203c expression, together with absolute numbers, morphology and viability of the cells, were evaluated with flow cytometry.

RESULTS

Exposure to specific allergen at 500ng/ml significantly activated blood basophils in subjects with confirmed hyperreactivity in context of CD63 and CD203c levels. However, application of 40-fold higher concentrations (used routinely in venom-specific immunotherapy) diminished the previously observed effects. Investigation of marker constitutively expressed also in non-atopic

healthy patients (CD203c) revealed that such phenomenon is strictly limited to allergic patients. We excluded influence of apoptosis or cytotoxicity since cell morphology and caspase-3 levels remained unchanged in samples stimulated with a high dose of the allergen.

CONCLUSION

For the first time, we demonstrated the concentration-dependent inhibitory effect of the specific Hymenoptera allergens on basophil activation. Further research is required to establish mechanism of that phenomenon. Obtained results underline BAT assay's usefulness in allergy diagnostics and monitoring; however, testing dose should be cautiously selected.

CONFLICTS OF INTEREST

The authors did not specify any links of interest.

Submission number: 000030
Prefix: P03

VARIATION OF SPECIFIC IGG AND IGG4 TO HYMENOPTERA VENOMS DURING VIT INDUCTION

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BACKGROUND

Systemic allergic reactions (SR) to Hymenoptera stings may occur in a significant proportion of the population (up to 5% general population, up to 32% of beekeepers). These reactions can be fatal and may lead to quality of life impairment for fear of further systemic reactions. Venom immunotherapy (VIT) is the elective treatment for patients who have had a SR to an insect sting, after assessment of IgE sensitisation (with in vivo and/or in vivo testing). Whereas the clinical efficacy of VIT is well documented, its molecular mechanisms are incompletely understood. Yet, it would be desirable to determine its clinical efficacy using laboratory parameters.

METHOD

We studied the changes in sIgG and sIgG4 serum levels in a cohort of 55 patients undergoing VIT with modified rush protocol in our Allergology unit, from april 2023 until may 2024. The cohort had a mean age of 47,5±15.3 years (median 49), 31% females, all Caucasians. Thirty-five (63,6%) patients underwent VIT for Yellow Jacket venom, 12 (21,8%) for Bee and 8 (14,5%) for Paper Wasp. We collected blood samples at the beginning and at the end of the VIT induction and dosed sIgG and sIgG4 at baseline (first induction date) and at the ninth and last day of induction (time 9). The method used for IgG and IgG4 dosing was ImmunoCAP (FEIA, Thermo Fisher Scientific Inc.).

RESULTS

We compared the mean values of IgG and IgG4 serum titres, specific for each venom used diring VIT (sIgG and sIgG4), at T1 and T9.We then stratified the analysis on the basis of the venom used, observing an increase in the mean values of sIgG and sIgG4 as shown in the table.

sIgG (mgA/L)	T1	T9	delta	St. dev. delta	p (T test for paired samples)
Overall	4,9	13,4	8,5	7,2	<0,000
Yellow Jacket	4,6	14,9	10,3	7,6	<0,000
Bee	6,6	14,6	8	5,5	<0,000
Paper Wasp	3,6	5,2	1,5	2,4	0,113
sIgG4 (mgA/L)	T1	T9	delta	St. dev. delta	p (T test for paired samples)
Overall	1,9	7	5,1	6,1	<0,000
Yellow Jacket	2,4	7,7	5,3	6,2	<0,000
Bee	1,3	8,9	7,6	6,8	0,003
Paper Wasp	0,4	1,1	0,7	0,6	0,022

CONCLUSION

We observed a significant increase in serum levels of sIgG and sIgG4 in the whole cohort and in the subgroups of patients undergoing VIT for different venoms. Our findings corroborate the limitated data available on this topic in the literature. It remains to be determined whether the increase in serum titres of sIgG and sIgG4 may be a marker of efficacy of VIT on the future risk of allergic reactions.

CONFLICTS OF INTEREST

The authors did not specify any links of interest.

Submission number: 000032
Prefix: P04

CLINICAL AND LABORATORY ASPECTS IN HORNET'S VENOM ALLERGY: DESCRIPTION OF A COHORT OF 38 PATIENTS FOLLOWED BY ALLERGY CLINIC IN CA'FONCELLO HOSPITAL, TREVISO

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BACKGROUND

Allergic reactions to hymenoptera stings range from mild to severe systemic reactions. VIT protects up to 98% of treated patients from reactions with new stings. A correct diagnosis and identification of the venom causing the allergic reaction is essential to make this therapy effective. In 38/220 patients of our Allergy Clinic in Ca'Foncello Hospital (Treviso) a VIT for hornet's venom was

started. The purpose of this study is to describe clinical and laboratory characteristics of patients with a diagnosis of hornet's venom allergy.

METHOD

Diagnosis of hornet's allergy was based on IgE specific assays, intradermal skin tests and anamnesis with possible identification of hymenoptera species responsible for allergic reaction. Laboratory and clinical data were retrospectively collected and analyzed using descriptive statistics and statistical significance tests. Allergic reactions were classified according to Mueller grading system.

RESULTS

35/38 (92%) patients are male. The referral reason was a type IV allergic reaction for 27/38 patients (71%). There is not a significant association between this grade of reaction and levels of serum tryptase > 8 ng/mL using Chi-Square Test (p= 0.221). Median IgE level to hornet's extract is 1.48 kU/L. IgE levels to Polistes (median 8.31 kU/L) and Vespula (median 8.35 kU/L) extracts are higher than IgE to hornet's extract respectively in 32/35 and 32/36 patients. IgE to Pol d 5 (median 9.21 kU/L) and Ves v 5 (median 8.04 kU/L) are higher than IgE to hornet's extract respectively in 27/28 and 25/29 patients. Interestingly, 8/11 patients are sensitized to Api m 5 (median 1.33 kU/L) without positive results to others bee's molecules.

CONCLUSION

Most of patients with hornet's venom allergy are male and show a type IV allergic reaction. Type IV reactions are not associated to high serum tryptase, so they could be related to the high amount of injected venom. Serological sensitization pattern in these patients usually includes IgE to Polistes and Vespula extracts and molecular components, suggesting that hornet's venom allergic patients could be sensitized to homologous molecules between different Vespidae species. In vitro tests may have a poor sensitivity in dosing IgE to hornet's venom considering the lower levels of antibodies to hornet than IgE level to other Vespidae species in almost all patients of this cohort. Finally, dosing IgE to Api m 5 may be a useful diagnostic tool in identifying hornet's venom allergy.

CONFLICTS OF INTEREST

The authors did not specify any links of interest.

Submission number: 000067
Prefix: P05

POTENTIAL BIOMARKERS TO MONITOR EARLY TOLERANCE INDUCTION IN HYMENOPTERA VENOM BASED IMMUNOTHERAPY

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BACKGROUND

Tolerance can be achieved in allergic patients upon administration of increasing doses of allergen over time. This so-called immunotherapy has shown to cause long-term tolerance induction by upregulating regulatory T Cells and specific IgG against the antigen. The regulatory mechanism leading to short-term tolerance induction remains unknown by large. Knowledge of this mechanism would help in better understanding of the rush and ultrarush immunotherapy, where tolerance is achieved within hours or days. Our study aims to investigate this mechanism by checking the high affinity receptor (FcεRI) density on the surface of basophil granulocytes and the soluble isoform in the serum, as well as the activation of basophils in patients undergoing immunotherapy for hymenoptera venom.

METHOD

We collect patient blood before and six hours after the initial doses of immunotherapy to check the reactivity of basophils using a FACS-based standardized basophil activation kit. The amount of soluble FcεRI in the serum is detected by ELISA and the surface density of FcεRI on basophils is determined by quantitative FACS analysis.

RESULTS

Already six hours after the start of immunotherapy we could show in eight patients a median increase in the amount of IgE-unoccupied FcεRI on the basophils of +3.2% (IQR -3.6 to +32.0). and an overall surface FcεRI (whether IgE-occupied or not) median decrease of -4.9% (IQR -11.2 to +6.2). In the preliminary analysis we saw no changes of the activation of basophils within the short period of time.

CONCLUSION

Preliminary results suggest that fast tolerance induction in immunotherapy might be caused by a general decrease of FcεRI surface expression as well as an increase in IgE-free FcεRI on basophils. In the ongoing study, we plan to increase patient numbers and to check for changes of soluble FcεRI in the serum, which previous studies showed to behave as an endogenous omalizumab.

CONFLICTS OF INTEREST

The authors did not specify any links of interest.

Submission number: 000023
Prefix: P06

ANALYSIS OF RELATIONSHIPS BETWEEN WHEAL SURFACE, SPECIFIC IGE AND AGE THROUGH MACHINE LEARNING IN PRE AND POST IMMUNOTHERAPY INTRADERMAL REACTIONS

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BACKGROUND

Venom immunotherapy (VIT) is the only treatment that could prevent further systemic reactions in patients with hymenoptera venom allergy (HVA). In literature, different percentages of effectiveness are reported depending on the type the considered insect, from the 77%-84% of patients treated with honeybee venom to the 91%-96% of patients receiving vespid venom. Several immunological mechanisms have been proposed to account for the clinical efficacy of VIT such as specific IgE decline, IgG4 induction and specific Treg cells induction. Moreover, it has been previously demonstrated that aging has an impact on the total IgE levels.

The aim of this study is to analyze through a cluster analysis approach the changes in IgE immune response after a 3-year course of VIT.

METHOD

A database with 30 patients followed by the allergology unit of the Polyclinic hospital in Bari, each representing a combination of patient age, specific IgE levels and wheal surface, has been analyzed. A Semi-Automatic Method (SAM), developed at the Allergy and Immunology Unit "M. Albanesi", with a superior accuracy in quantifying wheals resulting from skin prick tests and intradermal reactions has been used to converte color and shape variations into precise quantitative data. The collected data reflects the results of the first and last post-immunotherapy tests for intradermal reactions related to hymenoptera venom. In order to ensure that all the three variables (wheal surface, specific IgE and age) with different units of measurement, carry equal weight, the data have been normalized, prior to plot these values in a three-dimensional graph (cluster analysis).

RESULTS

The analysis of the 3 variables in a 3D graph show that pre immunotherapy data can be divided into two different clusters (aka C_1 and C_2) with 2 separated centroids. Interestingly after 3 years immunotherapy course the data were gathered into a single cluster with 1 single centroid (C_3). Pre-immunotherapy the majority of patients presented a type 4 reaction according to Mueller's classification, while post immunotherapy those ones, that experienced re-stings, presented only localized reactions without systemic or other organ system involvement. All patients with a high susceptibility to severe allergic reactions have experienced a significant reduction in their allergic reactivity after receiving immunotherapy treatment, in both young and adult subjects.

CONCLUSION

The cluster analysis revealed the immune modulation of IgE response induced by VIT. In particular, a homogeneous immune response seems to be obtained via VIT. Furthermore, the purpose of the project is to influence future clinical guidelines and therapeutic strategies, tailoring treatment based on individual patient characteristics.

CONFLICTS OF INTEREST

The authors did not specify any links of interest.

Submission number: 000021
Prefix: P07

THE IMPACT OF THE COMPONENT-RESOLVED DIAGNOSIS ON VENOM IMMUNOTHERAPY PRESCRIPTION

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BACKGROUND

In Hymenoptera venom allergy (HVA) history is often unreliable, and specific IgE (sIgE) to whole venom preparations do not allow for discrimination between primary sensitization and cross-reactivity in case of double-positivity to vespid and bee venom. We aimed to estimate the extent to which the component-resolved diagnosis (CRD) affected the selection of venom immunotherapy (VIT) in our patients.

METHOD

We included a total number of 23 HVA patients receiving VIT. sIgE to bee and vespid (yellow jacket and hornet) venom extracts, rApi m1, rApi m10, rVes v1, rVes v5 were determined. A more sensitive cutoff of ≥0.1 kU/L was used to confirm sensitization. Medical history was reviewed with regard to the culprit insect.

The outcomes included the difference in proportions of patients with double-positivity based on extracts and CRD (true double-positivity), and the number of patients in whom VIT prescription was affected by CRD.

RESULTS

Out of 23 HVA patients, 12 (52.2%) had positive sIgE to both bee and vespid venom extracts. After performing CRD, true double-positivity was found in only five (21.7%) patients (group 1), while the remaining seven patients were shown to be sensitized to a single venom only (group 2).

In group 1, adding the second venom for VIT was recommended in two patients, while in the other three patients, we did not opt for changing the prescription so far, due to the convincing history of tolerance to recurrent stings of the other Hymenoptera insect.

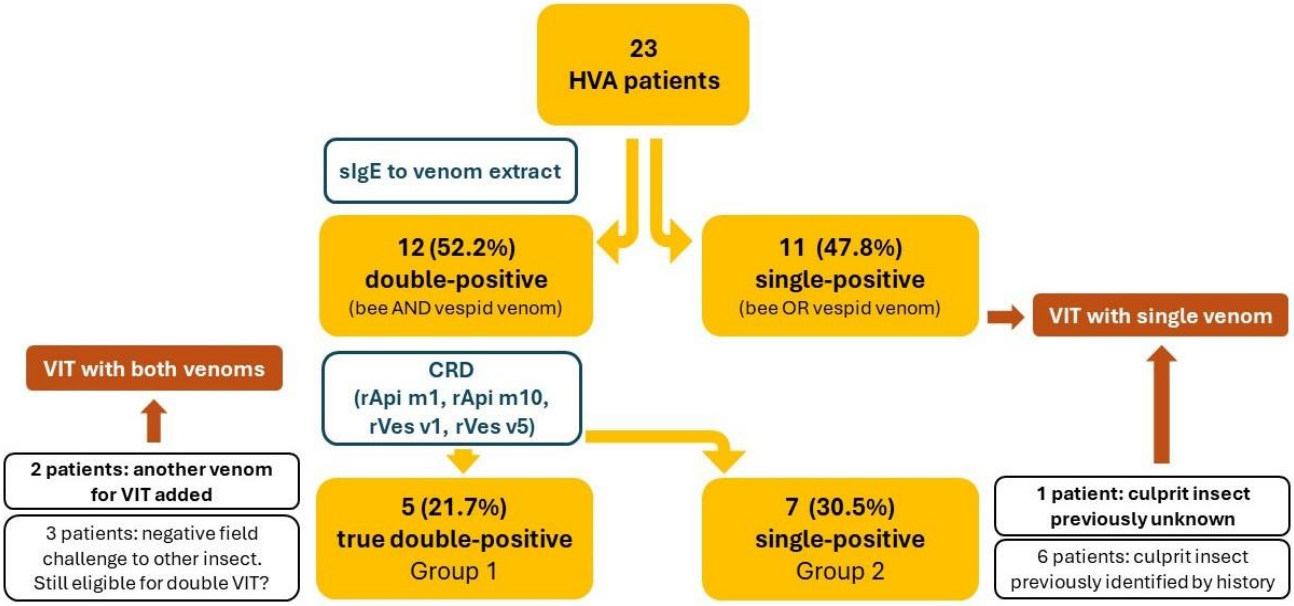
In group 2, CRD was able to determine the clinically relevant venom in a single patient with an inconclusive history. In the remaining six patients, in whom the culprit insect could be identified by history with a high level of certainty, the initial choice of VIT was affirmed.

CONCLUSION

In our cohort, CRD affected the selection of VIT in a relatively small but significant proportion (13%) of HVA patients. However, another three (13%) patients with true double-sensitization may also be considered eligible for treatment modification by adding another venom. As many patients with HVA are sensitized to more than one extract, CRD is essential in establishing precise diagnosis and guiding treatment.

Results

Results



CONFLICTS OF INTEREST

The authors did not specify any links of interest.

Submission number: 000046
Prefix: P08

SISTEMIC REACTION TO WASP STING WHITH IGE DEFICIENCY

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BACKGROUND

A 57 year old woman, who lives in a rural area of Catalonia, had an insect bite on her leg while looking at a wasp nest on her balcony in october 2022

After 10 minutes she presented symptoms of pharyngeal foreign body sensation, pharyngeal pruritus, dyspnea, sweating, vomiting, and skin erythema. The patient consults the primary care

health center receiving treatment with adrenaline 0.3 mg, hydrocortisone 100 mg, dexchlorpheniramine 5 mg and methylprednisolone 40 mg. No pharyngeal edema was evident on physical examination. Vital signs SPO2: 99%, BP 122/88mmHg, HR 102 bpm. The patient had previously suffered stings (wasps and bees) without any symptoms.

She had a clinical history of colon adenocarcinoma in 2021, treated with surgery and quimiotherapy. At the end of the second infusion of oxaliplatin she presents dyspnea and vomiting. Despite premedication in a new cycle she presents hypotension(78/55), Receiving treatment with adrenaline.

METHOD

Skin tests for hymenoptera venom (polistes, vespula and apis) were negative on 2 occasions.

Blood test analysis: total IgE <2 IU/ml, Tryptase 4.51 µg/L, IgE <0.1 for (vespula spp, polistes dominula, Ves v 5, Ves v 1, Pol d 5)

Total IgE is determined with the specific IgE reference curve and a value of 0.26 U/ml is obtained.

REMA Score <2.

RESULTS

With the suspicion of an IgE deficiency, a basophil activation test was requested, being positive mainly for polistes and in a lower degree for vespula.

She was diagnosed with a severe systemic reaction due to Polistes allergy and an IgE deficiency. Specific immunotherapy to polistes dominula was indicated with no reactions

CONCLUSION

- The availability of the basophil activation test allows to the diagnosis in this case, with a deficit of total IgE.

-Typical diagnostic tests are unable to confirm sensitization, due to the lack of total IgE.

-Total IgE deficiency is not included in the currrent Classification of primary immunodeficiencies

CONFLICTS OF INTEREST

The authors did not specify any links of interest.

Submission number: 000016
Prefix: P09

CONTROVERSY IN THE APPLICATION OF A STING CHALLENGE TEST IN A PATIENT WITH PRESUMED DOUBLE VENOM HYPERSENSITIVITY- A CASE REPORT

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BACKGROUND

A 55-year-old female patient was referred to our tertiary allergy center to continue bee venom immunotherapy (VIT) initiated 1.5 years ago. Her history included a severe allergic reaction following an insect sting three years prior, characterized by generalized urticaria, dyspnea, weakness, and nausea. Immediate treatment with intramuscular epinephrine by an emergency medical team led to a full recovery. Since then, she has neither experienced another episode of anaphylaxis nor been stung again.

METHOD

Initial diagnostic tests included skin tests for bee and wasp venom, both of which were positive at concentrations of 0.0001 µg and 0.001 µg, respectively. Molecular diagnostics were negative for all extracts and components. To determine the appropriate course of treatment, a live sting challenge was conducted. Both species were tested and induced local reactions, as well as non-specific symptoms such as lip and tongue numbness. However, since the patient reported sleepiness, general weakness, and a metallic taste after the bee sting, it was deemed positive. Tryptase levels were within limits for both challenges.

RESULTS

Despite the patient's suspicion of being initially stung by a wasp and the non-specific symptoms from the sting challenges, bee venom immunotherapy was initiated. This decision underscores the complexity and controversy surrounding the use of live sting challenges, especially in the absence of standardized protocols and guidelines.

CONCLUSION

Live sting challenges remain a controversial yet utilized tool in venom allergy workup. Our case emphasizes the importance of developing standardized protocols to guide clinical decisions and optimize patient outcomes in venom immunotherapy.

CONFLICTS OF INTEREST

The authors did not specify any links of interest.

Submission number: 000044
Prefix: P10

UTILITY OF COMPONENT-RESOLVED DIAGNOSIS IN VENOM IMMUNOTHERAPY QUALIFICATION - A CASE REPORT FROM A TERTIARY ALLERGOLOGY CENTRE

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BACKGROUND

A 29-year-old female patient was referred to our tertiary allergology clinic for venom immunotherapy. Her medical history revealed that 4 years prior, during a 10km run, she was stung by three wasps. Although she finished the run, she experienced facial swelling, shortness of breath, and generalized urticaria at the finish line. The emergency medical team administered i.v. steroids and antihistamine, leading to eventual recovery. Since then, she has not been stung.

METHOD

Skin tests were performed with positive results for bee venom and negative for wasp venom. As the results were inconclusive with the patient's reported history, further assessment was performed. Laboratory tests revealed a relatively low total IgE level (30 IU/ml) and specific IgE towards extracts were negative; tryptase levels were within norm.

RESULTS

Component-resolved diagnostics were performed, revealing rVes v5 (wasp venom) at 0.41 kU/l (Class 1), rApi m2 (bee venom) at 3.50 kU/l (Class 3), i3 wasp venom at 1.38 kU/l (Class 2), and i1 bee venom at 1.38 kU/l (Class 2). Api m3 and Pol d5 components were both negative (<0.1 kU/l).

Based on the comprehensive clinical evaluation, the patient was qualified for specific immunotherapy with wasp venom.

CONCLUSION

Component-resolved diagnostics (CRD) offer precise allergen identification, crucial for managing Hymenoptera venom allergies. In patients with low total IgE, applying lower cutoff values for major allergen components increases sensitivity, ensuring clinically significant sensitivities are detected. This leads to enhanced diagnostic accuracy and informs effective VIT decisions, improving patient outcomes.

CONFLICTS OF INTEREST

The authors did not specify any links of interest.

Poster discussion Session – Group 2 – Topic: Hymenopteram venom immunotherapy
Friday, 20 September 2024

Submission number: 000009
Prefix: P11

SAFETY OF A 4-STEP ULTRA-RUSH INDUCTION PROTOCOL IN WASP ALLERGY

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BACKGROUND

Ultra-rush (UR) protocols provide a quicker, more convenient and safe initiation of hymenoptera venom immunotherapy (VIT), enhancing patient adherence. A 5-step ultra-rush protocol (180 minutes) for wasp allergy has been described, with a good safety profile. We aimed to assess the safety of a 4-step (150 minutes) ultra-rush protocol.

METHOD

Retrospective analysis of the medical records of patients who initiated VIT with *Vespula* venom using a 4-step protocol (10-20-30-40ug, 150 minutes long) at our department over the past 5 years (Group A). Patients who started with a 5-step protocol (1-10-20-30-40ug, 180 minutes long) were also included (Group B) and data on demographics, previous reactions, and adverse reactions during VIT were collected and compared between the two groups. Mueller and WAO grading systems were applied to classify the allergic reactions.

RESULTS

A total of 40 patients were included, mostly male (73%) with a median age of 56.5 years (ranging 25-75). Atopy was observed in 13% of the patients, and cardiovascular diseases in 35%. Most patients (83%) reported having been stung more than once in their lifetime, and 93% experienced anaphylaxis following a wasp sting. The severity of the reactions was similar between the two groups. Wasp allergy was confirmed based on specific IgE and/or positive skin tests (30%).

VIT was initiated using a 4-step UR protocol in 20 patients, and a 5-step UR protocol in another 20 patients. All patients successfully completed the induction protocol. Reactions were observed in 4 patients (3 in group B) and all were classified as mild (WAO grade 1 and Mueller grade I). All were treated with antihistamines and one also received systemic corticosteroids. All reactions occurred after reaching a cumulative dose of at least 30ug.

Patients who reacted during the UR protocol had a history of grade III-IV (Mueller) or grade 3-5 (WAO) reactions, following a wasp sting. All baseline tryptase values were below 11.4 ug/L. In one patient that presented with a REMA score ≥ 2, systemic mastocytosis was excluded.

Ten patients (25%) were re-stung during the VIT maintenance and all experienced only local reactions.

CONCLUSION

Consistent with other series, wasp venom VIT is typically associated with less severe and less frequent adverse reactions. Our 4-step UR protocol demonstrated a similar safety profile to the 5-step protocol. It may be possible to shorten the protocols to 4-steps without compromising safety, in wasp venom allergic patients.

	Group A	Group B	Total
Male, n (%)	16 (80)	13 (65)	29 (73)
Age, median	59	50	56.5
Atopy, n (%)	2 (10)	3 (15)	5 (13)
Cardiovascular disease, n (%)	8 (40)	6 (30)	14 (35)
Previous stings, n (%)	17 (85)	16 (90)	33 (83)
Anaphylaxis, n (%)	18 (90)	19 (95)	37 (93)
Cardiovascular symptoms	7	13	20
Mueller, n			
I	5	2	7
II	1	3	4
III	9	7	16
IV	4	7	13
WAO, n			
1	2	1	3
2	4	1	5
3	8	9	17
4	2	3	5
5	4	6	10
Baseline tryptase (ug/L)	4.81	4.76	4.8
REMA score ≥2, n (%)	2 (10)	0	2 (5)
Total IgE (kU/L), mean	239	269	254
Vespula IgE (kU/L), mean	11.2	18.7	14.98
Vespula intradermal tests			
Positive (0.1ug/mL), n	2	0	2
Positive (1ug/mL), n	5	5	10
VIT induction reactions, n (%)	1 (5)	3 (15)	4 (10)
Re-stings, n (%)	5 (25)	5 (25)	10 (25)

Table 1. Characterization of patients under *Vespula* venom immunotherapy

CONFLICTS OF INTEREST

The authors did not specify any links of interest.

Submission number: 000028
Prefix: P12

SAFETY PROFILE OF HALF-DAY ULTRA-RUSH HYMENOPTERA VENOM IMMUNOTHERAPY PROTOCOL IN 22 OUTPATIENTS WITH HYMENOPTERA VENOM ALLERGY

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BACKGROUND

Venom immunotherapy (VIT) is highly effective and the recommended treatment for patients with a history of systemic anaphylactic reactions to Hymenoptera stings. Achieving a maintenance dose of immunotherapy in the shortest possible time is desirable in some situations. This study aims to report the 4-year experience with our half - day ultra - rush venom immunotherapy protocol in outpatients and to assess the safety of this protocol.

METHOD

This is a retrospective single-center study of 23 VIT inductions using half-day ultra-rush protocols conducted from 2020 to 2024 in 22 outpatients aged 17 to 69 years (13 males [59.1%], 9 females [40.9%]) with confirmed bee or wasp venom allergy, using depot venom preparations. The patients experienced 15 systemic reactions (SR) grade 2 and 8 SR grade 3 according to the Ring and Messmer classification. On day 1 of our protocol, an initial venom dose of 0.2 ml at 100 SQ-U/ml was followed by doses of 0.1 ml at 1000 SQ-U/ml, 0.1 ml at 10,000 SQ-U/ml, 0.1 ml at 100,000 SQ-U/ml, 0.3 ml at 100,000 SQ-U/ml, and 0.6 ml at 100,000 SQ-U/ml, administered at 30-minute intervals. Patients received one booster injection of 1 ml at 100,000 SQ-U/ml on day 15. Twenty-three ultra-rush VIT protocols were performed with honeybee (12 protocols) and wasp (11 protocols) venom, with one patient receiving injections of both venoms. All documented side effects were classified into local reactions and SR using the Ring and Messmer classification.

Results

Local reactions on day 1 were observed during 9 (18.9%) VIT induction procedures. There was no need to interrupt the treatment or reduce the dose. The bee venom group showed a non-significant trend towards a higher incidence of local reactions, resulting in more frequent antiallergic therapy. There were no immediate SRs on day 1 or day 15, despite the presence of patients with arrhythmias, antihypertensive medication use, and mastocytosis. No late reactions were observed. Epinephrine as rescue medication was never necessary.

CONCLUSION

The half-day ultra-rush protocol is a safe therapeutic option for Hymenoptera venom-allergic outpatients, displaying no SR in our study. The protocol appears to be safe even in high-risk and elderly patients, but further data are needed to confirm these findings.

CONFLICTS OF INTEREST

The authors did not specify any links of interest.

Submission number: 000013
Prefix: P13

MODIFIED ULTRARUSH PROTOCOL EFFICACY AND SAFETY IN HYMENOPTERA VENOM IMMUNOTHERAPY

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BACKGROUND

Ultrarush (UR) protocol is rarely used in the induction phase of venom immunotherapy (VIT). Adverse events range from 3 to 50 % but the severity of reactions is not always reported.

Our study reports the results of Rush (R), UR and shortened UR protocols in a wide cohort of well characterized patients.

METHOD

We included adult patients candidate for VIT from 1st January 2022 to March 2024 and we used 3-4 day R, traditional UR (tUR) or shortened UR (sUR) protocol, administering each dose every 30 min. and observing for 150 min. after the last dose. (Table 1)

Collected data included venom culprit, severity of reaction (Muller grade), basal tryptase levels, adverse reactions during induction and gained protection.

Extract venom used were from aqueous Anallergo (76 VIT) or Alutard Alk-Abellò (5 VIT).

Informed consent was obtained by all the patients.

RESULTS

Seventy one patients and 81 VIT were evaluated (10 patients received double VIT): 15 for Apis mellifera (A), 27 for Vespula (V), 18 for Polistes dominula (PD) and 21 for Vespa crabro (VC). Severity was grade 3 or 4 in 65 VIT, grade 1 or 2 in 15 and large local reaction (LLR) in 1. Tryptase levels (mcg/L) were < 5 in 29 cases, 5-8 in 37, 8-11.4 in 6 and > 11.4 in 9. (Figure1)

When Rema score was >= 2, haematological evaluation excluded systemic mastocytosis. Rush protocol was followed in 12 subjects, traditional UR in 20 and shortened UR in 49.

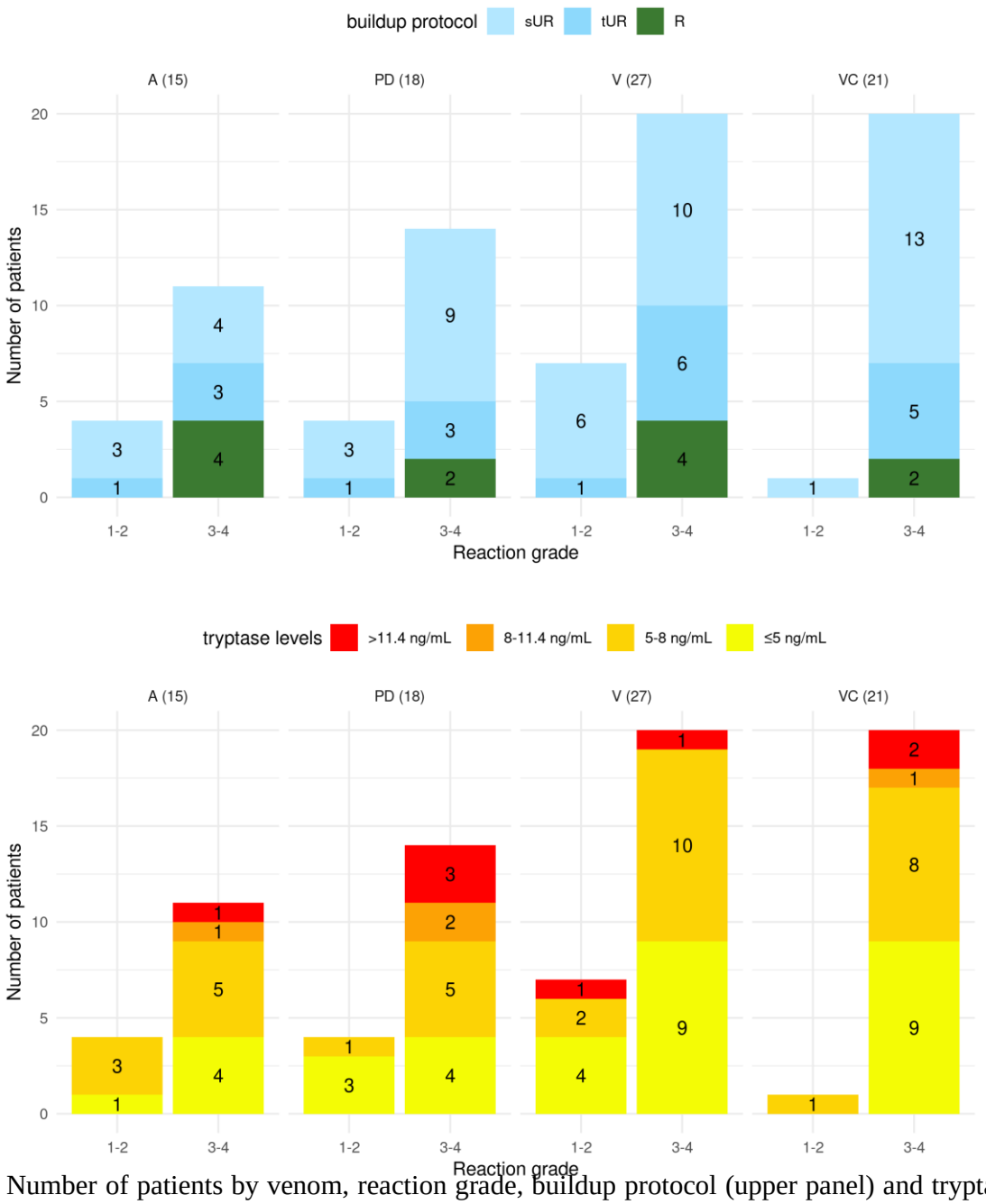
Systemic adverse reactions (SAR) occurred in 2 patients, both in A VIT (1 rush Alutard and 1 traditional UR Anallergo), with history of grade 3-4 reaction; none required adrenaline. LLR occurred in 14 cases, 1 (8.3%) in rush (PD), 4 (20%) in traditional UR (1 V and 3 VC) and 9 (18%) in shortened UR (2 A, 3 V, 4 VC).

Nine patients (7 with history of grade 3 or 4 reaction) were re-stung, without SAR.

CONCLUSION

The study demonstrates that UR protocol for VIT is both safe and effective also in the shortened UR irrespective of venom, reaction severity, tryptase levels.

Reducing the number of hospital admissions, it is advantageous both for patients and the health system



Number of patients by venom, reaction grade, buildup protocol (upper panel) and tryptase levels (lower panel)

	Dose (mcg)		
day	Rush	UR-Traditional	UR-Shortened
1	4 (0.01+0.1+1+3)	100 (1+3+6+15+30+45)	100 (2+8+15+30+45)
2	Vespid 35 (5+10+20) Honeybee 19 (1+3+5+10)	/	/
3	Vespid 100 (30+35+35) Honeybee 60(10+20+30)	/	/
4	--- Honeybee 100 (30+35+35)	/	/

Comparison of buildup protocols

CONFLICTS OF INTEREST

The authors did not specify any links of interest.

Submission number: 000029
Prefix: P14

HYMENOPTERA VENOM IMMUNOTHERAPY WITH ULTRA-RUSH PROTOCOL: EFFICACY AND SAFETY OF OMALIZUMAB PRETREATMENT IN PATIENTS WITH SYSTEMIC REACTIONS ON PREVIOUS ULTRA-RUSH

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BACKGROUND

Ultra-rush (UR) protocols allow the rapid achievement of maintenance dose in venom immunotherapy (VIT). Although there are no guidelines for the use of omalizumab (OMZ) in VIT, in the patients unable to complete the protocol due to systemic reactions (SR), OMZ pre-treatment seems to reduce the number and severity of breakthrough reactions. **Objectives:** To characterize the clinical and laboratory profile of a group of patients with SR on *Apis mellifera* VIT UR that started OMZ pre-treatment. We intended to evaluate the safety (number and severity of SR) and efficacy (cumulative tolerated dose of venom) of OMZ pre-treatment on VIT UR.

METHOD

A retrospective study was conducted in a group of 9 patients who repeated *Apis mellifera* VIT UR with OMZ pre-treatment after experiencing a SR in a previous UR. Patients received 4 monthly administrations of OMZ 300mg and repeated UR (210 minutes protocol, cumulative dose of 101.1µg) one week after the latest OMZ administration. Statistical analysis was performed using SPSS 26.

RESULTS

In this group, 67% of patients were male, median age was 47 years (27-60). Clinical evaluation revealed that 33% had atopy, 11% had asthma and all showed positive skin tests for *Apis mellifera* venom. Laboratory results are represented in Table 1. All patients had SR during the first UR attempt (II=3, III=4, IV=2), leading to the protocol interruption, with a median cumulative tolerated dose of venom of 12.1µg (2.1-81.1). After OMZ pre-treatment, 67% of patients completed UR without any reaction and 33% had breakthrough reactions (I=1, II=2), with a median cumulative tolerated dose of venom of 101.1µg (11.1-101.1). Statistically, there was a significant difference for the number of breakthrough reactions (p=0.031), its severity (p=0.014) and the cumulative tolerated dose of venom (p=0.011) in the paired analysis of this group before and after pre-treatment with OMZ. Regarding the maintenance phase of VIT, 2 patients maintained OMZ for the 5 years of VIT, 1 discontinued it after 4 years successfully, and the remaining 6 are still under VIT with OMZ pre-treatment.

CONCLUSION

OMZ pre-treatment proved to be a safe and effective procedure in patients with SR during previous UR, leading to a lower proportion and severity of SR and a higher cumulative tolerated dose of venom during UR. Additional studies are needed to identify potential clinical and laboratory biomarkers that can define the appropriate duration of adjuvant treatment with OMZ.

Patient	**Basal tryptase** (ng/mL)	**Total IgE** (kU/L)	**Specific IgE** (kU/L)					
			Apis mellifera	**Api m1**	**Api m2**	**Api m3**	**Api m5**	**Api m10**
1	13.3	166	10.30	8.66	0.01	0.93	0.02	2.08
2	2.1	29.2	30.40	27.90	0.03	0.02	0.00	0.64
3	4.3	1430	>100	>100	0.04	0.04	0.08	0.12
4	8.7	97.6	8.29	1.70	0.88	2.41	2.25	1.80
5	4.1	1364	>100	>100	51.20	0.59	0.91	50.20
6	2.8	64.1	14.50	13.20	0.00	0.27	3.40	0.00
7	6.5	60.3	>100	7.34	12.90	1.42	0.43	2.75
8	8.0	296	24.50	20.70	1.17	0.04	3.34	3.76
9	4.1	359	17.70	18.80	1.02	0.26	2.30	2.45
Median	4.3	166	24.50	18.80	0.88	0.27	0.91	2.08

Table 1. Laboratory results of all patients included in the analysis and median values for each parameter evaluated.

CONFLICTS OF INTEREST

The authors did not specify any links of interest.

Submission number: 000075
Prefix: P15

API M 10 SENSITIZATION: DOES IT MATTER?

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BACKGROUND

Honeybee sensitization profile may be relevant for the success of venom immunotherapy (VIT). Some authors suggest that predominant IgE sensitization to Api m 10 may be a risk factor for treatment failure in honeybee VIT, since Api m 10 may be underrepresented in extracts available for VIT and has been shown to degrade rapidly in venom extracts stored in solution.

METHOD

Patients who suffered a systemic reaction after a bee sting and were diagnosed with *Apis mellifera* venom allergy were treated with *Apis m.* VIT aqueous extract. Specific IgE (sIgE) to total bee venom and bee venom allergens (ImmunoCAP) was determined. VIT was administered using a build-up cluster schedule of 6 doses at two-weeks interval (4+2). Systemic adverse reactions (SAR) were recorded. VIT efficacy was assessed by outpatient honeybee sting challenge and/or field sting. The relationship between Api m10 sensitization and VIT efficacy was analyzed.

RESULTS

Sixty-two patients were included: 51 males, 11 females with a median age of 50 years (IQR 42 – 58.7 years). Forty-seven patients (75.8%) were sensitized to Api m 10. Nineteen patients developed a SAR to VIT. In 30 patients (48.38% of the total sample) the level of sIgE to Api m 10 was more than half the level of sIgE to total bee venom. Only one patient was monosensitized to Api m 10. Fifty patients were stung (31 sting challenge, 11 field sting, 8 both) and only 8 of them showed a systemic reaction. When comparing Api m10 dominant sensitization there were no differences in SAR or sting tolerance. Only 4 patients were initially treated with 200 mg (2 in each group). The rest (93.5%) were treated with the standard dose of 100 μg.

CONCLUSION

We found no significant association between sIgE Api m 10 predominant sensitization and lack of efficacy of VIT using aqueous venom extracts at the standard 100 mg dose.

CONFLICTS OF INTEREST

The authors did not specify any links of interest.

Submission number: 000073
Prefix: P16

IS IT NECESSARY TO USE A SISTEMATICALLY HIGH DOSE OF VENOM IMMUNOTHERAPY?

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BACKGROUND

Venom immunotherapy (VIT) is a highly effective treatment at 100µg doses. However, in some high-risk patients, such as beekeepers, higher doses are recommended to ensure protection.

Our aim is to analyze patients treated with doses > 100µg of venom, the reasons for this increase, their tolerance and the relationship with beekeeping.

METHOD

We performed a retrospective study of patients diagnosed with Hymenoptera venom allergy and treated with VIT at our allergy service between 2003 and 2023. Demographic characteristics, degree of index reaction, maintenance dose and tolerance to stings were analyzed. Patients requiring maintenance doses of 200µg or more, tolerance to dose escalation using a 30 minutes interval 100 + 100 µg and reasons for escalation were reviewed. Differences between beekeepers and non-beekeepers were analyzed.

RESULTS

During the study years, 466 patients started VIT. Of these, 348 patients were included in the study: 239 males, 109 females with a median age of 53 years (IQR 44 - 63.5 years). Clinical data are shown in Table I. Of these, 21 patients received doses of 200µg: 18 with bee venom and 3 with Polistes venom. Reasons for dose escalation were systemic reaction with field or controlled stings in 3 *Polistes* VIT and 13 bee VIT cases, predominant sensitization to Api m 10 in 2 cases and nonreduction of specific IgE in 3 cases. Fifteen percent of the 80 beekeepers required dose escalation to 200 µg. There were no differences in beekeeping or number of stings/year at a dose of 100 µg. Only one patient had throat itching when the dose was increased.

CONCLUSION

It is not necessary to use high doses of VIT in all beekeepers since a minority of them required doses of 200 µg. Dose escalation using a 30 minutes interval seems safe in our patients.

	N
Patients	348
Age Median (IQR)	53 (44 – 63,5)
Gender M/F	239 / 109
Müller grades N (%) I II III IV	 65 (18,67) 93 (26,72) 137 (39,36) 52 (14,94)
Venom N (100 µg /200 µg) *Apis* *Polistes* *Vespula*	 130 (112 / 18) 126 (123 / 3) 92 (92 / 0)
VIT 100 µg/ 200 µg (%)	327 (93,96) / 21 (6,03)
Beekepers (100 /200 µg)	68 /12

Table I. Clinical data

CONFLICTS OF INTEREST

The authors did not specify any links of interest.

Submission number: 000056
Prefix: P17

HYMENOPTERA VENOM ALLERGY IN PATIENTS AGED FROM 4 TO 18 YEARS

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BACKGROUND

Hymenoptera stings can trigger local or systemic allergic reactions. Venom Immuno Therapy (VIT) represents an effective and safe treatment for hymenoptera venom allergy. The aim of our study is to describe characteristics of patients referred to our center for hymenoptera venom allergy and the administration of VIT at young age (< 18 years old).

METHOD

We analyzed data from 16 patients aged from 4 to 18 years at diagnosis followed by our center between 01/2018 to 06/2023. Diagnosis was made on clinical history, positive intradermal skin tests and/or specific IgE assay to native or molecular allergens. Allergic reactions to hymenoptera stings were classified according to Muller criteria. Risk of mastocytosis was estimated by REMA SCORE.

RESULTS

Of the 16 patients considered 15 were male and 1 was female. Nobody of them was investigated for mastocytosis based on REMA SCORE. The referral reason was a type II reaction to hymenoptera sting for 1 patient, a type III reaction for 7 patients, and a type IV reaction for 8 patients. In 9/16 patients was found a sensitization to bee venom, 5/16 patient had allergy to Vespula species venom, and 2/16 patients were sensitized to Polistes venom. All these patients started VIT, 8/16 continued it for at least 5 years. In 5 patients VIT was safely discontinued after ≥ 5 years of maintenance therapy: 1/5 had a reduction in wheal diameter compared with baseline at intradermal skin test; 4/5 had a 2/3 reduction of specific IgE assay compared with baseline. One of these patients had also no reaction to re-sting. In 2/16 patients VIT has been continued for more than 5 years: in one case the reason was <2/3 reduction in specific IgE assay, for the other patient was a type III reaction after re-sting and a type II reaction after a VIT session for Polistes venom desensitization. 8/16 patients have no completed 5 years of VIT. Overall, 6/16 patients experienced a re-sting and 5/6 had no reactions. 3/16 patients had an allergic reaction to VIT: 2 presented a type I reaction with no need of any drugs during desensitization, 1 presented a type II reaction to re-sting with no need of treatment as well.

CONCLUSION

Prevalence of hymenoptera venom allergy results to be higher in adults and in males. Prevalence of sistemic mastocytosis is higher in adults. VIT for hymenoptera venom allergy is an effective and safe treatment and a type III or IV reactions should be a correct indication to start it.

CONFLICTS OF INTEREST

The authors did not specify any links of interest.

Submission number: 000018
Prefix: P18

REMEMBER ME? RECALL URTICARIA AT THE SITE OF THE PREVIOUS WASP STING OCCURING AFTER VENOM IMMUNOTHERAPY - CASE REPORT

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BACKGROUND

Local reactions (wheal surrounded by erythema) at the site of subcutaneous injection of venom immunotherapy (VIT) are frequent. Appearance of local reactions outside the injection area is uncommon. An urticarial response localized to an area of prior antigen exposure reactivated by various stimuli is called Recall urticarial (RU).

METHOD

We report a case of a patient with RU in a previous wasp sting area after injection of VIT.

RESULTS

A 42-year-old man was stung by a wasp in the right thigh in October of last year. It led to a local reaction, erythema and swelling at the sting site (less than 10 cm diameter) which withdrew spontaneously in a few hours. Two weeks later, he was stung by another wasp, but this time on the inside of his right upper arm. Soon afterwards, generalized pruriginous urticaria developed all over his body. Intravenous methylprednisolone and intramuscular chlorpheniramine were administered, then oral antihistamine was prescribed, which led to a complete regression of hives in the next few days. He had systemic reactions grade I Mueller to wasp sting. He had no previous history of allergic or autoimmune diseases. Several weeks later, blood tests showed that both basophil and eosinophil counts were normal. Total IgE level was 56.7 kU/L and serum baseline tryptase 4.1 mcg/mL. Skin tests with common inhalant and food allergens were negative, bee venom tested positive, wasp venom was not tested because of lack of reagents. Specific IgE was positive for Vespula spp (6.02 kU/L). VIT was started with Vespula spp extract with weekly increased up of venom extract subcutaneously, until a maintenance dose was reached weeks later. After almost every injection of VIT in the left upper arm, numerous hives appeared on his right arm, at the site of previous wasp sting. However, there were no local reactions on the injection site.

CONCLUSION

Specific allergens, such as allergen immunotherapy may activate local reactions in the previously antigen exposure areas, even if the antigens enter the body from another source, like an injection in the opposite arm. The mechanism of this type of reaction has not been clarified yet. Long-lasting local changes may occur at the previous wasp sting area. It is possible that the mast cells in that area are more prone to degranulation or that their number increases following the antigen exposure. Injecting the antigen in a distant site leads to mast cell degranulation through systemic antigen absorption or release of histamine-releasing factors.

CONFLICTS OF INTEREST

The authors did not specify any links of interest.

Submission number: 000050
Prefix: P19

OVERCOMING CHALLENGES IN VENOM IMMUNOTHERAPY: A CASE STUDY OF SUCCESSFUL TREATMENT IN A 19-YEAR-OLD MALE WITH SEVERE BEE STING ALLERGY

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BACKGROUND

Anaphylactic reactions to bee stings are life-threatening, demanding effective management strategies like venom immunotherapy (VIT) to prevent future episodes. This case report details the clinical course and treatment of E.I., a 19-year-old male, who underwent VIT following multiple severe allergic reactions to bee stings.

METHOD

Case Presentation: At age 10, E.I. experienced his first significant allergic reaction to a bee sting, presenting with rash on the face, ear, neck, and chest, along with a large local reaction over 10 cm in diameter, extending to his palm, accompanied by edema, heat sensation, and pruritis. At age 17, he suffered an anaphylactic shock, characterized by loss of consciousness and hypotension after a bee sting, necessitating emergency medical intervention. The third sting occurred on March 27, 2024, resulting in a delayed arrival to a health center and subsequent recovery after 9 hours of intubation and a comatose state in the intensive care unit.

Intervention: E.I. underwent VIT with Venom ALT-Ape following comprehensive diagnostic evaluations, including RAST, blood count, biochemical profile, complete urine analysis, serum tryptase levels, EKG, abdominal ultrasound, and spirometry. A rush hyposensitization protocol over five days was initiated, starting with 0.2 ml of 0.1 mcg bee venom/ml. Despite initial tolerance, E.I. experienced mild to moderate systemic reactions on subsequent doses.

RESULTS

E.I. experienced mild throat constriction, facial and ear edema, and erythema, progressing to more severe respiratory difficulty and systemic symptoms with higher doses. After careful dose adjustments and premedication, he successfully completed the treatment with progressively higher tolerated doses, culminating in the final dose of 1.0 ml of 100 mcg bee venom/ml, with only minor reactions.

CONCLUSION

This case underscores the complexities and challenges of VIT in patients with a history of severe anaphylaxis to bee stings. Despite initial adverse reactions, tailored dose adjustments and premedication enabled successful desensitization. This highlights the critical importance of

personalized VIT protocols and vigilant monitoring to ensure patient safety and efficacy in preventing future anaphylactic episodes. E.I.'s positive outcome provides valuable insights into managing similar cases and reinforces the necessity for individualized dose adjustment strategies in venom immunotherapy.

• **Day 3, Dose 3:** 0.2 ml of 100 mcg/ml resulted in mild throat constriction, chest tightness, difficulty breathing, facial flushing, and mild facial and lip edema. Treated with prednisolone 50 mg IV and rupatadine 10 mg.
• **Day 3, Dose 4:** 0.4 ml of 100 mcg/ml caused difficulty breathing, throat tightness, facial and ear rash, and esophageal burning sensation. Managed with treatment.
• **Day 4:** Started with 0.2 ml of 100 mcg/ml, followed by 0.4 ml, which induced breathing difficulty, laryngeal and facial edema, and rash. Treatment was interrupted due to reaction severity.
• **Day 5 (repeated Day 4):** Premedicated. Starting with 0.2 ml, progressing to 0.4 ml and 0.6 ml, both well tolerated. The final dose of 0.8 ml induced mild breathing difficulty, laryngeal and facial edema, and rash.
• **Day 6 (continued Day 5):** Premedicated. Starting with 0.6 ml, then 0.8 ml, and finally 1.0 ml, with only minor reactions of mild facial flushing.

Mild to moderate systemic reactions on subsequent doses

CONFLICTS OF INTEREST

I, Gjustina Loloci, declare a potential conflict of interest. I have previously worked as a Local Safety Officer for Allergy Therapeutics in Albania. Currently, I treat patients using their vaccines. The abstract includes a case of adverse effects from these products.

Submission number: 000051
Prefix: P20

RARE ADVERSE EVENTS IN RUSH VENOM IMMUNOTHERAPY: A CASE OF RECTAL PAIN AND DELAYED DIZZINESS

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BACKGROUND

Venom immunotherapy (VIT) is an effective treatment for patients with hypersensitivity to insect stings. The rush hyposensitization protocol, which accelerates the desensitization process, is associated with a higher incidence of adverse reactions compared to conventional protocols. While common reactions include local swelling and systemic symptoms such as urticaria and respiratory symtoms, rare adverse events are not well-documented.

METHOD

Objective: To report and analyze a rare case of rectal pain after defecation and delayed dizziness occurring during the rush hyposensitization protocol of VIT.

Methods: This case study involves a patient, F. S., born on 20.09.1981, undergoing rush Venom-ALT Ape for bee venom allergy. The patient reported experiencing rectal pain following defecation and dizziness occurring 3 hours post-injection on the third day of the treatment protocol. A thorough evaluation was conducted to ascertain the cause and appropriate management of these symptoms.

RESULTS

The patient's symptoms were rare and atypical for VIT. Rectal pain after defecation had not been previously documented as an adverse event of VIT. Dizziness occurring several hours post-injection was considered a delayed systemic reaction. Physical examination revealed no abnormalities that could directly explain the rectal pain. Neurological assessment was normal, with no immediate signs of central nervous system involvement. Both symptoms were carefully monitored, and supportive care was provided. The treatment protocol was adjusted to mitigate further adverse reactions.

CONCLUSION

This case highlights the importance of monitoring and reporting rare adverse events during rush VIT. Although rectal pain and delayed dizziness are not commonly associated with VIT, they can occur and should be considered in the overall management of patients undergoing this treatment. Given the timing and nature of the symptoms, it is plausible that they are related to systemic reactions from immunotherapy. Further studies are warranted to explore the prevalence and mechanisms of such rare adverse events in VIT.

CONFLICTS OF INTEREST

I, Gjustina Loloci, declare a potential conflict of interest. I have previously worked as a Local Safety Officer for Allergy Therapeutics in Albania. Currently, I treat patients using their vaccines. The abstract includes a case of adverse effects from these products.

Submission number: 000053
Prefix: P21

EFFICACY OF VENOM IMMUNOTHERAPY: A CASE SERIES OF FOUR PATIENTS TREATED FOR BEE STING HYPERSENSITIVITY

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BACKGROUND

Venom immunotherapy (VIT) is an established treatment for individuals with severe hypersensitivity to insect stings, notably those leading to anaphylaxis. This case series examines the efficacy of VIT in four patients with a history of severe allergic reactions to bee stings. The outcomes demonstrate the potential of VIT to significantly reduce the severity of reactions to subsequent stings, underscoring its importance in clinical practice.

METHOD

Bee stings can trigger severe allergic reactions, including anaphylaxis, in sensitized individuals. VIT aims to desensitize patients, reducing the risk and severity of future reactions. This report presents four cases that illustrate the efficacy of VIT in mitigating allergic responses to bee stings.

Case 1: F.S. (DOB: 20.09.1981) Stung three days after initial Venom-ALT Ape. Local erythema and edema, significantly improved from prior anaphylactic shock.

Case 2: V.J. (DOB: 28.08.2003) Stung 18 days after initial Venom-ALT Ape. Local erythema and heat sensation, no systemic symptoms, marked reduction in reaction severity.

Case 3: V.SH. (DOB: 14.02.1999) Sting challenge four months after completing four years of Venom-ALT Ape; stung again nine months post-VIT. Both instances showed only local reactions, indicating sustained efficacy of VIT.

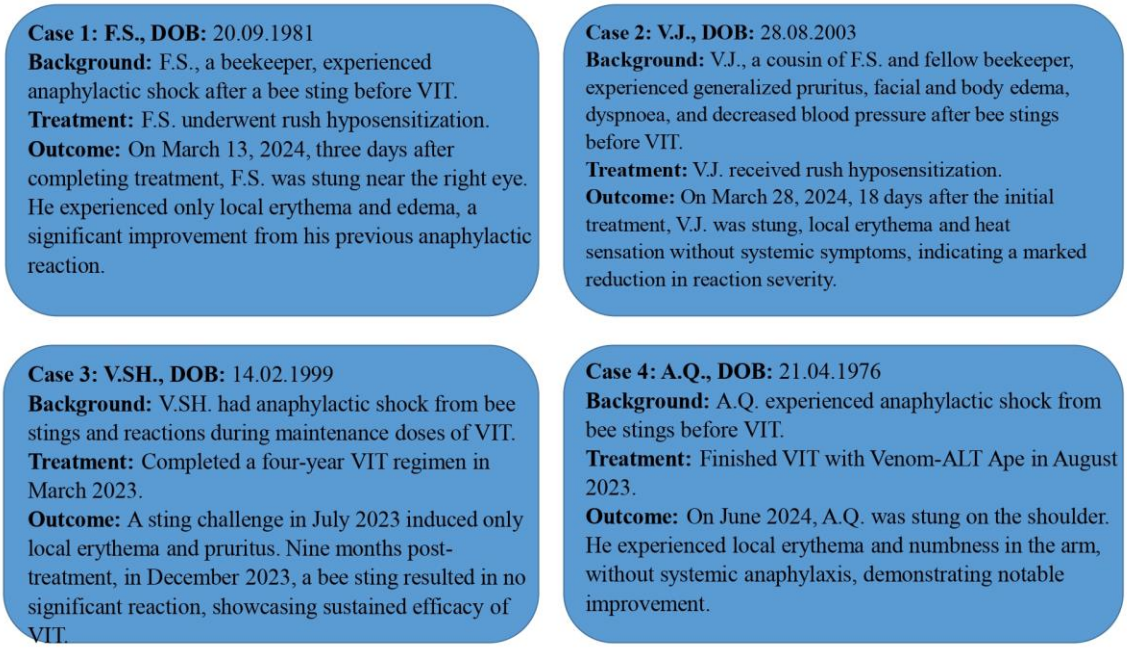
Case 4: A.Q. (DOB: 21.04.1976) Stung 10 months after completing five years of Venom-ALT Ape. Local erythema and arm numbness, no systemic anaphylaxis, notable improvement.

RESULTS

These cases highlight VIT's efficacy in reducing the severity of allergic reactions to bee stings. F.S. and V.J., treated with rush hyposensitization, showed significant improvement with only localized reactions to subsequent stings. V.SH.'s sustained desensitization, evident in both controlled and real-world stings, further supports VIT's long-term benefits. Despite A.Q.'s severe initial reaction, his post-treatment sting resulted in only local symptoms, indicating VIT's potential to mitigate life-threatening reactions.

CONCLUSION

VIT significantly reduces the severity of allergic reactions to bee stings, as demonstrated by the improved outcomes in these four cases. Transforming systemic anaphylactic reactions into localized, manageable symptoms underscores VIT's value in clinical allergy. Continuous monitoring and personalized treatment plans are essential to maximize VIT's benefits for individuals with venom hypersensitivity.



Case 1, Case 2, Case 3, Case 4

CONFLICTS OF INTEREST

I, Gjustina Loloci, declare a potential conflict of interest. I have previously worked as a Local Safety Officer for Allergy Therapeutics in Albania. Currently, I treat patients using their vaccines. The abstract includes cases demonstrating the efficacy of these products.

Poster discussion Session – Group 3 – Topic: Hymenoptera venom allergy and mast cell diseases
Friday, 20 September 2024

Submission number: 000063
Prefix: P22

INVESTIGATION OF ANAPHYLAXIS IN MASTOCYTOSIS MOUSE MODELS

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BACKGROUND

Mastocytosis is characterized by the expansion and activation of mast cells (MC) in various organs, particularly the skin and bone marrow (BM). It is associated with a mutation in the tyrosine kinase KIT (hKITD816V in over 90% of patients). Patients suffer from various symptoms of MC degranulation, including anaphylaxis, that can be life-threatening.

METHOD

Our lab utilizes novel mouse models expressing the mKitD814V mutation, the homologue of hKITD816V, in MC (Mcpt5-Cre x KitD814Vfl) or all BM-derived hematopoietic stem cells (Scl-CreER^{Tg} x KitD814Vfl) to study non-advanced and advanced systemic mastocytosis, respectively, aiming to explore anaphylaxis and novel treatment strategies. In both mouse models, we assessed the number of skin and organ MC as well as serum levels of mouse MC protease-1 (MCPT-1). To investigate IgE-mediated anaphylaxis, we sensitize mice with IgE@DNP and induce locally or systemically 24h later with DNP-HSA. Moreover, we investigated MRGPRX2-mediated anaphylaxis using C48/80 and ciprofloxacin, and bee-venom physiologic anaphylaxis. Anaphylaxis severity is measured by the drop of body temperature.

RESULTS

Both mouse lines showed a significant increase of MC in the skin compared to control littermates. In the Scl-CreER^{Tg};KitD814V line, we observe a continuous increase of skin MC until mice had to be sacrificed due to severe signs of disease (≤ 30 weeks), while in Mcpt5-Cre;KitD814V mice, MC only increase initially. This increase is accompanied by an elevation of MCPT-1 serum level. When inducing IgE passive anaphylaxis in both mouse models, no significant difference was observed between mutant mice and their control littermates. However, in both control and mutant mice, females were more susceptible to anaphylaxis-associated death compared to males. Interestingly, when we induce MRGPRX2-mediated anaphylaxis via C48/80 and ciprofloxacin, we observe that mutant mice are more sensitive than their control littermates.

CONCLUSION

Our mouse models thus replicate the phenotype of human systemic mastocytosis and allow studying characteristics and treatment of mastocytosis, including anaphylaxis. We currently explore Hymenoptera venom-induced anaphylaxis and the effect of KIT-targeting tyrosine kinase inhibitors on various MC functions.

CONFLICTS OF INTEREST

The authors did not specify any links of interest.

Submission number: 000012
Prefix: P23

SERUM TRYPTASE MEASUREMENT AT A UNIVERSITY HOSPITAL CENTER: PRACTICES AND INSIGHTS

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BACKGROUND

Our main objective was to assess the reasons for requesting serum tryptase measurements in a University Hospital Center. Additionally, we analyzed the location and timing of sample collection, as well as patient follow-up.

METHOD

A retrospective evaluation of serum tryptase measurements was carried out at a University Hospital Center for a twelve-month period. Demographic characteristics, setting and reason for sample request, timing of collection, analytical results, evaluation in specialty consultation, and, when available, clinical diagnosis were analyzed. Samples received from other hospitals were excluded.

RESULTS

A total of 548 serum tryptase measurements from 471 patients were analyzed [276 women (59%), median age 45 years]. The requests were mainly made in an outpatient setting (n=349; 66%), particularly by the specialties of Allergy and Clinical Immunology (n=232; 42%) and Hematology (n=70; 13%). Other requesting locations included the emergency department (n=129; 24%) and inpatient wards (n=55; 10%). Regarding the timing of collection, it corresponded to the acute phase in 179 cases (33%). Tryptase levels were elevated (>11.4 ng/mL) in 82 patients and increased relative to baseline values in 59% of patients with ≥2 measurements. The main reasons for requesting tryptase were anaphylaxis (n=177; 32%), angioedema/urticaria (n=145; 26%), mastocytosis/mast cell activation syndrome (MCAS) (n=99; 18%), and systemic hypersensitivity reaction to Hymenoptera venom (n=34; 6%). In the emergency department, the main reasons for requests were angioedema/urticaria (n=75; 58%) and anaphylaxis (n=46; 36%). Drugs were the most frequently suspected allergens (n=127; 27%), followed by foods (n=47; 10%) and

Hymenoptera venom (n=38; 8%). Follow-up in Allergy and Clinical Immunology consultation occurred in 377 patients (80%).

CONCLUSION

Tryptase is a valuable diagnostic tool, especially in anaphylaxis and mastocytosis/MCAS. In our cohort, tryptase measurements appear to be overutilized in contexts such as angioedema/urticaria, and potentially underutilized in anaphylaxis, considering that only one third of requests are made in the acute phase and that tryptase collection due to suspected anaphylaxis in the emergency department accounts for only 8% of total requests. These results highlight the need for further awareness of tryptase utility in distinct clinical settings.

CONFLICTS OF INTEREST

The authors did not specify any links of interest.

Submission number: 000069
Prefix: P24

MASTHAVE - A DIGITAL MONITORING APP DESIGNED FOR PATIENTS WITH MASTOCYTOSIS

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BACKGROUND

Mastocytosis is a rare and chronic disorder that affects various organs, including the skin, bone marrow, musculoskeletal system, gastrointestinal tract, spleen, and others. Patients present with a range of signs and symptoms, which make the diagnosis and management of the disease challenging. An app can offer a user-friendly approach to monitoring the disease course and organizing investigation results in a systematic fashion.

METHOD

The MASTHAVE app was developed by a team of experts in the treatment of mastocytosis. The relevant disease features and patient-reported outcome measures (PROMs) designed for mastocytosis have been defined and implemented in a manner that is readily understandable by those who are not experts in the field.

RESULTS

MASTHAVE was initially released to patients in Germany in June 2024. Further local language launches in Spain, Italy, France, Austria, Switzerland, and the USA are planned for October 2024 - early 2025. MASTHAVE is an innovative approach to improve interaction between patients with mastocytosis and their healthcare providers. Firstly, MASTHAVE supports the identification of signs and symptoms of the disease, possible triggers, disease activity and its impact on everyday life, detailed documentation of medical history and response to treatment, as well as results of previous examinations. Secondly, Mastocytosis-specific PROMs, such as the Mastocytosis Activity Score (MAS), the Mastocytosis Control Test (MCT), and the Quality of Life Questionnaire (MC-QoL) have been implemented and support disease evaluation in a standard manner. Finally, the app can provide a graphical summary of results that patients can share with their treating physicians, facilitating immediate and improved communication about the current disease status.

CONCLUSION

MASTHAVE provides vital support for mastocytosis patients and their physicians by enabling systematic and regular monitoring of disease signs and symptoms, medication intake, and treatment responses.

Main screen of MASTHAVE app

CONFLICTS OF INTEREST

The authors did not specify any links of interest.

Submission number: 000033
Prefix: P25

MOLECULAR PROFILE IN HYMENOPTERA VENOM ALLERGY IN PATIENTS WITH SYSTEMIC MASTOCYTOSIS

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BACKGROUND

Systemic Mastocytosis (SM) increases the risk of severe anaphylactic reactions to Hymenoptera venom. Accurate identification of the specific venom components responsible for allergic reactions is crucial for effective long-term venom immunotherapy (VIT), aimed at desensitizing patients to the allergen and preventing life-threatening anaphylaxis.

METHOD

This is a descriptive retrospective study of patients with mast cell diseases undergoing VIT. Demographic, clinical, molecular characteristics and CAP inhibition assays were analysed.

RESULTS

Fifteen patients (11 men) with a median age of 57,17 years [52,0-59,9] were included. Anaphylactic shock due to Hymenoptera venom was observed in 14 patients, with one experiencing anaphylaxis. All subjects had a REMA score ≥2. Eleven patients were diagnosed with bone marrow systemic mastocytosis, three with indolent systemic mastocytosis, and one with monoclonal mast cell activation syndrome. Median total IgE levels were 35,80 KU/L [11,50-104,00], and initial tryptase levels were 22,20 ug/L [10,38-31,78]. Based on skin tests and total sIgE levels, the sensitization profile comprised: 4 patients were monosensitized to *Polistes dominula*, one to *Vespula spp*, one to *Apis mellifera* and 9 had positive sIgE to both *Polistes dominula* and *Vespula spp*. CAP inhibition assays were conducted in 11 out of 15 patients, concluding: 5 patients were genuinely sensitized to *Polistes dominula*, 2 to *Vespula spp*, 3 presented co-sensitization to *Polistes dominula* + *Vespula spp* and one was genuinely sensitized to *Apis mellifera.* CAP inhibition assays couldn't be performed in 4 patients due to low sIgE levels. In the 9 patients with sIgE positive to both *Polistes dominula* and *Vespula spp*, CAP inhibition assay identified one genuine sensitizer in 6 of them (4 *Polistes dominula* and 2 *Vespula spp*), and confirmed co-sensitization in the remaining 3. Regarding immunotherapy, 8 patients are currently undergoing *Polistes dominula* vaccination, 3 *Vespula spp*, 3 patients receive double VIT for *Polistes dominula* and *Vespula spp* and one for *Apis mellifera*. VIT was initiated between 2005-2023 and, to date, all remain under treatment.

CONCLUSION

CAP inhibition assays are of valuable use in managing venom Hymenoptera allergy in patients with SM, particularly in selecting venom immunotherapy (VIT) for those experiencing hypersensitivity reactions to Hymenoptera stings.

CONFLICTS OF INTEREST

The authors did not specify any links of interest.

Submission number: 000047
Prefix: P26

NEGATIVE PREDICTIVE VALUE OF THE STING CHALLENGE IN PATIENTS WITH MASTOCYTOSIS: OUR EXPERIENCE

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BACKGROUND

Patients with mastocytosis are at higher risk than the general population for severe allergic reactions by hymenoptera stings. In these cases, lifelong venom immunotherapy (VIT) is the treatment of choice. In the absence of biomarkers, sting challenge is the gold standard for assessing the risk of systemic reaction. Our aim was to evaluate the sting challenges performed in our patients diagnosed of mastocytosis, as well as to analyze the predictive value of the test.

METHOD

Descriptive study of patients with systemic mastocytosis diagnosed of hymenoptera venom allergy to *Apis mellifera, Vespula spp.* and *Polistes dominula* (with positive skin tests and/or specific IgE > 0.35 KU/L to complete venom extracts and molecular profile) who received treatment with VIT and were subjected to the sting challenge.

RESULTS

15 patients were included, 12 males and 3 females with a mean age of 46. 2 patients were diagnosed with allergy to *Apis mellifera* venom, 11 to *Polistes dominula* and 2 to *Vespula spp.* and *Polistes dominula*, and treatment with VIT was initiated. All were subjected to sting challenge, performing a total of 20, 5 with *Apis mellifera*, 2 with *Vespula spp.* and 13 with *Polistes dominula*. They were tolerated in 100% of cases. Of the total, 8 patients with negative sting challenge were subsequently spontaneously stung. 6 patients tolerated the stung with a negative predictive value of 75%. Two patients presented mild symptoms, one flushing and tachycardia and another cervical pain and blurred vision after 3 simultaneous stings, maintaining normal vital signs.

CONCLUSION

We found that sting challenge is a safe, reproducible and currently irreplaceable test to monitor the efficacy of VIT in patients diagnosed with MS. We observed that in patients with negative sting challenge the probability of tolerating subsequent spontaneous stings exceeded 70%. It would be advisable to do more than one sting challenge in these patients.

CONFLICTS OF INTEREST

The authors did not specify any links of interest.

Submission number: 000043
Prefix: P27

PEDIATRIC MAST CELL DISORDERS: BE AWARE OF TANTRUMS

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BACKGROUND

Cutaneous mastocytosis may be associated with systemic symptoms due to mast cell mediators release. It is thought that alterations in KIT-structure and activity plays a key role in the pathogenesis of mastocytosis.

METHOD

We present a 3-year-old female patient diagnosed with urticaria pigmentosa due to multiple cutaneous lesions that started developing when she was 2 months old and increased progressively in number (>50), making the diagnosis of mastocytosis possible. The lesions worsened with cold, hot baths or anger. Serum basal tryptase was 24.8 µg/L, and an abdominal ultrasound was normal.

In July 2023 (at 2 years old), the patient experienced severe anaphylaxis with neurological involvement (loss of consciousness and hypotonia) and repeated vomiting, 30 minutes after eating chocolate she had tolerated several times before. She was having a tantrum at the same time. She was admitted to the emergency department and received intramuscular adrenaline along with antihistamines and corticosteroids, with a good response.

RESULTS

An allergological evaluation revealed low-level egg sensitization (sIgE egg white 0.28 kU/L, ovomucoid 0.33 kU/L), almonds (sIgE 0.21 kU/L), and hazelnut (sIgE 0.24 kU/L, rCor a 9 0.23 kU/L), and negative results for insect venom. An ALEX test showed low positive levels for melon profilin. She reported perioral urticaria with omelette and mustard. All involved foods were removed from her diet, and an epinephrine auto-injector was prescribed.

A genetic test using digital droplet PCR in peripheral blood identified a c-KIT mutation in c.2447A>T.p.Asp816Val (D816V mutation, allele frequency 0.07%). The patient was evaluated by the Hematology department and started treatment with daily antihistamines and disodium cromoglycate. According to the WHO diagnostic criteria for cutaneous and systemic mastocytosis, the patient meets two minor criteria (detection of mutation in blood and serum total tryptase >20 ng/mL); therefore, a bone marrow biopsy has not yet been indicated. Tryptase levels remain high, and no further anaphylactic episodes have occurred.

CONCLUSION

In patients with mastocytosis, especially in early childhood, tantrums as a form of stress can trigger or act as cofactors for anaphylactic reactions. This case highlights the difficulty of managing emotional stress in pediatric patients with mastocytosis to prevent severe allergic responses. Multidisciplinary work is therefore essential in order to diagnose, treat and manage this disease. The risk of unforeseeable reactions due to presence of triggering factors is unpredictable.

CONFLICTS OF INTEREST

The authors did not specify any links of interest.

Submission number: 000065
Prefix: P28

THIS POISON FLIES

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BACKGROUND

The purpose of the study is to demonstrate the different pattern of sensitisation that Vespa Velutina hypersensitivity can have.

METHOD

The study employed both in vivo and in vitro methods to assess the patient's allergic diagnosis and the treatment. In Vivo methods included: medical history, circumstances of stings, symptoms and treatments administered, and Skin Prick Tests (SPT) and Intradermal Tests (IDT) to test sensitivity from: *Vespula spp, Polistes sp, Polistes dominula* and *Apis mellifera.* In Vitro methods included: total Ig E (tIg E) , specific IgE (sIg E) to *Polistes dominula*, *Vespula spp* , *Apis mellifera*; tryptase levels and CAP inhibition study.

RESULTS

54-year-old male, with hypertension and dyslipidaemia, no personal or family history of atopy, treated with losartan/hydrochlorothiazide, amlodipine, plague control worker; 20-25 minutes after being bitten by a Vespa velutina on the right wrist, despite wearing a suit; he presented with: burning sensation in the wrist and forearm, sweating, hyperventilation and loss of consciousness. He received emergency treatment with antihistamines and corticosteroids, with clinical relief.

SPT and IDT were Positive for *Polistes spp.* at 1 mcg/ml and Negative for *Apis mellifera* and *Vespula spp.* In Vitro Testing: the tryptase level during the reaction was 44 ug/l, tIg E: 122 kU/L, sIgE for *Polistes dominula* (rPold5: 126 KU/L) an significant levels for *Vespula spp*. (rVes v1 and rVes v5) and *Apis mellifera* (rApi m1, m3, and m10) was observed. In CAP inhibition: significant inhibition was observed in homologous inhibition (97%) and heterologous inhibition of Vespula

(91%) when inhibited with *Polistes dominula* venom. Inhibition with the mixture of *Polistes* venoms with *Vespula* venoms did not provide significantly better inhibition than incubation with *Polistes dominula* venom alone.

CONCLUSION

The patient was diagnosed with anaphylactic shock due to the sting of *Vespa velutina*. Sensitisation to *Polistes dominula* (Pol d5), *Vespula spp* (Ves v1 and Ves v5) and *Apis mellifera* (Api m1, 3 and 10) was also observed. CAP inhibition has helped us to establish that the immunotherapy that best prevents severe reactions in this patient is immunotherapy with *Polistes dominula* venom.

CONFLICTS OF INTEREST

The authors did not specify any links of interest.

Submission number: 000025
Prefix: P29

SYSTEMIC MASTOCYTOSIS AND NON-STEROIDAL ANTI-INFLAMMATORY DRUG-INDUCED ANAPHYLAXIS: A CASE REPORT

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BACKGROUND

Systemic mastocytosis (SM) is characterized by abnormal proliferation and activation of clonal mast cells in extra-cutaneous organs, releasing preformed and newly synthesized mediators and contributing to allergic reactions. Anaphylaxis has a higher prevalence in patients with SM than the general population, mainly with hymenoptera venom stings and drugs.

METHOD

Case report

RESULTS

A 25-year-old female patient, Internal Medicine resident, was referred to our Allergy Department due to two episodes of non-steroidal anti-inflammatory drug (NSAID)-induced anaphylaxis. The first episode occurred after intake of Ibuprofen (otitis) and the second with Diclofenac (backache), with serum tryptase levels of 144 ug/L and 117 ug/L, respectively. In the Emergency Department she was treated with intravenous anti-histamines and corticosteroids. Baseline tryptase was 92 ug/L (1.0 to 15 ug/L). Bone marrow biopsy, myelogram and immunophenotypic study were conducted, confirming indolent SM. *c-kit* D816V mutation wasn't detected. NSAIDs eviction was advised and the patient was prescribed Ketotifen 1 mg once daily and Bilastine 20 mg once daily. Skin prick tests (SPT) with inhalants, cereals and peach non-specific lipid transfer protein were executed to exclude co-factor enhanced food allergy. The patient stopped taking daily anti-histamine and no

further anaphylactic episodes were stated. To study the NSAIDs hypersensitivity, oral drug provocation test (DPT) with Ibuprofen was performed, with malar and neckline erythema, headache and palpebral and ear edema 1 hour after administration (600 mg).

DPT was later performed with Etoricoxib, as an alternative NSAID, with no reaction. Paracetamol and Tramadol were tolerated by the patient as well. mRNA SARS-CoV-2 vaccination without premedication took place with no complications.

CONCLUSION

Clonal mast cell activation disorders are associated with an increased risk of adverse reactions to multiple drugs. NSAIDs and vaccines are often empirically avoided without evidence of reactions, depriving patients of needed medications and placing them at risk for unfavorable outcomes. In patients with a history of adverse reactions, testing is recommended to avoid mislabeling. This clinical case reinforces the importance of de-labeling with skin testing and/or provocation procedures, to prevent unnecessary avoidance of first-line medications.

CONFLICTS OF INTEREST

The authors did not specify any links of interest.

Submission number: 000037
Prefix: P30

SEVERE ANAPHYLAXIS FOLLOWING BEE STING WITH SLIGHTLY ELEVATED BASAL SERUM TRYPTASE: COULD IT BE MASTOCYTOSIS?

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BACKGROUND

Hymenoptera venom is one of the three most common causes of anaphylaxis, accounting for 48.2% of severe anaphylaxis cases. It is a significant allergen due to the severe reactions it can induce, with up to 42% of reactions to hymenoptera stings classified as severe.

The most important risk factors for severe systemic reactions (SSRs) due to hymenoptera stings are mastocytosis or elevated baseline serum tryptase.

METHOD

Case report: We present a case of a 50-year-old male, with history of SSR (anaphylaxis grade IV WAO) due to hymenoptera sting and significant cardiovascular comorbidities (non-ST-elevation myocardial infarction, ischemic cardiomyopathy and hypertensive cardiomyopathy). One year prior to allergological evaluation in our clinic, the patient was stung by a bee on his upper back,

during a seaside holiday. Within minutes, he developed generalized pruritus, dyspnea, abdominal discomfort, culminating with peripheral cyanosis and signs of cerebral hypoperfusion-blurred vision (the patient could not provide any data on the vital signs during the reaction). The administration of two doses of 300 micrograms of epinephrine was needed for symptom resolution. The allergological workup revealed the presence of specific IgE antibodies to bee venom (2,28 ku/l) and an elevated basal serum tryptase (BST) level (11,6 ng/ml compared to the upper normal limit of 11,4 ng/ml) in two consecutive determinations, which raised the suspicion of systemic mastocytosis. Consequently, the patient was referred to a haematology clinic and is currently under investigation.

RESULTS

Risk assessment for this patient identified multiple risk factors for a future SSR due to hymenoptera sting, including elevated basal serum tryptase, cardiovascular comorbidities and male sex. The patient was prescribed an EpiPen and was provided with exposure prophylactic measures. Furthermore, the patient is a suitable candidate for venom immunotherapy (VIT), which will be initiated as soon as the product becomes available in Romania.

CONCLUSION

In alignment with other cases previously documented in the literature, our case emphasizes the necessity for further hematologic evaluation in individuals presenting with SSR following a hymenoptera sting and slightly elevated BST. Furthermore, it is evident that the initiation of VIT is of paramount importance, particularly in view of the high risk of future SSR that this patient population is subject to.

CONFLICTS OF INTEREST

The authors did not specify any links of interest.

Submission number: 000074
Prefix: P31

THE ROLE OF OMALIZUMAB ON MASTOCYTOSIS-ASSOCIATED SYMPTOMS

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BACKGROUND

Omalizumab (OMA), a monoclonal anti-IgE antibody, is labelled for the treatment of asthma as well as chronic idiopathic urticaria. In systemic mastocytosis (SM), OMA seems to be a promising treatment option, preventing anaphylaxis and improving chronic mediator-related symptoms in patients who do not achieve symptom control with standard therapy as reported in previous case reports and few case series. The only two existing randomized placebo-controlled study have documented an improvement in mediator related-symptoms in the group of treated patients, without reaching statistical significance. Specifically, ROAM study investigated the efficacy of OMA at

the dosage of 375 mg monthly while in XOLMA study, a few patients underwent OMA doses according to IgE and their body weight.

METHOD

We describe the case of an 80-yo-woman affected by SM, wild-type for the cKIT gene, indolent variant according to the World Health Organization's diagnostic criteria.

RESULTS

Indolent SM was diagnosed as a result of severe anaphylactic reactions to drugs (beta-lactam antibiotics and vitamin B6) by laboratory and instrumental work-out. Serum basal tryptase level was equal to 24 ng/ml and there were no associated-mediator symptoms, nor a history of spontaneous or insect bite-induced anaphylaxis. The follow-up in the subsequent three years did not show any significant clinical manifestations. Then, the patient presented frequent episodes of widespread body transient itchy wheals, sometimes associated with angioedema of the lips and face, resistant to 2nd generation H1antihistamines administrated up to three times a day.The clinical picture suggested the chronic presence of idiopathic spontaneous urticaria and angioedema. Considering these findings and the need for multiple courses of oral corticosteroids in a patient with osteopenia as a comorbidity, OMA therapy was started at the dosage of 300 mg every four weeks without obtaining any effectiveness after six months.

CONCLUSION

We experienced a case of ineffectiveness of OMA in a patient affected by indolent SM with chronic urticaria and angioedema manifestations. Currently, it is believed that OMA can regulate the activation state of mast cells and the subsequent release of mediators, but the mechanisms of action of OMA in mast cell disorders and SM pathogenesis are not fully understood. Indeed, the hypothetical dosage of OMA to control the reactivity of mast cells is still unknown. Due to the existence of multiple and complex mast cell inflammatory pathways, the management of mast cell-dependent diseases, such as SM with chronic urticaria manifestations, is not always predictable. The growing understanding of the pathogenic mechanisms may allow identifying the personalized therapeutic strategy, particularly when the activation of mast cells is not solely IgE-mediated.

CONFLICTS OF INTEREST

The authors did not specify any links of interest.

Submission number: 000014
Prefix: P32

THE ALLERGIST'S CENTRAL ROLE IN MULTIDISCIPLINARY CARE: FROM A HYMENOPTERA STING TO A MASTOCYTOSIS DIAGNOSIS

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BACKGROUND

Systemic mastocytosis is a rare group of conditions caused by an increased number of clonal mast cells in the body's tissues. Patients affected by this disease are more likely to develop anaphylaxis. Hymenoptera stings are the most common triggers leading to a diagnosis. It is particularly important to achieve a complete assessment of the patient due to a very wide range of disease subtypes and, since the release of mediators occurs in various organs and tissues, it is necessary to refer the patient to different specialists.

METHOD

This descriptive case report highlights the importance of a long-term multidisciplinary follow-up. To carry out this analysis, this report will focus on a 78-year-old woman diagnosed with indolent systemic mastocytosis, attended by our allergology department since 2022.

RESULTS

In 2022 the patient suffered an anaphylactic shock, syncope first, with urticaria and emesis occurring shortly after, caused by a hymenoptera sting. Serum IgE levels for extractive and molecular allergens as well as skin tests highlighted sensitization to Vespula spp. venom and immunotherapy was initiated. Secondly, the patient was referred to a hematology specialist due to high serum tryptase. A bone marrow assessment confirmed indolent systemic mastocytosis and a molecular biology evaluation showed the c-KIT D816V mutation. Furthermore, given a known osteoporosis condition since 2005, the patient was referred to a bone unit for a reassessment and put on bisphosphonates therapy. As a result, after three years, her bone mineral density values improved. Additionally, the patient regularly undergoes abdominal ultrasounds, all of which have shown no abnormalities. It is also relevant that the patient has previously undergone surgeries under general anesthesia and imaging with contrast agent without developing adverse drug reactions. Finally, the patient has never presented gastrointestinal or dermatological mediator-release symptoms.

CONCLUSION

In conclusion, this case highlights the need of a multidisciplinary approach for patients with systemic mastocytosis diagnosis and the importance of referring them to specialised physicians. Usually, allergists are the first tasked with assessing a probable diagnosis of systemic mastocytosis and, in case of hymenoptera venom allergy, they are the ones who frequently monitor the patient's progress. Therefore, allergists need a good knowledge of this condition in order to promptly refer the patients to the appropriate specialist.

CONFLICTS OF INTEREST

The authors did not specify any links of interest.

Submission number: 000035
Prefix: P33

HIMENOPTERA BITE IN PROFESSIONAL BOTANY, WITH SUBSEQUENT DIAGNOSIS OF SYSTEMIC MASTOCYTOSIS

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BACKGROUND

Systemic mastocytosis is a group of diseases that cause systemic symptoms secondary to the activation and release of mast cell mediators. These symptoms may appear due to an identifiable trigger, whether or not specific IgE is detected against it. Or without a trigger being identified. The most common cause of mast cell activation is the bite of Hymenoptera.

METHOD

Male, 60 years old, botanist by profession. During the month of June, while he was working outdoors, he received a sting from a Hymenoptera on his right arm. He identifies it as an Asian wasp. He believes that in childhood he received a wasp sting, but is not sure. Minutes later after the bite he began to experience intense dizziness, without losing consciousness, as well as dyspnea, nausea and headache. Edema in the bite area, without edema or skin lesions at other levels. A colleague takes him to the emergency room.

RESULTS

Upon arrival at the emergency room, he presented hypotension (SBP 75/50 mmHg), desaturation (satO2 89%) and tachycardia (112 bpm). Antihistamine, corticosteroid and intramuscular adrenaline, and serum therapy was administered. He was monitored and left to evolve, with a good response. Tryptase was normal (6.2 ng/mL). Subsequently, he was referred to the Allergology service where skin tests were performed on Hymenoptera, which were positive for Vespula and Vespa velutina. In analytics, were positive of Vespula and Vespa velutina. He was referred by his allergist to a reference center for mastocytosis study, subsequently confirming the diagnosis of systemic mastocytosis. Vaccination for Vespula was indicated, Vespa velutina vaccine not available.

CONCLUSION

In patients with systemic reactions to Hymenoptera stings, the presence of mast cell disorders, whether mast cell activation syndromes or systemic mastocytosis, must be ruled out, as well as the presence of hereditary alpha-tryptasemia. Identification is important since Hymenoptera bites are the most common cause of mast cell activation and immunotherapy is indicated indefinitely.

CONFLICTS OF INTEREST

The authors did not specify any links of interest.

Submission number: 000034
Prefix: P34

HYMENOPTERA VENOM-ASSOCIATED ANAPHYLAXIS IN A PATIENT WITH INDOLENT SYSTEMIC MASTOCYTOSIS WITHOUT SKIN INVOLVEMENT

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BACKGROUND

The association between Hymenoptera venom allergy (HVA) and clonal mast cell-related disorders (cMCD) was clearly established decades ago. The frequency of HVA in mastocytosis is 20–50 % and raises to 60–80 % in patients affected by indolent systemic mastocytosis without skin involvement (ISM (-)).

METHOD

We present a case of an ISM (-) patient with anaphylaxis triggered by a honeybee sting.

RESULTS

A 34-year old female patient was diagnosed with indolent systemic mastocytosis by a hematologist, during thrombophilia examination after 3 miscarriages. The bone marrow biopsy revealed multifocal dense infiltrates of mast cells, baseline serum tryptase was elevated (37 mcg/L), KIT point variant at codon 816 was not detected, and the patient had no skin lesions or other systemic findings. One month after the diagnosis, the patient experienced severe Hymenoptera venom - triggered anaphylaxis with hypotension and loss of consciousness, in the absence of other clinical manifestations. She was then referred to an allergist. Four weeks after the reaction, an immunoglobulin E (IgE) – mediated HVA was proven by skin prick test and specific IgE against Apis mellifera. Specific venom immunotherapy (VIT) was indicated, however, it was postponed due to the pregnancy. The patient delivered a healthy boy, with hematological premedication and under continuous medical supervision. VIT is about to start now, with special precautions.

CONCLUSION

The symptoms of HVA are one of the most frequent clinical presentation in ISM (-) patients. These findings suggest that the impact of cMCD on Hymenoptera venom-triggered anaphylaxis could be underestimated. Patients with HVA-associated anaphylaxis, typically with cardiovascular manifestations, should be evaluated for cMCD before starting VIT.

CONFLICTS OF INTEREST

The authors did not specify any links of interest.

Poster discussion Session – Group 4 – Topic: Hymenoptera in a changing world
Friday, 20 September 2024

Submission number: 000006
Prefix: P35

DETERMINING THE SAFETY OF SWITCHING IMMUNOTHERAPY BETWEEN DIFFERENT MANUFACTURERS IN INSECT VENOM IMMUNOTHERAPY - A REAL-WORLD EXPERIENCE

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BACKGROUND

Insect venom specific immunotherapy (VIT) is a proven and effective therapy to induce tolerance in patients with insect venom allergy. The insect venom used for VIT is of natural origin and is composed of the insect venom from Apis spp. or Vespula spp. Despite significant differences in the amount and composition of the allergens due to different processing strategies, similar treatment efficacy has been described for the different preparations. Some are supplied as aqueous extracts, while others are depot formulations. Nevertheless, these differences may be associated with preparation-specific side effect profiles. In addition, patients allergic to insect venom often have an individual sensitization profile that may be associated with severe anaphylactic reactions. Thus, the characteristics of the venom preparation and the individual sensitization profile of the patient may be of particular importance when supply bottlenecks necessitate switching to another preparation. Further data are needed to minimize the costly prolongation of the post-VIT monitoring period due to safety concerns.

METHOD

In our retrospective clinical study, we evaluated 168 patients (52% female, 48% male) with honeybee insect venom allergy (10%), wasp venom allergy (87%, 1% hornet) and combined insect venom allergy (2%). Our patient cohort included 3 patients with systemic mastocytosis and 9 patients with elevated basal mast cell tryptase of unknown clinical significance (mean 15.68 µg/l). At the time of the switch, all patients were in the maintenance phase of the VIT, 2 (1%) on reduced insect venom dosage, 161 (96%) on normal (100 µg) and 5 (3%) on increased dosage (150 µg resp. 200 µg). We changed the insect venom preparation from an exclusively lyophilized preparation to a preparation with a reduction of anaphylaxis-related molecular antigens and the use of a depot preparation with aluminum hydroxide. Patients were monitored for two hours. In eight cases, patients were monitored on the ward for 24 hours.

RESULTS

There were no anaphylactic events (0%) during the switch to the other supplier's preparation.

CONCLUSION

In our large cohort of patients (N = 168), we observed no adverse side effects associated with switching from lyophilized to aluminum depot formulations with different processing strategies. Thus, we show that there is no need to extend the monitoring period. This applies exclusively to the two insect venom preparations used in our study.

CONFLICTS OF INTEREST

The authors did not specify any links of interest.

Submission number: 000039
Prefix: P36

HYMENOPTERA VENOM ALLERGY IN TOLOSALDEA, GIPUZKOA, SPAIN: A RETROSPECTIVE AND DESCRIPTIVE ANALYSIS OF 15 PATIENTS

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BACKGROUND

Vespula and Vespa species cause the majority of the anaphylaxis in Tolosaldea. Gipuzkoa represents a doorway for Vespa Velutina Nigrithorax (VVN) to northern Spain and it is considered a public health problem. Our aim was to describe the epidemiological, demographic and clinical characteristics, sensitization profile and the current treatment of patients with Hymenoptera venom allergy (HVA) in Tolosaldea.

METHOD

A retrospective and descriptive analysis was conducted on patients with HVA (from 2021 to may 2024) currently undergoing follow-up in the Allergy Department. The severity of systemic reactions (SR) was assessed according to Müller's classification (MC). Sensitization pattern was determined through sIgE and basal tryptase was measured. Mast cell clonality were predicted by the REMA score. KIT^{D816V} and molecular studies to assess the TPSAB1 genotype were performed in peripheral blood of patients with REMA score >2. Statistical tests were used for the association of variables.

RESULTS

The median age was 65 years (22-79 years) and 86,67% were males. All lived in a rural environment and 40% had high risk of exposure (1 beekeeper). 13 (86,67%) had anaphylaxis and two had large local reactions (LLR). 14/15 identified the culprit insect (CI) and there was correlation between previous mild stings (PMS) and SR with *Vespula spp.* ($p<0.05$). All patients

with SR to VVN identified *Vespula spp*. in PMS. Most reactions happened in the first 15 minutes (60%) with no differences regarding the CI. No differences were found between the CI and age, sex or occupation. According to MC, 46,15% had grade IV reaction. Laboratory tests are shown in the Table. Anaphylaxis happened in 6/13 to *Vespula spp*., in 4/13 to VVN, in 2/13 to *Apis mellifera* and in 1/13 to *Vespa crabro.* Three patients had a REMA score >2. In these patients, the KIT mutation was negative and one had TPSAB1 3α:2ß genotype. Currently, 14/15 patients are receiving venom immunotherapy (VIT) with Alutard ALK-Abelló Lab.: 2 with *Apis mellifera* and 12 with *Vespula spp.* with no adverse reactions.

CONCLUSION

Anaphylaxis is the main reason for consultation for HVA in Tolosaldea. There´s an association between PMS and SR with *Vespula spp. Vespula spp*. is the most frequent Hymenoptera in SR followed by VVN. VIT has shown to be safe in these patients.

Table. Laboratory results of sensitization profile and basal tryptase in patients with systemic reaction.

	n	%	Median	IQR
Serum specific IgE, kU_A/L				
Apis mellifera	11	91.66	0.21	0.09-1.01
Polistes spp.	11	91.66	0.83	0.42-6.05
Pol d 5	8	66.66	1.92	0.66-7.54
Vespula spp.	11	91.66	2.13	1.67-4.72
Ves v 1	7	58.33	0.09	0.09-3.68
Ves v 5	8	66.66	2.53	1.26-5.84
VVN	7	58.33	1.67	0.47-2.89
tIgE, kU/L	12	100	208	96.6-628
Baseline tryptase, µg/L	12	100	5.42	4.45-5.88

Abreviations: IQR, Interquartile Range; VVN, Vespa Velutina Nigrithorax.

Table. Laboratory results of sensitization profile and basal tryptase in patients witg sysptemic reaction.

CONFLICTS OF INTEREST

The authors did not specify any links of interest.

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Prefix: P37

HYMENOPTERA VENOM ANTIGEN-SPECIFIC IMMUNOTHERAPY: A 17-YEAR-LONG EXPERIENCE OF A CHILEAN CENTER

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BACKGROUND

Allergy to hymenoptera venom affects up to 5% of those stung by Hymenoptera species. In Europe, the prevalence of systemic reactions due to Hymenoptera venom is 0.3-8.9% in adults and up to 3.4% in children, affecting 14-32% of individuals frequently exposed, such as beekeepers. Antigen-specific immunotherapy (ASI) is the only effective treatment that protects from systemic reactions in the case of future stings, with an efficacy of 91-96% in vespids and 77-84% in bees.

Access to ASI in Chile is limited to a few public and private centers, most of which are located in Santiago. This study presents a 17-year-long experience of a Chilean center.

METHOD

Data was obtained from electronic clinical files and manual registries at the allergy center for all 42 patients who have received hymenoptera ASI since 2007.

RESULTS

Patients began treatment between the ages of 3 and 66 years, with a median of 14. 64% of them are men. 93% of the patients are allergic to bees, and 76% have a connection to agriculture and/or beekeeping, either through their own occupation, their relatives', or where they live. Two patients have mastocytosis. 31% have atopic diseases.

Nine allergic to bees patients underwent molecular IgE studies. All tested positive for Api m1, followed by Api m2 (78%) and, among those tested for Api m3 and m10, all resulted positive. Consensibilization to vespids, whether by molecular or specific IgE, was found, but without clinical significance. Altered tryptase was only found in the mastocytosis patients.

All patients began ASI with conventional protocols and received immunotherapy for 2 to 74 months, with a median of 30 months. Seven patients experienced systemic reactions to immunotherapy, which occurred during the build up phase or when changing batches. Eight patients presented spontaneous stings during immunotherapy, but none had systemic reactions.

Six patients are actively undergoing immunotherapy, and among the inactive patients, only 15 completed treatment, two changed centers, and 19 abandoned treatment.

CONCLUSION

In this series, most of the patients have an allergy to bees, which reflects the reality in Chile. Molecular sensitization profiles show polisensitization, with Api m1, m2, m3 and m10 as major allergens.

Molecular diagnosis is scarcely available in Latin America, and in Chile, it's been available since 2017. Molecular sensitization profiles and future implementation of controlled sting challenges will allow us to improve decision making when treating these patients.

Api m1	Api m2	Api m3	Api m5	Api m10	Ves v1	Ves v5
0,83	3,86	0,23	0,37	1,52	1,97	0,83
0,93	0,16	0,12	0,08	0,11	0,06	0,11
0,94	3,28	N/D	N/D	0,4	<0,1	0,91
1,9	<0,1	1,31	<0,1	1,01	<0,1	<0,1
2,4	7,4	0,2	<0,1	6,09	<0,1	<0,1
2,91	0,91	1,61	N/D	N/D	N/D	N/D
4,7	2,31	0,59	0,97	4,29	0,05	0,02
5,18	<0,1	3,23	<0,1	15,5	<0,1	<0,1
61,1	13,2	N/D	N/D	N/D	N/D	<0,1

Fig 1. Molecular IgE studies of nine patients previous to immunotherapy

Molecular IgE studies of nine patients previous to immunotherapy

CONFLICTS OF INTEREST

The authors did not specify any links of interest.

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Prefix: P38

SIMULTANEOUS IMMUNOTHERAPY INITIATION WITH TWO HYMENOPTERA VENOMS: EXPERIENCE OF 8 CASES

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BACKGROUND

Hymenoptera venom hypersensitivity is potentially fatal; venom immunotherapy (VIT) is indicated after severe reactions, because it is safe and effective in reducing allergy symptoms in the case of a new sting. However, this treatment can be administered only in hospital setting, and the initial updosing phase should be titrated carefully over time, in order to limit adverse reactions. When there is the need of reaching a good protection fast, it would be convenient to concentrate the updosing phase as much as possible, provided that there are no safety concerns. Few data are available on simultaneous dual VIT, and recommendations on this topic are mainly based on expert consensus. Aim of this work is to share our experience on simultaneous dual VIT with vespid venoms.

METHOD

We retrospectively assessed data of the patients with hymenoptera venom hypersensitivity who initiated VIT at Padova university hospital from 2010 to 2024. The medical records of patients with double sensitization to different hymenoptera venoms who performed a simultaneous dual VIT were thoroughly reviewed. Informed consent was given by all the patients participating in the study.

RESULTS

Among 370 patients who initiated VIT, 8 performed simultaneous dual VIT, because of double sensitization along with the need of a fast updosing phase. All of these 8 patients were male, with a mean age of 68,25 years and a standard deviation of 15,11 years (range 40-86 years). 4 patients complained severe reactions (Mueller grade III or IV), while 4 patients had less severe reactions (Mueller grade I or II). After assessment of history, IgE concentration and skin testing, 4 patients were found sensitized to polistes spp and vespula spp, 3 patients resulted sensitized to v. crabro and vespula spp, and 1 patient resulted sensitized to v. crabro and polistes spp. The patients initiated VIT in 2014 (3 patients), 2015 (2 patients) and 2017 (3 patients). The schedule was as follows: the aqueous extracts of the two purified hymenoptera venoms were administered subcutaneously in increasing concentration in day 1 (baseline) and in days +3/4, +8/12 and +15/18 from baseline, reaching the full dose of both venoms at 15/18 days. This procedure was well tolerated and all the patients reached the full dose; 6/8 patient complained local pruritus and/or local swelling, with one patient needing to slow down the schedule adding an additional time point before reaching the full dose. Depot extracts were administered after about 30 days from baseline, and all patients subsequently began monthly administration. All the patients were stung again by hymenoptera without significant reactions and are currently receiving immunotherapy administration on a 12 weeks interval, without side effects.

CONCLUSION

In our limited experience, simultaneous dual VIT with vespid venoms seems a safe and effective strategy when a fast updosing phase is needed.

CONFLICTS OF INTEREST

Travel grants received form Alk-Abello

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IMMUNOTHERAPHY WITH VESPA VELUTINA NIGRITHORAX: TWO CASES OF SUCCESSFUL ULTRA-RUSH INDUCTION PROTOCOL

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BACKGROUND

Vespa velutina nigrithorax (VVN), also called asian hornet, is an insect native from South-East Asia and considered an invasive species in other countries. As other *Hymenoptera,* severe allergic reactions can be prevented with venom immunotherapy (VIT). However, there is still a lack of knowledge about VIT with VVN venom.

METHOD

To describe two cases of VVN VIT submitted to a 210-minutes (Birnbaum J et al, 2003) ultra-rush induction protocol and theirs follow up in our Immunoallergology clinic.

RESULTS

Case 1: Female, 55 years, developed generalized urticaria and dyspnea few minutes after VVN sting in peri-orbital zone. Allergic investigation found positive skin prick test and intradermal tests with VVN venom (Roxall®) - table 1. During the tests, the patient developed lip pruriginous oedema, treated with oral steroids and antihistamines. VVN specific IgE (sIgE) was 23,7 kUA/l. VVN VIT (Roxall®) using an *ultra-rush* induction protocol was prescribed in June 2023, under pre-medication with anti-histamine and montelukast, with no complications besides bilateral large local reaction in injection sites. Serial assessment of VVN sIgE at 3 and 6 months of VIT was, respectively, 13,5 kUA/l and 10,1 kUA/l.

Case 2: Male, 30 years, describes an episode of cough, dyspnea, local oedema and oropharyngeal tightness few minutes after VVN sting in peri-orbital zone. Allergic investigation found positive skin prick test and intradermal tests with VVN venom (Roxall®) - table 1. VVN sIgE was 22,4 kUA/l. The patient started VVN VIT (Roxall®) under *ultra-rush* induction protocol in July 2023, under pre-medication with anti-histamine and montelukast, with no adverse events. In this patient, sIgE to VVN after 6 months of treatment was 4.48 kUA/l .

Both patients identified the culprit stinging insect as being VVN and none was stung again.

Table 1 indicates the specific IgE values and the results of skin test of both patients.

CONCLUSION

VVN VIT seems to be safe as both patients tolerated an *ultra-rush* induction protocol with no systemic adverse events. None of the patients was stung again but we have identified a reduction in sIgE after 6 months of VIT.

Table 1 - Investigation in the Immunoallergology clinic of both patients

	Case 1	Case 2
Skin tests before VIT (largest papule diameter) - mm		
Skin prick test		
Vespula spp.	neg	neg
Polistes spp.	neg	neg
VVN	6	neg
Intradermal test		
Vespula spp. 0.01 mcg/mL	neg	neg
Vespula spp. 0.1 mcg/mL	neg	neg
Vespula spp. 1 mcg/mL	10	neg
Polistes spp. 0.01 mcg/mL	neg	neg
Polistes spp. 0.1 mcg/mL	neg	neg
Polistes spp. 1 mcg/mL	neg	neg
VVN 0.01 mcg/mL	10	8
VVN 0.1 mcg/mL	12	10
VVN 1 mcg/mL	14	12
sIgE before VIT- kUA/l		
sIgE V*espula spp*	52.2	6.54
sIgE *Ves v1*	13.4	2.33
sIgE *Ves v5*	44.2	0.04
sIgE *Polistes spp*	58.4	1.57
sIgE *Pol d 5*	44.7	0.03
sIgE *VVN*	23.7	22.3
Basal tryptase level - mcg/ml	9.1	2.9
sIgE After VIT- kUA/l		
sIgE *VVN 3 months*	13.5	Not determined
sIgE *VVN 6 months*	10.1	4.48
Abbreviations: neg - negative; Pol d - polistes dominula; sIgE - specific IgE; Ves v - *Vespula vulgaris;* VIT - venom immunotherapy; VVN - *Vespa velutina nigrithorax*		

Table 1 - Investigation in the Immunoallergology clinic of both patients

CONFLICTS OF INTEREST

The authors did not specify any links of interest.

Submission number: 000058
Prefix: P40

A CASE OF ANAPHYLAXIS FROM XYLOCOPA VIOLACEA STING

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BACKGROUND

Xylocopa violacea (XV) is a solitary bee in Central-Southern Europe and it belongs to Apidae family like *Apis mellifera* (AM) and *Bombus terrestris* (BT). We describe a case of anaphylaxis after XV sting and identification of its protein components.

METHOD

Our patient with clear history of anaphylaxis after XV sting more than 25 years ago, underwent allergologic work up consisting of skin test with venom extracts (Anallergo), basophil activation test (Bühlmann Laboratories) and s-IgEs (ThermoFisher scientific) for venom extracts and molecules. Immunoblotting and EAST-inhibition with patient's serum and venoms from XV and AM were carried out. Finally, SDS-PAGE with XV, AM and BT venoms was also performed.

RESULTS

Positive results were obtained with intradermal test at concentration of 1 µg/ml of AM venom. S-IgEs were positive for AM venom extract (0.23 kUa/L) and rApi m10 (0.12 kUa/L); basophil activation test confirmed positivity for AM venom (36.9%).

However, neither EAST-inhibition nor immunoblotting could demonstrate any reactivity of patient's serum to AM and XV venoms. Interestingly, SDS-PAGE showed different protein profiles among Apidae venoms. In XV most represented proteins were melittin, apamin and phospholipase A2 (PLA2). Another relevant protein seemed to be CAP VA5.

CONCLUSION

In our patient, tests demonstrated sensitization to AM venom, probably due to cross-reactive allergens in AM and XV venoms.

A limitation of our study is the long interval between clinical event and performing of tests. Indeed, *in vivo* and *in vitro* reactivity to AM venom was low. Also, EAST-inhibition and immunoblotting were negative.

Being a previous XV sting very unlikely in our patient, we may speculate that the reaction to XV sting was secondary to prior sensitization to AM PLA2, which shares sequence identity of 58% with AM PLA2.

Our data shows that XV PLA2 is likely to be a clinically relevant allergen in XV.

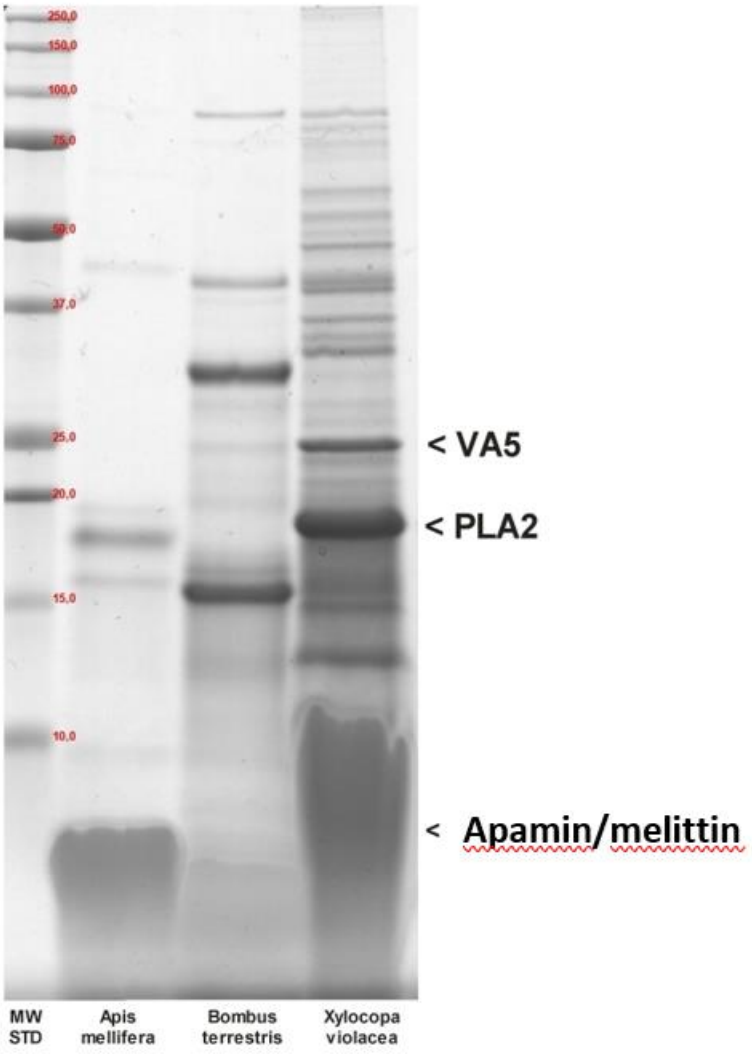

Figure 1. SDS-PAGE with AM, BT and XV venoms

CONFLICTS OF INTEREST

D.Labardi and N. Orsi Battaglini work in Anallergo, S. Turillazzi works in Insect Pharma Entomotherapy, Florence, Italy

Submission number: 000041
Prefix: P41

EFFICACY AND SAFETY OF HYMENOPTERA VENOM ALLERGY IMMUNOTHERAPY (VIT) AND THE LONGER MAINTENANCE SCHEDULE (12 MONTHS) IN OCCUPATIONAL EXPOSED (OE) PATIENTS

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BACKGROUND

Sensitization to Hymenoptera venom is 15-25% in general population is higher in workers occupationally exposed reaching 31-38%; the risk of systemic reaction (SRs) is reported between 14 to 45%, higher in not a risk population (0.3-7.5%). Therefore, there is a strong indication of VIT in these patients. However, the conventional schedule (monthly maintenance doses) can be time consuming and can reduce an optimal adherence to thetreatment. Aim of the study: the evaluation of efficacy and safety of VIT in occupationally exposed compared to a group of subjects without work related risks. A 3 months interval in maintenance was also administered in a selected group of OE subjects

METHOD

A population of 116 patients with previous severe systemic reactionsto HV (grade 3 or 4 according to Muller classification) with skin and specific IgE positivity were evaluated. In the group of occupationally exposed patients were included 44 subjects, whereas the control group consisted of 72 patients. All patients were evaluated for systemic reactions in the field (severity, use therapy).

RESULTS

After 10 or 15 years of treatment the frequency of stings on the field was 2.5 in work exposed patients and 1.4 in controls. SSR were registered after the treatment in 0.4% of occupationally exposed patients vs 0.18 in controls. Epinephrine was administered in three cases in the occupational exposed patients and in one case incontrols. No LLR and SR were observed in the group of patient susing a 12 maintenance weeks and the efficacy was comparable with the conventional schedule.

CONCLUSION

Our study confirms the efficacy and safety ofVIT, which is comparable in occupationally expose patients and in control. The longer maintenance schedule may be convenient as less time consuming and may increase the adherence to treatment.

CONFLICTS OF INTEREST

The authors did not specify any links of interest.

Submission number: 000052
Prefix: P42

SEVERE ADVERSE REACTIONS FOLLOWING INTERRUPTED VENOM IMMUNOTHERAPY IN A 42-YEAR-OLD FEMALE DUE TO PRODUCT UNAVAILABILITY: A CASE REPORT

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BACKGROUND

Venom immunotherapy (VIT) is a critical intervention for patients with hypersensitivity to insect stings, preventing potentially life-threatening allergic reactions. However, interruptions in the treatment regimen can lead to adverse events upon re-administration of the therapy.

METHOD

Case Presentation: A 42-year-old female patient, M.A., on February 16, 2024 experienced significant adverse events following the re-administration of venom immunotherapy. The patient had undergone a treatment interruption of two months due to a lack of product availability from the manufacturer. Upon resuming therapy with a reduced maintenance dose of 0.5 ml at a concentration of 100 mcg of Venom-ATL Ape, she developed severe adverse reactions.

Adverse Events: Post-administration, the patient exhibited multiple symptoms indicative of anaphylaxis:

Generalized urticaria

Generalized pruritus

Dizziness

Dysphagia

Dyspnoea

A significant drop in blood pressure from 124/79 mmHg to 105/71 mmHg (a reduction of 20 mmHg)

RESULTS

The lack of product availability leading to a prolonged interruption in VIT resulted in a reduction of the patient’s tolerance to the venom allergen. Consequently, even a reduced maintenance dose triggered severe systemic reactions. This case underscores the critical need for consistent availability of immunotherapy products to prevent interruptions that can compromise patient safety. Ensuring a reliable supply chain for essential medications requires coordinated efforts at a

broader, possibly European level, given the international nature of pharmaceutical manufacturing and distribution.

CONCLUSION

Interruption in venom immunotherapy due to product unavailability can significantly impact patient safety, leading to severe adverse reactions upon treatment resumption. Continuous monitoring and management of the supply chain for critical therapeutic products are imperative to maintain effective and safe treatment regimens for patients undergoing immunotherapy. Coordinated efforts at a broader, possibly European level, are essential to address the challenges posed by international pharmaceutical manufacturing and distribution.

CONFLICTS OF INTEREST

The authors did not specify any links of interest.

Submission number: 000007
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THE PREVALENCE OF INSECT ALLERGY IN CERTAIN GROUP OF PATIENT PRESENTED IN "YLLI" POLYCLINIC

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BACKGROUND

Insect venom is one of the most frequent elicitors of anaphylaxis. The majority of cases of anaphylactic reaction occur after a sting by honeybee, due to the higher frequency of attacks.

METHOD

459 patients were examined, from the period August 1, 2023-December 31, 2023, presented for diagnosis at the "Ylli" Clinic, Pristina.

RESULTS

We examined 459 patients from the time period August 1, 2023-December 31, 2023).Most of our patients have demonstrated: Rhioconjunctivitis 86(18.73%),Bronchial asthma 83 (18.08%),44 Urticaria (9.58%),42 Dermatitis (9.15),Rash 33(7.18),Angioedema (3.7%),17 Anaphylaxis (3.7%),11 Urticaria with Angioedema (2.3%),11Conjunctivitis (2.3%),12 Prurit (2.6%),8 Dermografismus (1.74%),Rhinosinusitis 6(1.3%),4 Sinusitis (0.87%),2 Contact dermatitis (0.4%),Vasculitis 2(0.4%),1 Reactio medicamentosa (0.2%),1 Headache(0.2%),1 Rash(0.2%),1 AERD(0.2%),1 Epistaxis (0.2%),and 125(27.23%) without initial dgn. 450 of them were positive for pneumoallergens (92.02%), 296 (60.54%) were allergic to certain foods, and only 15 of them (3.07%) were allergic to insects.

Patients allergic to insects 15 (m/f=8/7), most of them clinically manifested Anaphylactic Reaction (7), 3 of them Generalized Urticaria, Rhinoconjunctivitis (2), Bronchial Asthma (1), Generalized Erythema (1) as well as Dermographism (1) patients.

Of those 15 allergic patients, 6 (40%) of them were allergic to bee venom, 6 (40%) to wasp venom, 6 (40%) to vVespv 5, hornet venom 4 (26.67%), mosquito 7 (46.67%).

The highest level of sensitization of our patients was level 4, with crusts registered

CONCLUSION

Even the systemic reaction to the insect venom ranges from 3.3-5% of general adult population, it could be life threatening reaction.

CONFLICTS OF INTEREST

The authors did not specify any links of interest.

Submission number: 000038
Prefix: P44

ADHERENCE TO STORAGE CONDITIONS OF EPINEPHRINE AUTOINJECTORS IN PATIENTS UNDERGOING VENOM IMMUNOTHERAPY: A REAL-WORLD STUDY

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BACKGROUND

Aherence to correct storage conditions of self-administered adrenaline preparations is a frequently discussed but under-researched issue that can significantly impact the safety of patients with a history of anaphylaxis. Epinephrine autoinjectors (EAIs) should ideally be stored at 20–25°C, with acceptable excursions between 15–30°C. With the increasing frequency of extreme weather events due to climate change, maintaining these conditions has become more challenging. Our objective was to assess the compliance and adherence to proper storage conditions of adrenaline autoinjectors among patients undergoing venom immunotherapy (VIT), treated at a tertiary allergology center.

METHOD

We bought 90 0.3 mg EpiPen Senior® EAIs from a local pharmacy wholesaler and distributed one to each patient undergoing VIT at our Clinical Department of Pneumonology and Allergology. The distribution took place >12 months before the expiration date, following extensive training and education on proper adrenaline usage and storage. All patients returned their autoinjectors after

twelve months. At the end of the expiration period, the autoinjectors were discharged into test tubes, and the epinephrine concentration was measured using high-performance liquid chromatography. Additionally, each patient filled a questionnaire on their compliance and adherence regarding storage conditions during the study period.

RESULTS

Eighty patients returned their epipens intact, and one patient used his epipen after a bee sting. The mean concentration of epinephrine in the returned autoinjectors was 99.45% (mean effective dose 0.2984 mg). Patients with severe anaphylaxis (grade III or IV) were more likely to carry their adrenaline at all times and presented better compliance and fewer reported storage errors. Additionally, patients with a history of bee venom anaphylaxis were more likely to adhere to the correct storage conditions compared to those allergic to wasp venom (OR=1.7, $p<0.05$).

CONCLUSION

Component-resolved diagnostics (CRD) have emerged as a valuable tool in the precise identification of allergenic sensitivities, particularly in the context of Hymenoptera venom allergies. By analyzing specific allergenic proteins, CRD allows for a detailed assessment of a patient's immune response to individual components of venom, providing a clearer picture than traditional whole-extract testing. Furthermore, in patients with low total IgE levels, standard cutoff values for major allergens may not adequately reflect their sensitization status. Therefore, applying lower cutoff values for major allergens in such patients can enhance the sensitivity of the tests, ensuring that even minimal but clinically significant allergen-specific IgE levels are detected. This approach helps in avoiding misdiagnosis and ensures that appropriate immunotherapy is administered, improving patient outcomes.

CONFLICTS OF INTEREST

The authors did not specify any links of interest.