

# Ultrarush immunotherapy in a patient with occupational allergy to bumblebee venom (*Bombus terrestris*)

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**Summary.** Bumblebee venom allergies, though uncommon among the broad public, pose a significant risk in plant industry and scientific occupation. Since a significant IgE cross-reactivity between bumblebee and honeybee venom has been described in several cases and bumblebee venom for immunotherapy has been available only from a few suppliers, SIT with honeybee venom was frequently used for bumblebee venom allergic patients in the past. We present the case of occupational bumblebee allergy in a biologist who developed anaphylactic reactions with subsequent stings. He was lacking cross-reactivity to honeybee venom, therefore we initiated immunotherapy with bumblebee venom extract. Two months after reaching the maintenance dose of 80 µg, the efficacy of the treatment was demonstrated by sting challenge.

**Key words:** *Bombus terrestris*, bumblebee venom, cross-reactivity, hymenoptera, specific immunotherapy.

## Introduction

Although immediate-type allergies to bumblebee stings are very rare, in spite of potentially life-threatening forms of hymenoptera venom allergy, they become increasingly important since the introduction of bumblebees for pollination in plant industry [1,2]. Bumblebees for pollination provide a more effective pollen movement and are early indicators of problems in plant environment or health. Thus, occupational bumblebee venom allergy is increasingly common in greenhouse employees, and scientists belong to the high hymenoptera venom is a safe and effective method to protect these patients, but lack of efficacy has often been described in bumblebee allergic patients treated with honeybee venom [3]. This is due to a low or missing degree of cross-reactivity between honeybee and bumblebee venoms in some patients.

This paper describes the case of a patient with severe occupational allergy to bumblebee venom (BBV) who showed no cross-reactivity to honey-bee venom (HBV) and was successfully treated with BBV.

## Case Report

We report the case of a 27-year-old male biologist, investigating reproduction of bumblebees, who developed progressively severe allergic reactions after subsequent stings at his workplace, resulting in a large local swelling, massive urticaria, Quincke edema and asthma.

Diagnosis of venom-specific allergy was confirmed with skin tests. They were performed with purified venom extracts of *Bombus terrestris* (BBV), *Apis mellifera* (HBV) and *Vespula spp.* (VV), which were purchased from ALK-Abéllo (Hørsholm, Denmark). Intradermal skin tests revealed clearly positive reactions to BBV at 0.00001 µg/ml, HBV at 0.1 µg/ml and a mild reaction to VV at 1.0 µg/ml.

Specific IgE levels were increased with 13.2 kU/L for BBV (Class 3), 36.40 kU/l for HBV (Class 4) (IgG level: 23.30 mg/l) and 1.52 kU/l for VV (Class 2) using the Pharmacia CAP method (Pharmacia & Upjohn Diagnostic, Uppsala, Sweden). Cross-reactivity, assayed by CAP-inhibition (Pharmacia & Upjohn, Uppsala,

Table 1. Serological results.

	Concentration of Inhibitory component	HBV kU/l	HBV %	VV kU/l	VV %	BBV kU/l	BBV %
Control	0 µg/ml	23.40		0.89		10.8	
Inhibition with BBV	100 µg/ml	3.43	87%	0.35	98%	9.85	9%
Inhibition with VV	100 µg/ml	23.3	0%	0.34	100%		

BBV, bumblebee venom; VV, vespid venom; HBV, honeybee venom

Sweden), was very low (<10%) (Table 1). Therefore we diagnosed a primary sensitization to *Bombus terrestris* with a grade III systemic reaction to BBV and a latent sensitization to HBV and VV.

Based on the above mentioned findings we initiated immunotherapy with aqueous purified BBV extract (ALK-Abéllo, Hørsholm, Denmark), following a strict rush protocol with escalating doses. 15 minutes after a 20 µg dose of ultrarush induction (31.1 µg), the patient complained of generalized pruritus and received oral corticosteroids (100 mg prednisone) and intravenous antihistamine (Tavegyl 2 mg). Again 15 minutes later he presented an urticarial rash of the flexures of both arms, neck and cleavage, rhinoconjunctivitis and mild asthma. Blood pressure and heart rate were normal. Rhinoconjunctival symptoms disappeared within the next hour but the patient developed confluent urticaria, encompassing pelvic and femoral region. We decided to stop ultrarush henceforth and administered a maximum total dose of 50 µg BBV on the following day under premedication with antihistamines without any intricacies. Conventional immunotherapy was then continued on an outpatient basis.

A maintenance dose of 80 µg was finally reached within 5 weeks of treatment, thereafter administered in 4-week intervals and successfully tolerated ever since under antihistaminic prophylaxis. Four months after ultrarush SIT treatment started, the course of specific IgE was analyzed and showed a decrease of BBV-IgE (10.20 kU/l, Class 3), HBV-IgE (12.10 kU/l, Class 3; specific IgG 14.90 mg/l) and VV-IgE (1.22 kU/l, Class 2; specific IgG 5.43 mg/l).

The protective effect of SIT was proven by another bumblebee sting at workplace two months after having reached the maintenance dose. No systemic, but only a mild local cutaneous reaction occurred.

## Discussion

Since bumblebees are not very aggressive and do not sting under natural conditions, BBV allergies are of no remarkable importance in the general population.

However, they pose a widespread significant risk particularly in plant industry and scientific occupation by subsequent stings. The prevalence of BBV allergy is controversially discussed: approximately 6% of all hymenoptera venom allergic patients have been found to be BBV allergic [4].

SIT is a safe and effective treatment to protect occupationally exposed patients and the side effects seem to be comparable to those of HBV and VV immunotherapy [5]. In some cases there is a high degree of cross-reactivity between HBV and BBV, and SIT with HBV is sufficient for patients with BBV allergy [6, 7]. Our patient experienced a grade III reaction to BBV. Sensitization was confirmed by intradermal skin test and CAP with BBV extract, however cross-reactivity to HBV was not measurable. This case as well as previous studies show that cross-reactivity should be carefully analyzed before SIT. In patients with a low or lacking degree of antigenic cross-reactivity to HBV, due to the enormous array of allergenic substances in BBV like phospholipase A<sub>2</sub>, casein hydrolyzing protease and small amounts of hyaluronidase and acid phosphatase, SIT with venom from the appropriate species of bumblebees is advisable [3,5,8]. Otherwise SIT with HBV might end up unsuccessfully in such patients [9].

The therapeutic benefit in our patient was established through a re-sting at his workplace. Neither a large local reaction nor systemic reactions occurred. The course of specific IgE to BBV as an accepted clinical marker for the effectiveness of SIT corresponded to data about SIT in bee- or vespid-allergic patients in whom specific IgE decreased during immunotherapy [10].

Current data suggest that the frequency and severity of local and to a minimal extent also of systemic reactions are reduced under pretreatment with antihistamines [11,12] and even long-term outcomes in preventing allergic reactions are improved [13]. In our case rapid venom immunotherapy was hardly tolerated during the induction phase, but well tolerated under premedication. Whether high cumulative doses or number of injections are directly proportional to the incidence of systemic reactions has not been confirmed yet in a prospective randomized controlled trial.

A nearly 100% efficacy is achieved with a maintenance dose of 100 µg, 50 µg results in only 79% protection from re-sting challenges [14]. In our patient 80 µg were sufficient for efficacious immunotherapy, but individual varieties should be considered when adapting the rush protocol to the patient.

All in all, our case shows that SIT with BBV is a safe and efficacious therapeutic method in patients who cannot avoid reexposure to bumblebees. SIT should be performed with the appropriate hymenoptera venom and preferably under pretreatment with antihistamines. Moreover, clinical benefit can reliably be confirmed by bumblebee sting challenge.

## References

1. Kochuyt AM, Van Hoeyveld E, Stevens EA. Occupational allergy to bumble bee venom. *Clin Exp Allergy* 1993;23(3):190-5.
2. de Groot H, de Graaf-in 't Veld C, van Wijk RG. Allergy to bumblebee venom. I. Occupational anaphylaxis to bumblebee venom: diagnosis and treatment. *Allergy* 1995;50(7):581-4.
3. Bucher C, Korner P, Wüthrich B. Allergy to bumblebee venom. *Curr Opin Allergy Clin Immunol* 2001;1(4):361-5.
4. Barr SE. Allergy to hymenoptera stings. *Jama* 1974;228(6):718-20.
5. de Jong NW, Vermeulen AM, de Groot H. Allergy to bumblebee venom. III. Immunotherapy follow-up study (safety and efficacy) in patients with occupational bumblebee-venom anaphylaxis. *Allergy* 1999;54(9):980-4.
6. Stapel SO, Waanders-Lijster de Raadt J, van Toorenenbergen AW, de Groot H. Allergy to bumblebee venom. II. IgE cross-reactivity between bumblebee and honeybee venom. *Allergy* 1998;53(8):769-77.
7. Reisman RE, Muller UR, Wypych JI, Lazell MI. Studies of coexisting honeybee and vespid-venom sensitivity. *J Allergy Clin Immunol* 1984;73(2):246-52.
8. Hoffman DR, El-Choufani SE, Smith MM, de Groot H. Occupational allergy to bumblebees: allergens of *Bombus terrestris*. *J Allergy Clin Immunol* 2001;108(5):855-60.
9. Stern A, Wüthrich B, Mullner G. Successful treatment of occupational allergy to bumblebee venom after failure with honeybee venom extract. *Allergy* 2000;55(1):88-91.
10. Wilson AB, Deighton J, Lachmann PJ, Ewan PW. A comparative study of IgG subclass antibodies in patients allergic to wasp or bee venom. *Allergy* 1994;49(4):272-80.
11. Reimers A, Hari Y, Muller U. Reduction of side-effects from ultrarush immunotherapy with honeybee venom by pretreatment with fexofenadine: a double-blind, placebo-controlled trial. *Allergy* 2000;55(5):484-8.
12. Berchtold E, Maibach R, Muller U. Reduction of side effects from rush-immunotherapy with honey bee venom by pretreatment with terfenadine. *Clin Exp Allergy* 1992;22(1):59-65.
13. Muller U, Hari Y, Berchtold E. Premedication with antihistamines may enhance efficacy of specific-allergen immunotherapy. *J Allergy Clin Immunol* 2001;107(1):81-6.
14. Golden DB, Valentine MD, Kagey-Sobotka A, Lichtenstein LM. Regimens of Hymenoptera venom immunotherapy. *Ann Intern Med* 1980;92(5):620-4.

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