

Insect sting anoxic encephalopathy after stopping venom immunotherapy

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Key words: anoxic encephalopathy; discontinuing immunotherapy; negative tests; venom allergy.

The risk of the re-occurrence of a systemic reaction (SR) after stopping venom immunotherapy (VIT) is elevated in adult age, honeybee venom allergy, patients with severe pretreatment SR, SR during VIT to treatment injections or restings, elevated basal serum tryptase and mastocytosis (1).

We report a case of anoxic encephalopathy secondary to a yellow-jacket sting-induced anaphylactic shock in a young patient who had previously received more than 5 years of VIT.

The patient was 34-year old when he had an anaphylactic shock in August 1993 after a yellow-jacket (YJ) sting. He was found to be sensitive to honey bee and YJ venoms, while skin tests were negative to wasp venom. The Pharmacia CAP-System was positive to bee (class 2) and YJ (class 2) venoms, negative to wasp venom.

In December 1993, the patient began YJ immunotherapy, reached a maintenance dose of 100 mcg, with no SR. Maintenance injections were given progressively at regular 4–6–8 week intervals over time, without any SR. During immunotherapy the patient tolerated three *Vespid* stings.

In June 1999, an intradermal skin test with YJ venom was doubtful (1 mcg/ml), while the Pharmacia CAP-System was negative. Skin and serological tests were negative to honey bee and wasp venoms; VIT was stopped in July 1999.

The patient was, nevertheless, advised to carry a self-administered epinephrine kit with him at all times.

He tolerated a new YJ sting after stopping VIT. In April 2000, intradermal YJ and wasp venom skin tests were negative, the CAP-System likewise was negative. In July 2001 the patient was restung by an YJ while out jogging, he did not have his epinephrine kit at hand and there was no emergency room nearby. He developed a severe anaphylactic shock with subsequent ischemic encephalopathy, resulting in permanent physical and mental disability. The patient's family refused to consent to medical tests (e.g. hematic blood samples to measure specific IgE and tryptase levels) except a nonbiptic dermatological examination, which ruled out urticaria pigmentosa.

Literature reports a few patients who had previously experienced anaphylactic shock, some of whom had negative skin and/or serological tests after several years of VIT and later developed SR, even fatal, to subsequent stings after VIT discontinuation (2–4).

To the best of our knowledge this is the first case of a near fatal insect sting reaction with ischemic encephalopathy, resulting in permanent physical and mental disability, occurring in a young healthy patient after stopping VIT, which had run for more than 5 years. Indolent systemic mastocytosis or urticaria pigmentosa cannot be completely ruled out, as neither bone marrow nor skin biopsies were performed and serum tryptase levels evaluated. Indeed, the literature reports two fatal cases of insect sting anaphylaxis in females with mastocytosis where VIT had been discontinued (2). A recent report describes the significant association between a reaction to the sting

challenge during VIT and an elevated basal serum tryptase in *Vespula*, but not in bee venom-allergic patients (5). Even the patient in question had presented indolent systemic mastocytosis or elevated basal tryptase levels, he received several tolerated in-field stings both during VIT and the first year after its discontinuation. Data of this kind suggests that baseline serum tryptase concentration should be determined in all patients with a history of severe reactions and that VIT should probably be continued indefinitely in these patients (6), irrespective of insect type, even in the young. Progressively prolonging the intervals between injections should be considered. Nevertheless, after VIT has ceased it is strongly advisable that the patients carry epinephrine, especially when isolated from medical facilities, even though a re-sting has been tolerated.

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Urticaria-angioedema reaction caused by propafenone

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Key words: drug allergy; propafenone; urticaria-angioedema.

Hypersensitivity reactions to drugs mainly involve the cutaneous, respiratory, and cardiovascular systems, but the rate and kind of reactions may widely change according to the different drugs. Propafenone is an agent used in cardiac arrhythmias thus far reported as mainly responsible of respiratory reactions (1–4). Here we describe for the first time a skin reaction with urticaria-angioedema in a patient treated with propafenone.

The patient was a 51-year-old woman referred to our Allergy Unit for urticaria-angioedema with daily manifestations. Wheals were scattered in all the body but more abundant in the trunk and arms, and angioedema affected especially lips and eyelids. The patient was under treatment with enalapril 20 mg u.i.d., propafenone 150 mg b.i.d, and acetylsalicylic acid (ASA) 100 mg u.i.d. for hypertension and extrasystolic arrhythmia.

The clinical history was negative for atopy or previous hypersensitivity reactions to drugs.

Considering the major role for ASA in skin reactions and the current absence of arrhythmia we discontinued the treatment with ASA but no changes in symptoms were observed. Also ACE-inhibitors agents are frequently involved in angioedema and thus enalapril was substituted with the calcium antagonist amlodipin for treating hypertension, but also this measure did not have any effect on symptoms. Since 6 weeks had elapsed from their first presentation, standard investigations for chronic urticaria, and namely for allergic, physical, infectious and (by means of autologous serum skin test) autoimmune causes, were done, but all the results were negative.

Finally, to rule out a responsibility of propafenone, at first not considered because of the absence of reports of urticaria-angioedema reactions to such agent, and following consultation with the cardiologist, the drug was withdrawn. After 48 h urticaria and angioedema began to decrease in intensity, and a complete resolution occurred in 1 week. To achieve certainty, after 1 month the drug was readministered with rapid reappearance of wheals and angioedema of the lips and a new resolution following the definitive stopping of treatment.

It has been suggested that the asthmogenicity of propafenone is because of its structural similarity to the beta-blocker propanolol (2), and thus the respiratory reactions seem caused more by the drug's mechanism of action than by hypersensitivity. Regarding skin reactions, only recently a case of exanthematous pustulosis was reported (4), and the present description adds a classical picture of hypersensitivity with urticaria and angioedema, which suggests to reconsider propafenone as a possible cause of allergic reactions.

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Ranitidine-induced anaphylaxis: detection of serum specific IgE antibody

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Key words: anaphylaxis; IgE; ranitidine; skin tests.

Although an IgE-dependent mechanism was suggested for anaphylactic reactions to ranitidine, the presence of serum specific IgE antibodies to ranitidine has not been demonstrated (1, 2). We report a case of severe anaphylaxis to ranitidine, in which specific IgE antibody was demonstrated.

A 55-year-old asthmatic man was presented with skin rash with pruritus, dyspnea, irritability, and syncope which developed 30 min after taking one tablet of ranitidine (150 mg, Zantac®; Glaxo-SmithKline-Korea, Seoul, Korea). His blood pressure (BP) was 60/40 mmHg, and forced expiratory volume in 1 s (FEV₁), forced vital capacity (FVC), and FEV₁/FVC were 1.35 l (44% of predicted), 3.16 l (81% of predicted), and 43%, respectively. After treatments with epinephrine, antihistamine, steroid, bron-

Our case suggests that ranitidine could induce an IgE-mediated anaphylaxis.