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Successful Desensitization with Honey Bee Venom: A Case Report

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Abstract

Venom immunotherapy has been shown as an effective and safe treatment for preventing sting induced anaphylaxis. Immunotherapy (IT) with honey bee extract has also been used in the cases of venom hypersensitivity, but it did not prove protective. Here, a 6 years' old boy presented to emergency room with clinical recurrent anaphylaxis. He developed systemic reaction with symptoms such as, nausea, vomiting, diarrhea, breathlessness immediately after honey bee sting near to his house. The patient showed positive skin prick test against honey bee antigen. His specific serum IgE was 0.620 OD before immunotherapy and decreased to 0.001 OD after 1.5 years of immunotherapy. His total serum IgE was 2200 IU/ml at the start of immunotherapy. After being given the immunotherapy in maintenance dose for 1 year, he did not experience anaphylaxis by fresh honey bee sting. His total serum IgE for honey bee decreased to 460 IU/ml after 1.5 years of venom IT. The bee venom immunotherapy for 2 years is effective in prevention of anaphylaxis in case of bee hypersensitivity.

Keywords: Anaphylaxis, Skin prick test, Specific IgE, Venom allergen, Immunotherapy

INTRODUCTION

Ants, bees, wasps, and hornets, are insects of the order hymenoptera. Usually they threaten human beings only by their prodigious numbers and ruthless, organised, and persistent pervasiveness. One sting by bee and related species may provoke fatal anaphylaxis in a sensitized person. Anaphylaxis is increasingly recognized as an important mode of death in different parts of the world. Apart from drugs and foods, stings by hymenoptera are among the most familiar precipitants. Undoubtedly, the prompt use of self-injectable epinephrine could prevent most cases of severe anaphylaxis, but desensitisation offers even greater insurance against sting reactions. In people who had anaphylactic reactions to bee and wasp stings, desensitisation[1] by injection of increasing doses of the appropriate hymenoptera venom, was first validated in 1978. The mechanism of desensitisation remains uncertain but earlier notions of an induction of IgG "blocking" antibody have yielded to evidence that, in hypersensitive individuals, immunotherapy[2] causes a switching of the abnormal Th2 cytokine response (interleukins 4 and 13), which stimulates secretion of IgE by B cells, to Th1 responses stimulating secretion of interleukin 2 and interferon gamma. The effectiveness of venom immunotherapy against hymenoptera-sting anaphylaxis is supported by clinical evidence[3].

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CASE REPORT

A six year old boy suffered honey bee sting while playing near to his house. This resulted in symptoms such as nausea, vomiting, diarrhea, and breathlessness within minutes, followed by drowsiness and impaired breathing associated with high pulse rate and low blood pressure. When examined by the emergency physician about 30 minutes after the sting, the patient was in shock, feeling drowsy and had severe breathing problem. Local haemorrhage, edema and pain at the sting-site occurred, but no systemic bleeding or hemorrhagic diathesis developed. Hydrocortisone, antihistamines and physiological saline were administered intravenously, the patient was intubated and artificial ventilation initiated. On the sting area a massive swelling at the right hand and a moderate edema of the forearm had developed with swollen lips. Blood pressure was 70/40 mm Hg, and cardiac rate was 135 beats/min. Steroid, antihistamines and adrenaline was administered at regular intervals. Patient comes to normal after 24 hours. Artificial ventilation was terminated on 2nd day and the patient was discharged from the hospital. His condition was normal except his lips were slightly swollen.

The history of the patient suggests that, he received bee sting twice at the interval of one year, but did not show systemic reactions. He experienced a severe systemic reaction when stung by bee third consecutive time. It happened twice earlier at the age of 4th and 5th year. His family history showed that his grandmother was having asthma. After recovered fully from systemic reactions, he was brought at Department of Pulmonary Medicine, University of Delhi, Delhi (India) and started with venom immunotherapy. After being given the IT in maintenance dose for 1 year, he never had anaphylaxis on receiving the bee stung.

MATERIALS AND METHODS

Skin prick tests were done using different concentrations (0.001, 0.01 and 0.1 μg/ml) of bee venom allergen (*Apis Mellifera;* Pharmalgen, Allerayde, Nottinghamshire UK).

Venom immunotherapy (VIT) was started to the patient after skin prick tests. Patient was given VIT with gradually increasing doses of venom allergen from 0.1 μg/ml to 100 μg/ml. A maintenance dose of 100 μg/ml was given for 1 year. Total and specific serum IgE levels were measured before starting, at 6 months and after 1.5 years of VIT.

RESULTS

A 6 year old boy was evaluated for three episodes of urticaria, angioedema, dyspnea, and loss of consciousness due to bee sting which resulted in systemic reaction. Skin prick test was strongly positive to bee venom even at the lowest concentration (0.001 μg/ml). Specific IgE in patient's serum to venom antigen was 0.620 OD (before VIT) and 0.200 and 0.001 OD after continuing VIT for 6 months and 1.5 years, respectively. Total serum IgE to bee venom was 2200 IU/ml at the start of immunotherapy and it decreased to 1600 IU/ml at 6 month and further to 460 IU/ml at 1.5 years. A total of 2.5 years of VIT was taken by the patient and discontinued later on his own. The patient has not reported any further systemic reactions with bee sting.

DISCUSSION

Of the invertebrates, insects particularly hymenoptera sting commonly cause anaphylaxis. In stinging bees, wasps, and ants, the ovipositor of females has been modified into a stinger. This venom delivery system is a powerful defence against vertebrates. In the case of humans, insect sting and venom delivery may be life-threatening when the individual is sensitized to allergens present in the venom.

About 1% of children and 3% of adults are reported to experience systemic allergic reactions, but these may be underestimates due to inadequate data[4]. Many people die each year from hymenoptera stings, but some of them may not have prior history of allergic reactions[5]. Allergic reactions to hymenoptera stings are more common in men and can occur in any age group, but are often more severe in adults over 30 years of age. Treatment of hymenoptera sensitivity includes prevention of stings if possible and immediate treatment of reactions when they occur. The proper identification of the offending insect and immunotherapy with venom preparation is also recommended[6]. Epinephrine and HI _ H2 antihistamines may be life-saving when administered early during an anaphylactic reaction. For diagnosis of hymenoptera sensitization, skin testing and RAST are available including several venom preparations[6]. The successful VIT can prevent systemic reactions in sensitized patients.

Pharmacotherapy treatment for prevention of anaphylactic reactions is not always available. Immunotherapy is currently possible only for hymenoptera venom. Therapy with whole insect body extracts was proved to be no better than placebo whereas venom immunotherapy was reported 95% effective[1,7]. The indications for venom immunotherapy require a history of previous systemic allergic reaction to a sting and a positive diagnostic test for venom-specific IgE. Those with a recent history of anaphylaxis and a positive skin test have a 30% to 70% chance of systemic reaction to a subsequent sting[1,8]. A low risk (<10%) has been observed in children and adults with a history of large local reactions, and in children with systemic reactions limited to cutaneous signs and symptoms[9,10]. Venom immunotherapy is not required in these low-risk cases, but some patients still request treatment because of their fear of reaction and the impact on their quality of life. Children with moderate or severe systemic reactions have chance up to 30% of reaction to a sting even decades later[9]. Unfortunately, there is no test that predicts which patients will progress to more severe reactions. Even intervening stings without reaction do not eliminate the risk of anaphylaxis to a later sting.

Initial venom immunotherapy can follow any of several recommended schedules. Treatment is usually recommended with each of the venoms giving a positive skin test. Therapy is 98% effective in completely preventing systemic allergic reactions to stings when treatment includes mixed vespid venoms (300 mcg total dose), but complete protection is achieved in only 75% to 85% of patients utilizing 100 mcg of any single venom (e.g. honeybee, yellow jacket or Polistes wasp).

Adverse reactions to venom immunotherapy occur no more frequently than with inhalant allergen immunotherapy[11]. Systemic symptoms occur in 10-15% of patients during the initial week of treatment, regardless of the regimen used. Most reactions are mild, and fewer than half require epinephrine injection. Virtually all patients can achieve the full dose even after initial systemic reactions. In the unusual case of recurrent systemic reactions to injections, therapy may be streamlined to single venom and given in divided doses, 30 minutes apart. Large local reactions to injections are common, occurring in up to 50% of patients. Unlike standard inhalant immunotherapy, the uniform target dose in venom immunotherapy may make it necessary to advance the dose in the face of large local reactions, beyond what might otherwise be considered the “maximum tolerated dose”.

The duration of venom immunotherapy is indefinite according to the recommendation in the product package insert. Initial efforts to stop treatment when the RAST became negative were successful, but only a few patients become RAST-negative within 5 years of treatment[12,13]. Extended study of a large number of adults has shown that when venom immunotherapy is stopped after five years, the chance of a systemic reaction will remain 10 percent for each sting even more than 10 years after stopping treatment and even if skin tests become negative[4,14]. When sting reactions occur after stopping venom immunotherapy, most are quite mild and almost always are less severe than the pre-treatment reaction. A higher frequency of relapse occurs in patients who had very severe (near-fatal) sting reactions before therapy, those who had a systemic reaction during therapy (to a sting or a venom injection), those with honeybee allergy, and those who had less than five years of therapy[4,15]. Patients with any of these four high-risk characteristics may need to be treated indefinitely, but there are no data on the outcome after more than 15 years of treatment. Some patients will prefer to continue venom treatment for security and improved quality of life. Children who had 3 to 5 years of venom immunotherapy have a very low chance of systemic reaction even 10 to 20 years after stopping the treatment[9].

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