

# Uterine Contractions: An Unusual Side Effect of Venom Immunotherapy

F Karakurt,<sup>1</sup> A Kargili,<sup>1</sup> B Bozkurt,<sup>2</sup> B Kasapoglu,<sup>3</sup> M Ikizek<sup>3</sup>

<sup>1</sup>Fatih University Medical School Department of Internal Medicine, Division of Endocrinology, Ankara, Turkey

<sup>2</sup>Fatih University Medical School Department of Pulmonology, Division of Allergy and Clinical Immunology, Ankara, Turkey

<sup>3</sup>Fatih University Medical School Department of Internal Medicine, Ankara, Turkey

## ■ Abstract

Venom immunotherapy (VIT) is an efficient treatment modality for preventing further sting-induced anaphylactic reactions in patients with Hymenoptera venom allergy. The main side effects of VIT include local and systemic allergic reactions with a variable risk of up to 46%. We report the case of a woman who experienced rapid-onset hypocalcemia and regular uterine contractions on 3 occasions within 30 minutes of receiving *Apis mellifera* VIT. To the best of our knowledge, this is the first report of uterine contractions as a side effect of VIT. The importance of this event is clear, as VIT has now been approved for pregnant women. We provide recommendations to physicians using this modality.

**Key words:** Venom immunotherapy. Uterine contractions.

## ■ Resumen

La inmunoterapia con veneno es una modalidad de tratamiento eficaz para la prevención de reacciones anafilácticas inducidas por picadura en pacientes con alergia al veneno de himenópteros. Entre los principales efectos secundarios de la inmunoterapia con veneno se encuentran las reacciones alérgicas locales y sistémicas con un riesgo variable de hasta el 46%. En este artículo se recoge el caso de una mujer que experimentó hipocalcemia de rápida evolución y contracciones uterinas regulares en 3 ocasiones 30 minutos después de recibir inmunoterapia con veneno de *Apis mellifera*. A nuestro saber y entender, esta es la primera notificación de contracciones uterinas como efecto secundario de la inmunoterapia con veneno. La importancia de este acontecimiento está clara, puesto que la inmunoterapia con veneno está aprobada para su uso en mujeres embarazadas. Se proporcionan recomendaciones para los médicos que utilizan esta modalidad de tratamiento.

**Palabras clave:** Inmunoterapia con veneno. Contracciones uterinas.

## Introduction

Hymenoptera, including honeybee (*Apis mellifera*) and yellow jacket (*Vespula germanica* and *Vespula vulgaris*), can cause sting-induced systemic and allergic reactions in susceptible patients. Patients with Hymenoptera venom allergy can be treated efficiently with venom immunotherapy (VIT) to prevent further sting-induced anaphylactic reactions [1]. Several dosing options are available, including conventional, rush, and ultrarush schedules [2-4]. Induction takes several weeks with the conventional schedule, several days with a rush

schedule, and several hours with an ultrarush schedule. The main side effects of VIT include local and systemic allergic reactions with a variable risk of up to 46% [5]. VIT is the most commonly used approach in systemic immunotherapy and can now be administered to pregnant women.

We report the case of a woman who experienced regular uterine contractions on 3 occasions due to rapid-onset hypocalcemia within 30 minutes of receiving *Apis mellifera* VIT. Her condition resolved with calcium infusions. To the best of our knowledge, this is the first report of uterine contractions as a side effect of immunotherapy.

## Case Report

A 45-year-old woman was referred to the allergy department due to a systemic allergic reaction including urticaria, bronchospasm, and nasal congestion after a bee sting. She had been monitored by the endocrinology department for about 5 years with a diagnosis of hypoparathyroidism after total thyroidectomy. She was taking calcium lactate gluconate 2940 mg/d, calcium carbonate 300 mg/d, and calcitriol 1 µg/d and had no accompanying systemic diseases. Intradermal tests for both *Apis mellifera* and *Vespula* species were performed before induction of VIT. She experienced an allergic reaction to 10 ng/mL of *Apis mellifera*. Since it was spring, the rush schedule was administered [6], with smaller doses for the first 4 consecutive days and then 100 µg monthly for 3 years. The results of a physical examination and a serum biochemistry workup were all within normal ranges, with a calcium level of 8.4 mg/dL at the beginning of VIT. No side effects were observed during the first 4 days of the induction period. One month later she came for the first maintenance dose. Levocetirizine was administered before the injection. About 30 minutes after the injection, an induration measuring 3 cm appeared at the injection site and she experienced sudden cyclic uterine contractions every 3 minutes. She defined the pain as that of labor contractions. The serum sample taken at that moment revealed a calcium level of 5.0 mg/dL. Although the reason for the hypocalcemia was not clear, the contractions subsided after a calcium infusion. One month after the injection, the same contractions were observed again, with a sudden drop in serum calcium levels to 5.4 mg/dL. Again, calcium infusions were administered. On the third occasion, we administered the injection after a calcium infusion and no contractions were observed.

## Discussion

Bee VIT is a highly effective, specific treatment to prevent life-threatening reactions in patients with Hymenoptera allergy. It is administered to diminish the risk of a subsequent systemic allergic reaction and thus prevent morbidity and mortality. VIT involves reaching the appropriate dose of allergen to induce tolerance to Hymenoptera venom with the lowest rate of systemic reactions [7]. Whatever the schedule, a maintenance dose of 100 µg is usually recommended. In rush protocols, patients are given higher doses of venom over a shorter period of time than conventional protocols to achieve the maintenance dose more rapidly [8].

However, this treatment can cause adverse reactions, the most severe of which are systemic. The main local effect is redness and swelling at the injection site; the main systemic effects are itching, anxiety, palpitations, nausea, vomiting, chest tightness, dizziness, diarrhea, sleepiness, confusion,

fainting, and low blood pressure. There have been no reports of hypocalcemia or electrolyte imbalance due to VIT. Although life-threatening reactions are rare, physicians qualified to deal with these reactions should administer VIT carefully.

To the best of our knowledge, this is the first reported case of hypocalcemia and uterine contractions after VIT. We cannot explain the mechanism responsible for this effect; however, the fact that it occurred 3 times and resolved with calcium infusions leads us to believe that it is related to VIT. Such a side effect is increasingly important, as VIT can now be administered during pregnancy.

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### ■ Dr. Benan Kasapoglu

Emek mah. 4. Cadde No: 1/3  
06500 Bahcelievler/  
Ankara, Turkey  
E-mail: benankasapoglu@hotmail.com