

Transient bradycardia during vespid venom immunotherapy

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Summary

A woman developed generalized symptoms of hypersensitivity when she was stung requiring treatment with adrenalin.

Intradermal venom skin tests showed immediate hypersensitivity to yellow hornet and white-faced hornet thus fulfilling the criteria to receive appropriate venom immunotherapy.

During the course of modified rush immunotherapy with yellow hornet and white-faced hornet venoms, she developed transient but progressive bradycardia necessitating interruption of the venom immunotherapy. Transient bradycardia recurred when venom immunotherapy was resumed but it was possible to reach a maintenance dose of 100 µg protein for each venom.

Bradycardia has been reported to be induced in experimental animals by oriental hornet venom as well as other venoms, through a direct cholinergic action. It appears that a similar effect may occur in man in susceptible individuals during venom immunotherapy.

Introduction

The constituents of venoms are numerous and have been reviewed by Habermann (1972). Using isolated guinea pig hearts, scorpion venom was found to cause bradycardia which usually preceded the cardiac stimulating effect of the venom. The bradycardia could be blocked by atropine and was thought to be of cholinergic nature (Corrado, Antonio & Diniz, 1968). Cardiac stimulation was blocked by the use of propranolol. Kaplinsky, Ishay & Gitter (1974) gave intravenous oriental hornet venoms to dogs and slight cardiac slowing was one of cardiovascular effects observed; however it disappeared upon vagotomy and/or atropinization.

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Local or systemic symptoms of hypersensitivity including pruritus, urticaria, angioedema or tachycardia with hypotension can occur in patients receiving venom immunotherapy. We believe this is the first case report of bradycardia during venom immunotherapy.

Case Report

A 24-year-old housewife who lives on a farm was stung on the back in August 1979. She immediately developed generalized pruritus, angioedema and urticaria. There was no shortness of breath or wheezing. She was treated at a local hospital with adrenalin and antihistamines. She had been stung by bees in the past without problems.

Skin testing

The patient was seen at the Health Sciences Centre in April 1980. Intradermal skin tests with 0.02 ml venom (Pharmacia AB, Uppsala, Sweden) at a concentration of 0.001 $\mu\text{g/ml}$ venom protein of yellow hornet and white-faced hornet were positive, 1+ and 3+ respectively. The yellow-jacket venom skin test at a concentration of 0.1 $\mu\text{g/ml}$ was 3+ positive but she had a negative skin reaction to honey bee and wasp venoms. She therefore fulfilled the criteria to receive venom immunotherapy (Lichtenstein, Valentine & Sobotka, 1979).

In August 1980 she was admitted to hospital for immunotherapy with yellow and white-faced hornet venoms. The regimen of venom immunotherapy was modified slightly from that recommended by Pharmacia. Examination prior to immunotherapy showed that she was 155 cm tall, weighed 89 kg and had a regular pulse of 64 per minute and blood pressure of 120/60 mmHg. The remaining examination was normal.

Subcutaneous injections with increasing doses of each hornet venom were given alternatively at 30 min intervals in the upper arms. The initial dose was 0.1 ml of 0.001 $\mu\text{g/ml}$ venom protein concentration of each venom. The dose of this concentration was increased as follows: 0.2 ml, 0.4 ml, 0.8 ml. The concentration was then increased tenfold and administered in the same manner, to eventually achieve a maintenance dose of 100 μg of venom protein for each venom (Golden *et al.*, 1980).

Results

The pulse 10 min after injection was noted to be 58/min after she had received a total of 0.4330 μg of venom protein and was 44/min after a total of 1.333 μg of venom protein (Fig. 1). The bradycardia was initially transient and venom injections were continued

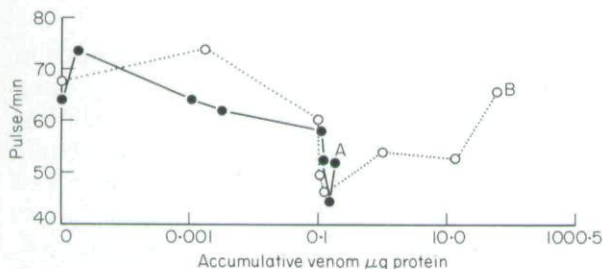


Fig. 1. Post-injection lowest pulses during venom immunotherapy. ●—●, Pulse during first admission; ○—○, pulse during second admission; A, immunotherapy discontinued (first admission); Maintenance dose achieved.

when the pulse rose to 60/min or more. However, immunotherapy was discontinued at point A (Fig. 1), because bradycardia persisted for several hours. The lowest blood pressure noted was 90/60 mmHg. No allergic symptoms developed.

She was readmitted a few weeks later for further venom immunotherapy. The injections were given alternatively at 45 min intervals, and were restarted at one tenth of the amount of venom administered in the final injection of the previous series. After receiving a total of 0.30 μ g venom protein, bradycardia began to develop shortly after each injection. With a pulse rate of 46/min her blood pressure was 98/62 mmHg. She complained of fatigue, but no symptoms of hypersensitivity occurred. At times the pulse was irregular. However venom immunotherapy was continued cautiously until a maintenance dose of 100 μ g of venom protein was attained. She was sent home to continue on a monthly dose of 100 μ g of each venom (Fig. 1), and she has had no problems in the last 7 months.

An electrocardiogram done prior to immunotherapy was normal with a rate of 65/min while later during an episode of bradycardia the EKG was otherwise normal. SMA-12, electrolytes, fasting blood sugar, IgG and IgE were normal.

Discussion

Although the risks of anaphylaxis while administering purified venoms in man are well recognized, this type of idiosyncratic or direct toxic effect of Hymenoptera venom during immunotherapy has not to our knowledge been previously described. The bradycardia in this case appears to be due to direct toxicity, since its severity increased with the total dose of venom administered.

It would seem likely that the constituent(s) of the venom and mechanisms responsible for the development of bradycardia in this patient are the same as those described in experimental animals, although these have not been identified. If so, then atropine might be used for dangerous degrees of bradycardia unresponsive to conservative measures complicating venom immunotherapy, such as might occur in patients receiving propranolol or other beta-adrenergic blockers.

Acknowledgment

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References

- CORRADO, A.P., ANTONIO, A. DINIZ, C.R. (1968) Brazilian scorpion venom (*Tityus Serralutus*). An unusual sympathetic postganglionic stimulant. *Journal of Pharmacology & Experimental Therapeutics*, **164**, 253.
- GOLDEN, D.B.K., VALENTINE, M.D., KAGEY-SOBOTKA, A. & LICHTENSTEIN, L.M. (1980) Regimens of hymenoptera venom immunotherapy. *Annals of Internal Medicine*, **92**, 620.
- HABERMANN, E. (1972) Bee and wasp venoms. The biochemistry and pharmacology of their peptides and enzymes are reviewed. *Science*, **117**, 314.
- KAPLINSKY, E., ISHAY, J. & GITTER, S. (1974) Oriental hornet venom: Effects on cardiovascular dynamics. *Toxicon*, **12**, 69.
- LICHTENSTEIN, L.M., VALENTINE, M.D. & SOBOTKA, A.K. (1979) Insect allergy. The state of the art. *Journal of Allergy & Clinical Immunology*, **64**, 5.

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