

Correspondence

Allergic reaction to snake venom after repeated bites of *Vipera aspis*

Sirs, We observed a snake biologist studying the two indigenous poisonous snakes living in Switzerland, *Vipera aspis* and *Vipera berus* [1], who had been bitten twice by a *Vipera aspis* within 4 years. After the first bite in 1987 he developed a severe haemorrhagic oedema spreading from the arm to the chest and finally to the groin. Initially he suffered from swelling of the tongue, dyspnoea and diffuse abdominal pain. He was treated with amoxicillin, frusemide and analgesics; no antivenom was given. After the second bite in July 1991 he presented 30 min after the event with a generalized confluent rash of the urticarial type and a typical angioedema of the face involving the mucous membranes of the mouth. The second finger of the right hand—where he had been bitten—was oedematous. Pulse rate was 85/min, blood pressure 120/70 mmHg, the lung sounds were weak and during expiration wheezing could be heard. Clinical examination revealed no further abnormalities, laboratory results were normal and no hints of a coagulation disorder could be found.

Because of this clinical picture we wondered whether an allergic reaction could explain the signs after the second bite. The presence of IgE against the venom of *Vipera aspis* in the patient's serum, but not in controls, could be demonstrated in a dot assay. For higher sensitivity the test was performed by a chemiluminescence method with a biotinylated anti-IgE and avidine-peroxidase (V. Aubert, PhD; see Fig. 1). The skin-prick test with native venom of *Vipera aspis* was positive in the patient with a weal of 6 × 8 mm (venom-dilution 1:10). No swelling and only slight erythema were seen in the three controls. Total IgE was 106 IU/ml (norm: ≤ 220 IU/ml).

Repeated bites by poisonous snakes occur more frequently than generally assumed, particularly in professional or amateur herpetologists [2,3]. Allergic reactions to repeated snake bites have been suspected in several

earlier reports [3] but in most cases no serological investigations have been performed [2–8].

Considering the high frequency of allergic and anaphylactic reactions to other animal venoms, especially of bees and wasps, a high allergenic potential of snake venoms would not be surprising. The snake venoms of *Vipera aspis* and *Vipera berus* consist of a complex mixture of enzymes and non-enzymatic proteins [9]. The occurrence of IgE-mediated disease to snake venoms might be more frequent than suspected since the clinical picture does not easily allow a distinction as to whether some of the signs (oedema, nausea and abdominal pain, cardiovascular reactions with hypotension and shock) are of toxic or immunologic origin. Allergic reaction is mainly expected in persons with prior bites, but even sensitization without a history of a poisonous snake bite has been documented in a man working in the venom-asservation on a snake farm [10]. It is important to recognize that professionals dealing with poisonous snakes and persons who suffer from repeated snake bites can not only develop a toxic but also an allergic reaction, because adequate diagnosis and therapy of an anaphylactic reaction can be life-saving. Anaphylactic reactions are probably an underestimated factor in fatal snakebites [7].

This case report demonstrates that, independent of atopy, a sensitization against snake venom can occur. In our patient the reaction to the first bite (swelling of the tongue, dyspnoea and diffuse abdominal pain) may suggest allergy and considering the symptoms after the second snake bite with urticaria and angioedema, we wondered whether an IgE-mediated mechanism was at least in part responsible for the clinical picture. Although the presence of IgE against the snake venom was only demonstrated after the second event, one can not exclude that already the symptoms after the first exposure were partially due to an IgE mediated mechanism since the patient was in repeated contact (skin, possibly inhalation) with snake venom during his work.

If a sensitization can be proved by immunological

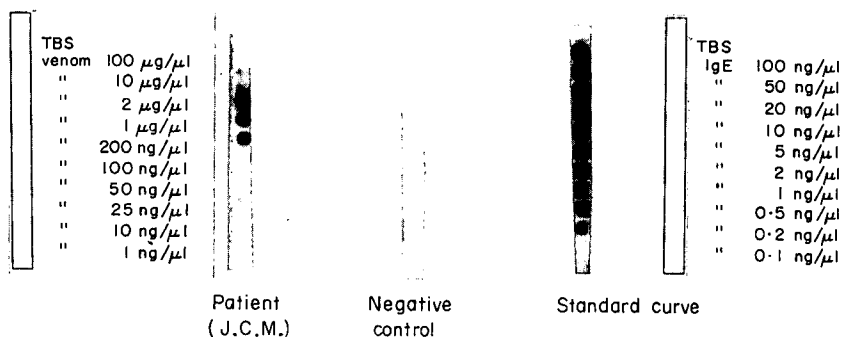


Fig. 1. Detection of *Vipera aspis* venom specific IgE (by chemiluminescence).

testing, exposure to snake venom should be avoided, eventually through change of profession. The high toxicity of native snake venoms exclude an immunotherapy and an effective vaccine with a detoxified venom is not available to our knowledge. For emergency situations the patient should carry an adrenalin-injector or -inhaler.

References

- 1 Stahel E, Wellauer R, Freyvogel TA. Vergiftungen durch einheimische Vipern (*Vipera berus* und *Vipera aspis*). Schweiz med Wschr 1985; 115:890-6.
- 2 Schmutz J. Accidents dûs à des serpents exotiques en Suisse. Thesis, University of Zürich, 1985: 7-10.
- 3 Parrish HM, Pollard CB. Effects of repeated poisonous snakebites in man. Am J Med Sci 1959; 237:277-86.
- 4 Clement JF, Pietrusko RG. Pit viper snakebite envenomation in the United States. Clin Toxicol 1979; 14:515-38.
- 5 Ellis EF, Smith RT. Systemic anaphylaxis after rattlesnake bite. J Am Med Ass 1965; 193:401-2.
- 6 Robert M. Morsures de serpents. Méd et Hyg 1981; 39:378-84.
- 7 Schmutz J, Stahel E. Anaphylactoid reactions to snakebite. Lancet 1985; 2:1306.
- 8 Schmutz J. Accidents dûs à des serpents exotiques en Suisse. Thesis, University of Zürich, 1985:39.
- 9 Iwanaga S, Suzuki T. Enzymes in snake venoms. In: Chen-Yuan Lee, Ed. Snake venoms. Berlin: Springer, 1979:61-158.
- 10 Wadde AA, Rabson AR. Development of specific IgE antibodies after repeated exposure to snake venom. J Allergy Clin Immunol 1987; 80:695-8.

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Allergic skin reaction after inhalation of budesonide

Sirs, Inhaled glucocorticosteroids are essential drugs in treatment of asthma. Glucocorticosteroids are also drugs of choice in many inflammatory dermatoses and allergic rhinitis. Contact allergy to glucocorticoids has recently been shown to be a rather common phenomenon. Among glucocorticoids causing contact hypersensitivity is budesonide [1,2] used both as skin, nasal and inhaled preparations. Skin reactions due to contact allergy have so far been seen after use of topical and nasal preparations [1, 2]. We report a patient with an allergic skin reaction due to inhaled budesonide.

A 59-year-old woman had worked in a bread store for 10 years. Previously she had been found to be allergic to

dog epithelium in a skin-prick test. Patch testing for contact allergy due to an episode of complicated dermatitis had earlier resulted in allergic reactions to chloroallyl-hexaminiumchloride, formaldehyde, fragrances, hexachlorophen, imidazole dinitylurea, methanamine, resins, trihydroxyethylhexa-hydrotriazine and vioform, as well as four glucocorticoids, alclomethasone dipropionate, betamethasone dipropionate, hydrocortisone-17-butyrate and tixocortol pivalate.

Due to continuous respiratory symptoms simultaneous with periods at work in the bread store, she was hospitalized for an assessment of possible occupational disease. She was found to have occupational asthma and allergic rhinitis to wheat flour which was confirmed by positive RAST, prick, and inhalation challenge tests.

When entering the ward she had a dermatitis in the volar aspect of the right elbow. During investigations she was given budesonide powder as Pulmicort® (Turbuhaler®) 800 µg twice and Rhinocort® nasal spray 50 µg two sprays thrice during a day. On the next morning she had erythematous flares on the lips, nose, cheeks and neck, while dermatitis in the right crook bend of the arm had worsened; additionally her mouth was sore.

Patch tests with budesonide at 0.25% and 0.025% in ethanol resulted in allergic (erythematous and oedematous) reactions on the fourth day after application of the tests. Prick tests for Rhinocort nasal spray and Pulmicort powder were negative as well as a chamber scratch test with Pulmicort powder.

Total serum immunoglobulin E (IgE) was 2100 kU/l. Rhinocort-RAST and Pulmicort-RAST, that is, a human serum albumin conjugate (HSA) of budesonide, did not reveal clear IgE binding from the patient serum. However, in immunospot (modified dot blot) analysis, IgE antibodies from the patient serum did bind to the spot of Rhinocort® aqua sample, but not to its HSA conjugate nor to the Pulmicort® Turbuhaler sample or its HSA conjugate. The control serum from a patient, who had not used glucocorticoids and with a normal serum total IgE value, did not show any IgE binding.

The patient was challenged with Pulmicort powder inhalations of 200 µg, 400 µg and 800 µg at one-hour-intervals in the morning; the earlier cubital fossa dermatitis flared up 30 min after the last inhalation. She was given an additional dose of 800 µg of budesonide on the same evening; on the next morning there were two more erythematous flares situated on the neck. The skin reactions disappeared within 24 hr although she was given three more 800 µg budesonide doses. No other reactions were observed. Rhinocort nasal spray challenges performed after 4 days were negative.

Budesonide is used in various forms including dermatological preparations, nasal spray and metered dose