

Contact urticaria and anaphylactoid reaction induced by topical application of nitrogen mustard

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SUMMARY

A 36-year-old woman and a 16-year-old boy, both suffering from mycosis fungoides, developed urticaria and an anaphylactoid reaction after topical whole body application of nitrogen mustard. Prick tests with nitrogen mustard solution produced a weal and flare response.

Both patients had previously been treated intermittently with total body applications of nitrogen mustard for 2½ years and 1 year respectively without complications.

It is well known that topically administered drugs may elicit reactions of the delayed hypersensitivity type, allergic contact dermatitis, but immunological reactions of immediate type hypersensitivity after topically applied medications are less well known (Warin & Champion, 1974). However, anaphylactic reactions have been reported following topical treatment with neomycin (Pippen, 1966), bacitracin (Comaish & Cunliffe, 1967), and an ointment containing neomycin and bacitracin (Roupe & Strannegaard, 1969) and after its application on an endotracheal catheter (Eriksen, 1963). Maucher (1972) described two patients with severe hypersensitivity reactions to systemic penicillin who developed urticaria at the penicillin patch test site that was later followed by systemic allergic reactions. Daugherty, Zackheim & Maibach (1973) have reported an urticarial response and anaphylactoid reaction after topical application of mechlorethamine.

This paper describes two cases of immediate hypersensitivity reactions after topical application of nitrogen mustard, Erasol.

CASE REPORTS

Case 1

A 36-year-old woman with mycosis fungoides of 5 years' duration, in stage II according to van Scott & Kalmanson's (1973) classification, was treated intermittently with whole body applications of nitrogen mustard (40 mg of the drug in 40 ml aqueous solution per treatment). The treatment was repeated once a month, 25 times in all. After the 24th and 25th application, within 30 min she developed generalized pruritus and nausea followed by sweating, burning and a prickling sensation together with tightness of the chest. One and a half hours after treatment she had generalized urticaria.

Her pulse rate was regular with a frequency of 112 beats per min, blood pressure 130/80 mmHg. Her body temperature was 38.9°C. Auscultation of her chest was normal. Following oral antihistamine treatment (cyproheptadine 20 mg) all symptoms disappeared.

Case 2

A 16-year-old boy, with mycosis fungoides in stage II of 1½ years' duration, had been treated intermittently (once a month) with universal topical applications of nitrogen mustard, after initial 'tolerance induction' to the drug (van Scott & Kalmanson, 1973). Attempts to induce tolerance were performed by intravenous injections of 200 µg of nitrogen mustard weekly for 5 weeks.

Two days after treatment 17 and 4 months after the last intravenous injection, he developed urticarial lesions for the first time. They disappeared 5–10 min after administration of cyproheptadine. Generalized urticaria also appeared after three later topical treatments. Urticaria was accompanied by a prickling sensation, sweating and universal itching. All symptoms vanished within 1 h.

In both patients prick tests were performed with freshly prepared aqueous solutions of nitrogen mustard (Erasol) in the following concentrations: 10^{-10} , 10^{-6} , 10^{-5} , 10^{-4} , 10^{-3} , 10^{-2} . All necessary resuscitation equipment was readily available. Following nitrogen mustard at the concentration of 10^{-2} both patients produced after about 15 min an erythematous reaction which approximately 1½ h later turned into a weal and flare response limited to the test area. Five volunteers showed no reactions to nitrogen mustard at this concentration.

Serum levels of immunoglobulin E (IgE) were 76 and 62 µg/l, respectively (normal values: 60–1000 µg/l). Values of complement factors C₃ and C₄ as well as C₁-esterase inhibitor before and after topical treatment were all normal.

A biopsy from the urticarial lesions confirmed the clinical diagnosis.

DISCUSSION

Allergic contact dermatitis is a common complication of topical treatment. However, topical administration of drugs may also result in immediate type reactions.

Anaphylactoid reactions after topical treatment may occur after a patient has developed delayed hypersensitivity to a drug (Pippen, 1966) or without signs of previous contact dermatitis (Comaish & Cunliffe, 1967; Roupe & Strannegaard, 1969; Daughters *et al.* 1973).

The two cases described in the present report provide further evidence that percutaneously administered nitrogen mustard may give rise to an anaphylactoid reaction.

Both our patients tolerated nitrogen mustard well and responded excellently to therapy. One patient had received tolerance induction (van Scott & Kalmanson, 1973), the other one had not. Neither had elevated total IgE in serum, as has been found by other workers in patients with mycosis fungoides (Tan *et al.*, 1973) and in a number of our other mycosis fungoides patients (Zachariae *et al.*, 1975).

With all necessary precautions available for treating a severe anaphylactic shock, and giving antihistamines prior to whole body painting, it has been possible to continue the treatment.

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