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CLINICAL REPORT

1,2-Ethanedithiol-induced Erythema Multiforme-like Contact Dermatitis

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Contact dermatitis simulating erythema multiforme can be caused by many allergens. The chemical agent 1,2-ethanedithiol, which serves as a protective group in chemical synthesis, has hitherto only been implicated as an irritant. We report on a 22-year-old female chemistry student who developed widespread erythema multiforme-like lesions after local contact with 1,2-ethanedithiol. Many target lesions were observed bilaterally on her hands, forearms, arms, and on her forehead. One such lesion was histologically compatible with erythema multiforme. The patient had a positive patch test to 1,2-ethanedithiol, whereas none of 30 healthy subjects showed a positive reaction. However, eight of the 30 controls (26.7%) developed irritant reactions to 1,2-ethanedithiol. Cautious handling of the compound is a prudent precaution. ***Key words: allergic contact dermatitis; erythema multiforme; 1,2-ethanedithiol.***

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Erythema multiforme (EM)-like contact dermatitis is a non-eczematous allergic contact dermatitis (1), which is histopathologically indistinguishable from EM (2). The EM-like contact dermatitis can be caused by potent contact allergens including topical medicaments, chemicals and plants (1). True EM, on the other hand, is usually a consequence of infection with herpes simplex virus (HSV) (3).

Compounds that are chemically very reactive and widely used represent candidate contact allergens. One such compound is 1,2-ethanedithiol (CAS540-63-6; HS-CH_2-CH_2-SH). The chemical agent is widely used as a protective group in many chemical experiments. However, to the best of our knowledge, EM-like contact dermatitis caused by 1,2-ethanedithiol has not been hitherto reported in the literature. We report a case of systemic EM-like contact dermatitis induced by 1,2-ethanedithiol. To elucidate the potential of skin irritancy or contact sensitivity after contact with 1,2-ethanedithiol, a prospective patch testing study was undertaken on healthy volunteers.

CASE REPORT

History

The patient was a 22-year-old Taiwanese female, who was a university graduate student in chemistry. She had no past medical history of mycoplasma or HSV infection. In the year prior to her admittance to our hospital, she had periodic and minimal contact with 1,2-ethanedithiol during the course of laboratory experiments. In July 2001, an accident resulted in the spillage of a large amount of the compound over her right forearm. Within 24 h, many variously sized, erythematous, oedematous, target lesions appeared on her right forearm (Fig. 1). This was followed by the bilateral spread of EM-like lesions to her hands, forearms, and arms, as well as to her forehead on the third day following the spill. By the fifth day after the spill, the skin lesions had worsened and the patient had developed fever, malaise, and dizziness. Laboratory examinations revealed an elevated white blood cell count (10.6×10^9/l, as compared to the normal range of $4.0 - 10.0 \times 10^9$/l).

Upon a diagnosis of EM-like contact dermatitis, the patient was hospitalized and treated intravenously with methylprednisolone (160 mg/day) for three consecutive days. Prednisolone was then administered orally until the skin lesions had cleared.

Histopathology

A skin biopsy specimen was taken from one of the EM-like lesions. Microscopic examination of the biopsy sections showed frequent dyskeratosis, focal epidermal

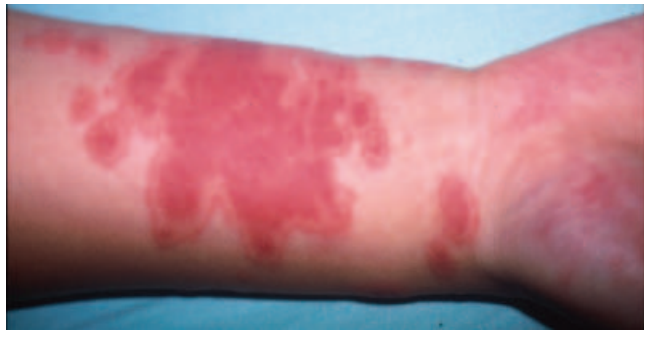

Fig. 1. Several circular, wheal-like erythematous plaques and target-like lesions with confluence located on the right forearm.

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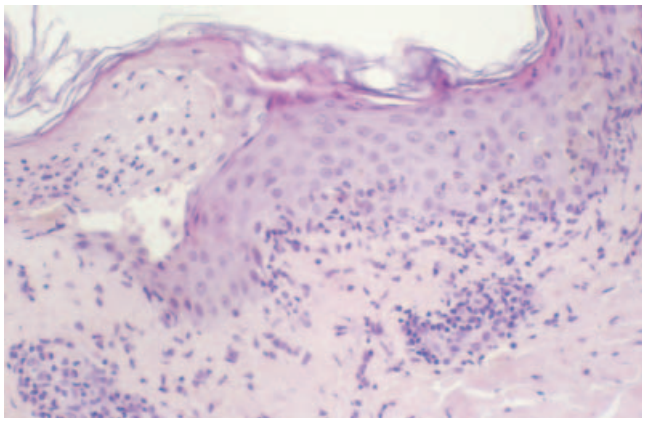

Fig. 2. Histopathological examinations showed frequent dyskeratosis, focal epidermal keratinocyte necrosis, basal vacuolization, and cleft formation in the dermal-epidermal junction (haematoxylin & eosin, original magnification × 200).

keratinocyte necrosis, basal vacuolization, and cleft formation in the dermal-epidermal junction (Fig. 2). These microscopic features were compatible with EM.

Patch testing

Patch testing was performed according to international standards (4). Briefly, test substances were applied to the upper back with Finn chambers, where they remained in contact with the skin for 48 h. Observations were made at 72 and 120 h.

Reactions were scored according to the scale recommended by the International Contact Dermatitis Research Group (ICDRG). A positive result was defined as an erythema with infiltration (1+), erythema with infiltration and papules (2+), or erythema with infiltration, papules and vesicles (3+) (4). The patient was patch-tested with the European standard series and 1,2-ethanedithiol concentrations of 1% and 5% prepared in petrolatum.

After 72 h the patient produced negative results to the European standard series but had positive reactions (1+) to both concentrations of 1,2-ethanedithiol. After 120 h, the 5% concentration of 1,2-ethanedithiol produced a 3+ positive reaction (Table I).

CONTROL STUDY

Thirty healthy volunteers (12 men and 18 women, aged 22–64 years, mean age 27.7±8.2 years) were enrolled in the study. None of them had received systemic medications or topical steroids, nor had they a previous contact history of exposure to 1,2-ethanedithiol. The study was approved by the ethical committee of the National Taiwan University Hospital and informed consent was obtained from each participant.

Table I. *Results of patch testing in the patient*

	Day 3	Day 5
European standard series	Negative	Negative
1,2-Ethanedithiol (1% pet.)	1+	1+
1,2-Ethanedithiol (5% pet.)	1+	3+

Patch testing was performed as summarized above. All of the control subjects were patch-tested with 1% and 5% 1,2-ethanedithiol in petrolatum. The effect of contact exposure was assessed 72 h after application of the patch.

All of the control subjects registered a negative reaction to both concentrations of 1,2-ethanedithiol. However, the 5% concentration produced an irritant reaction in 8 of the 30 control subjects (26.7%) within 5–10 min after applying the Finn chambers to the back.

DISCUSSION

As summarized in Table II, many allergens have been reported to cause EM-like contact dermatitis (1, 5–26). To the best of our knowledge, until the present report, 1,2-ethanedithiol has not been implicated in allergic contact dermatitis.

Clinically, EM-like contact dermatitis manifests as erythematous, oedematous plaques with target lesions (3). The skin lesions can be localized in the contact area or can occur more generally on the trunk and extremities (3). Pathologically, EM-like contact dermatitis shows the same features as EM (3).

EM is currently considered to represent a cell-mediated immune reaction usually targeting keratinocytes that express HSV antigens (27). On the other hand, EM-like contact dermatitis appears to be principally elicited by type IV hypersensitivity (3), although widespread, cutaneous lesions or systemic symptoms, such as were evident in the present case may instead result from circulating immune complex (type III hypersensitivity) (15, 23). The positive patch testing result in our patient suggests that type IV hypersensitivity is involved in the pathogenesis of EM-like contact dermatitis.

In addition to the cutaneous manifestations, the patient had systemic toxic signs including fever, malaise, and dizziness. It has been reported that one patient died of EM-like contact dermatitis and toxic epidermal necrolysis after exposure to spray cologne (28). Thus, toxic complications and severe systemic complications can occur in EM-like contact dermatitis, and may be life-threatening.

1,2-Ethanedithiol is a chemical agent used as a protecting group in chemical synthesis (29). It is readily volatile and vaporizes easily. The fetid odor associated with its presence can be detected in the air even at a very low concentration (1 ppm) (30). The compound can cause eye and skin irritation. Indeed, in the present control study more than one-quarter of the healthy

Table II. *Review of EM-like contact dermatitis with a positive patch test*

Causative agent (Ref.)	Age/sex	Involved site	Form/phase of the contactants
Topical medicament			
Bufexamac (5)	34/M	Local, then systemic	Ointment
Budesonide (6)	19/F	Hand, face, forearms	Ointment
Bufexamac (7)	52/M	Face, trunk	Ointment
Povidone-iodine (8)	30/M	Limbs, trunk	Topical
Phenylbutazone (9)	65/F	Thorax, right axilla	Ointment
Proflavine (10)	24/M	Legs and knee	Powder
Lincomycin (11)	37/F	Ear, face, neck, trunk	Ointment
Mephenesin (12)	30/M	Arms, legs	Ointment
Chemicals			
Ethyl ethoxymethylene cyanoacetate (13)	36/M	Face, extremity	Crystal
Beta-cyclocostunolide (14)	26/M	Upper limbs	Oil
Rubber gloves (1)	48/F	Bilateral forearms	Solid
Natural rubber latex (15)	26/F	Thigh, face	Solid
Oxybenzone (16)	44/F	Forearm, leg	Sunscreen
Dimethoate (17)	41/F	Trunk, back, hand	Insecticide
Plants			
Rhus (lacquer) (18)	43.8 (mean) M18, F13	Body	Ingestion
Rhus (lacquer) (19)	54/M	Hand, arm, trunk	Contact
Sesquiterpene (20)	31/F	Presternal, trunk	Solid
Rosewood (21)	36/M	Neck, thigh, penis	Solid
Primula (22)	30/F	Back, hands, forearms	Plants
Others			
Hair dyes (23)	70/F	Hands, forearms, lip, thigh	Liquid
Capsicum (24)	65/F	Right knee, body	Tincture
Epoxy sealant (25)	46/F	Upper extremity, arm, hand	Paints
Cutting oil (26)	48/M	Forearm, hand, trunk	Liquid

volunteers displayed an irritant reaction, including erythema, itching, and a burning sensation almost immediately after the patch application of the compound.

Given this irritant potency, 1,2-ethanedithiol should be used in a ventilated fume hood and handled with protective gloves, goggles and clothing (31). Finally, as examplified by the present case, because 1,2-ethanedithiol can be inhaled or transcutaneously absorbed, the possibility of systemic contact dermatitis cannot be excluded. Cautious handling of 1,2-ethanedithiol is recommended.

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