Erythema Multiforme Induced by Topical Application of Viru-Merz® Ointment

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Viru-Merz® ointment, 1% tromantadine hydrochloride, is a topical antiviral agent used for recurrent herpes simplex. There are many reported cases of contact dermatitis by tromantadine. But erythema multiforme-like eruptions in association with Viru-Merz® ointment has not been reported. A 31-year-old woman, who applied Viru-Merz® ointment for a recurrent herpes simplex labialis, developed an allergic contact dermatitis. Erythema multiforme like eruptions with typical target feature followed around the eczematous lesions on the face, and spread progressively on the neck and trunk. A patch test revealed positive reaction to Viru-Merz® ointment. (Ann Dermatol 13(1) 66~69, 2001).

Key Words : Tromantadine, Contact dermatitis, Erythema multiforme

Viru-Merz® ointment, 1% tromantadine hydrochloride, is a topical antiviral agent used for recurrent herpes simplex. Since Fanta et al reported a case of contact dermatitis by this ointment in 1976, several cases have been reported. But erythema multiforme-like eruptions in association with Viru-Merz® ointment-induced contact dermatitis has not been reported. We report a case of erythema multiforme induced by this ointment. She developed contact dermatitis after using Viru-Merz® ointment, and then Erythema multiforme-like eruptions. To the best of our knowledge, this is the first report on the erythema multiforme in relation with allergic contact dermatitis by Viru-Merz® ointment.

CASE REPORT

A 31-year-old woman presented with acute pruritic eczematous lesions with edema and grouped vesicles on the perioral area, and multiple erythematous targetoid lesions on her face and trunk. She had suffered from recurrent herpes labialis for ten years and treated with acyclovir ointment. Three weeks before a visit to our hospital, pruritic grouped vesicles developed on her lower lip, and healed with topical acyclovir ointment, but one week later vesicular lesion recurred again on right upper lip. Viru-Merz® ointment prescribed at a private clinic was applied for 2 days. After this, the lesions were aggravated with sudden swelling and severe oozing vesicles on the lips. Multiple erythematous targetoid lesions also developed on the face and trunk two days before visit.

Cold urticaria and allergy to beer and sulfa drugs were on her past medical history. But family history was unremarkable. Physical examination revealed grouped oozing vesicles within a well-demarcated edematous plaque on the right perioral area and multiple variable sized wheals and targetoid lesions on the face, neck and upper trunk (Fig. 1). Laboratory tests showed normal or negative blood cell count, liver function test, urinalysis and erythro-
cyte sedimentation rate. And anti-herpes virus IgG was positive. A biopsy specimen from the targetoid lesion on her back showed spongiosis and a few necrotic keratinocytes in the epidermis, vacuolar changes in the basal layer and mononuclear inflammatory cells infiltrate in dermoepidermal junction and perivascular areas in the upper dermis (Fig. 2A, 2B). Patch tests with Korean standard series, acyclovir ointment and Viru-Merz® ointment showed a positive reaction to Viru-Merz® ointment only (Fig. 3). She was diagnosed as erythema multiforme induced by contact dermatitis due to Viru-Merz® ointment and treated with oral steroids and antihistamines. The lesions disappeared in 10 days during the treatment. After the therapy, she had several attacks of herpes labialis, however, erythema multiforme like eruptions did not develop again.

Fig. 1. Grouped oozing vesicles within a well-demarcated edematous plaque on the right perioral area and multiple variable sized wheals and targetoid lesions on the face.

Fig. 2. A biopsy specimen from the targetoid lesion on her back (Fig 2A, arrow) showed spongiosis and a few necrotic keratinocytes in the epidermis, vacuolar changes in the basal layer and mononuclear inflammatory cells infiltrate in dermoepidermal junction and perivascular areas in the upper dermis (Fig. 2B).

Fig. 3. Patch test with Viru-Merz® ointment showed a positive reaction.
DISCUSSION

Viri-Merz® ointment (Merz & Co. Frankfurt/Main, Germany) is a commercial

name of 1% tromantadine hydrochloride (N-2-di-
methyl-aminoethoxyacetlyl-amino-amantadine), in-
hibitor of early and late events in herpes simplex
virus replication. It is used in the treatment of all
skin disorders caused by the herpes simplex virus, as
well as herpetic keratitis.

Fanta et al.1 reported a study of 240 patients with
herpes simplex treated with tromantadine, in
which 12 cases developed an allergic contact der-
matitis. Since then, many cases of contact der-
matitis caused by the agent have been reported.1–6
Santucci et al.1 reported that the sensitization to tro-
mantadine in molecular basis is due to the ring
structure, adamantane, and not to the amine group
present. Acute contact dermatitis by topical tro-
mantadine is frequently reported, but systemic
type contact dermatitis was extremely rare.1

The patch test by Viri-Merz® ointment in this pa-
tient showed a typical allergic contact dermatitis.
The target shaped lesions in this patient was com-
patible to EM on the base of clinical feature and
histopathological findings. Several contact aller-
gens including plants, exotic woods, various
chemical compounds have been reported to pro-
duce erythema multiforme-like eruptions in the
literature.1–4 In Korea, erythema multiforme-like
eruptions related to application of Rhus, Gramoxone
and diphenylcyclopropenone (DPCP) have been
reported.1–8 The clinical severities of the erythema
multiforme by contact allergen have been reported
to be from a mild localized exanthem to life-
threatening toxic epidermal necrolysis. They were
usually superimposed on acute allergic contact
dermatitis. In this patient, erythema multiforme
eruptions also started from the contact site of perioral
area, and spread into the other sites of face, neck and
trunk. The pathogenesis of erythema multiforme
in relation to allergic contact dermatitis remains
unclear. Irvine et al.17 suggested that a circulating an-
tibody to the absorbed allergen could result in im-
mune complex formation and its subsequent depo-
sition in the microvasculature, resulting in type 3 hy-
persensitivity reaction.

The erythema multiforme caused by contact der-
matitis might be differentiated from herpes associated
erythema multiforme (HAEM). It is strongly sug-
gested that erythema multiforme which occurred
in this patient should be related to the contact
dermatitis by Viri-Merz® ointment, rather than
that of HAEM. The following is the reasons. First,
she had a single episode of erythema multiforme
eruptions on the face and trunk, which were not
predilection sites for HAEM.11 Second, the initial
eruption of erythema multiforme developed on
the applied area of Viri-Merz® ointment, and simi-
lar eruptions spread over the trunk later. Third, in
our follow-up observation, recurrent attacks of
herpes labialis did not accompany with erythema
multiforme-like eruptions after contact dermatitis
episode.

As far as we know, this is the first case of erythema
multiforme in association with Viri-Merz® oint-
ment-induced contact dermatitis.

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