

# A Case of Allergic Contact Dermatitis to Ribavirin

Chee Won Oh, M.D., Mi Youn Park, M.D.\*, Jeong Hee Hahm, M.D.\*

*Department of Dermatology, College of Medicine Gyeongsang National University,  
Chinju, Korea*

*Department of Dermatology, College of Medicine, Ewha Womans University,  
Seoul, Korea\**

Allergic contact dermatitis to topical agents mostly results from vehicles and preservatives and rarely from the active ingredients. Ribavirin, an active ingredient of Viramid® cream, is a synthetic nucleoside derivative with broad spectrum activity against a wide variety of DNA and RNA viruses. We report an 18-year-old woman, who had a perioral edematous patch with exudative crusts after topical application of Viramid® cream (Ilsung pharmaceutical Co., Korea) for the treatment of herpes labialis. A patch test showed that the sensitizer was ribavirin, the active ingredient of the antiviral agent, Viramid® cream. (*Ann Dermatol* 5:(1) 44-46, 1993)

*Key Words:* Allergic contact dermatitis, Ribavirin

Ribavirin (1-β-D-ribofuranosyl-1, 2, 4-triazole-3-carboxamide), a synthetic nucleoside derivative, is an active ingredient of Viramid®, broad spectrum antiviral agent, which inhibits replication of DNA and RNA virus, and has a virustatic action. Sensitization to an antiviral agent, especially not to the base but to its active ingredient, is not common. Among antiviral agents, currently reported contact allergens are idoxuridine<sup>1,2</sup>, tromantadine hydrochloride<sup>1,3,6</sup>, and acyclovir<sup>7</sup>. Allergic contact dermatitis from ribavirin is not yet documented in the literature.

We describe a case of allergic contact dermatitis following topical application of Viramid® cream (Ilsung pharmaceutical Co., Korea, Table 1) for the treatment of herpes labialis.

## REPORT OF A CASE

An erythematous swollen patch and exudative crusts on the perioral area and chin with an itching sensation following topical application of

Viramid® cream on the lower lip developed in an 18-year-old woman. She has been suffering from atopic dermatitis since childhood and the appearance of grouped vesicles on her lips for the past several years. The family history was unremarkable. Three months prior to onset of this lesion, painful grouped vesicles developed on her lower lip, for which she applied an interferon ointment (Green cross Co., Korea), Lipclean® (Sang-a pharmaceutical Co., Korea), and Viramid® cream resulting in symptomatic aggravation. After stopping all topical agents, the lesion spontaneously disappeared. Three days prior to onset of this lesion, painful grouped vesicles recurred and she reapplied Viramid® cream on her lower lip. An oozing erythematous swollen patch developed on her perioral area and exudative crusts appeared and spread over her chin (Fig. 1). Patch tests to European standard series, cosmetic ingredients series, preservatives series, and vehicle series (Chemotechnique Co., Sweden) all revealed negative results. Among the salves which she had used, patch testing to interferon ointment and Lipclean® showed a negative reaction, but to Viramid® cream revealed 1+ reaction at 48 hours and 96 hours, respectively. We performed patch tests for the ingredients of Viramid® cream and the result showed positive reaction to ribavirin at 3.0% and

Received June 19, 1992.

Accepted for publication September 29, 1992

**Reprint request to:** Chee Won Oh, M.D., Department of Dermatology, College of Medicine, Gyeongsang National University, Chinju, Korea

higher concentrations (Table 2).



**Fig. 1.** The oozing erythematous swollen patch and exudative crusts on her perioral area.

## DISCUSSION

These days, the incidence of allergic contact dermatitis due to various topical agents seems to be increasing because of frequent use of topical agents in dermatologic disorders. Allergic contact dermatitis results from vehicles, preservatives and rarely from active ingredients of topical agents<sup>8</sup>.

The activity of ribavirin is quite effective not only against dermatologic disorders such as herpes simplex, herpes zoster, or measles, but also against systemic disorders such as hepatitis A, or influenza. Systemic use of ribavirin may induce hematologic abnormalities such as a decrease in hemoglobin, hematocrit, or the number of erythrocytes, but known adverse effects of topical application were very rare.

Only a few cases of contact sensitization to topical antiviral agents have been reported<sup>1-7</sup>. Amon et al (1975) described 4 cases of allergic contact dermatitis from idoxuridine, a pyrimidine analogue, and suggested cross reactivity to brominated and chlorinated, but not fluorinated, pyrimidine analogues<sup>2</sup>. Several cases of allergy to tromantadine hydrochloride were reported<sup>3-6</sup>: Fanta and Mischer (1976) described 12 cases of positive reactions with 1% tromantadine hydrochloride in the serol gel base, but all reactions to the base were negative<sup>3</sup>. In Van Ketel's patient, patch tests indicated concomitant sensitization to tromantadine hydrochloride and the serol base, the composition of which was unknown<sup>4</sup>. Lembo et al (1984) thought that methyl paraben or

**Table 1.** Composition of Viramid® cream

1. Main ingredient	ribavirin	30.0 mg/g
2. Vehicles	white petrolatum	133.0 mg/g
	emulsifying wax	70.0 mg/g
	mineral oil	51.5 mg/g
3. Emulsifier	cetomacrogol 1000	14.5 mg/g
4. Preservative	methyl paraben	1.0 mg/g
5. Solvent	distilled water	add

**Table 2.** Patch test results of ingredients of Viramid® cream

Ingredients	Concentration	Vehicle	48 hr	96 hr
Ribavirin	1.5%	distilled water	-	-
	3.0%	distilled water	+	+
	6.0%	distilled water	+	++
	15.0%	distilled water	+	++
	30.0%	distilled water	++	++
White petrolatum	as is		-	-
Emulsifying wax	30.0%	petrolatum	-	-
Mineral oil	as is		-	-
Cetomacrogel 1000	30.0%	petrolatum	-	-
Methyl paraben	5.0%	petrolatum	-	-

sorbic acid itself might be the sensitizing component in the serol base<sup>5</sup>. Although tromantadine hydrochloride is an antiviral drug derived from amantadine, Santucci et al (1984) suggested that the molecular basis of sensitization to tromantadine was due to the ring structure adamantradine and not to the amine group present<sup>6</sup>. Acyclovir, another antiviral drug, is a guanine derivative with an acyclic lateral chain. 5% acyclovir in propylene glycol is recommended for topical use<sup>9</sup>, but Camarasa and Serra-Baldrich (1988) described clear contact sensitivity to 5% acyclovir in aqueous solution<sup>7</sup>.

In our case, all vehicles tested in the vehicle series and minor ingredients in the Viramid® cream, such as vehicles, emulsifier, preservative, and solvent, were all negative and no remarkable cross reactivity was present. The patient presented positive reaction to ribavirin at 3.0% and higher concentrations. With more frequent use of topical antiviral agents, even with relatively few case reports on allergies against these antiviral agents, the chances of more frequent potential allergy patients against topical antiviral agents are easily predictable through this case report.

## REFERENCES

1. Angrlini G, Vena GA, Meneghini CL: *Contact allergy to antiviral agents. Contact Dermatitis 15:114-115, 1986.*
2. Amon RB, Lis AW, Hanifin JM: *Allergic contact dermatitis caused by idoxuridine: pattern of cross reactivity with other pyrimidine analogues. Arch Dermatol 111:1581-1584, 1975.*
3. Fanta D, Mischer P: *Contact dermatitis from tromantadine hydrochloride. Contact Dermatitis 2:282, 1976.*
4. Van Ketel WG: *Allergic dermatitis from Viru-Merz ointment, tromantadine hydrochloride and serol base. Contact Dermatitis 8:71, 1982.*
5. Lembo G, Balato N, Cusano F et al: *Allergic dermatitis from viruserol ointment probably due to tromantadine hydrochloride. Contact Dermatitis 10:317, 1984.*
6. Santucci B, Picardo M, Cristaudo A: *Contact dermatitis to tromantadine. Contact Dermatitis 10:317-318, 1984.*
7. Camarasa JG, Serra-Baldrich E: *Allergic contact dermatitis from acyclovir. Contact Dermatitis 19:235-236, 1988.*
8. Yoo BK, Kim HJ, Kim YK: *Allergic contact dermatitis to topical medicamentosa. Korean J Dermatol 23:447-455, 1985.*
9. Fiddian AP, Yeo JM, Stubbings R et al: *Successful treatment of herpes labialis with topical acyclovir. Br Med J 286:1699, 1983.*