

Kaposi's varicelliform eruption associated with the use of tacrolimus ointment in two neonates

Sir,

Steroid or tacrolimus ointments which are widely used for atopic dermatitis (AD) in Japan, are actually immunosuppressive. Long-term use of these ointments induces various adverse effects including serious skin infections, skin atrophy or rebound phenomenon.^[1] Therefore, I have been treating AD patients for more than 15 years, without using these immunosuppressive ointments.^[1] However, these adverse effects are not well known to many doctors in Japan. Moreover, there is no warning associated with tacrolimus ointment use for young children or neonates with AD in Japan. Kaposi's varicelliform eruption (KVE) is a dissemination of the cutaneous herpes simplex virus (HSV) or in some rare instances, other virus infections.^[2]

A report described the treatment of KVE in a 40 year-old woman with AD with an oral steroid and steroid ointment.^[2] KVE was also found to be evoked by tacrolimus ointment in adult patients with AD.^[3,4] Thus, KVE developed in a 29 year-old man with AD after four days of using tacrolimus ointment.^[3] In addition to this, it was also reported that KVE relapsed in a 32 year-old woman with AD following tacrolimus ointment treatment on her face.^[4] However, the fact that KVE is associated with tacrolimus ointment is not well known in Japan. Moreover, KVE has not been previously reported in neonates. I report here two neonatal cases of KVE associated with the application of tacrolimus ointment. Taking photographs of both cases was not permitted by the parents for religious and ethical reasons.

Case 1: The first patient was a baby boy born at term gestation by spontaneous delivery. Eczema was noted on his face on day 8 and he was treated with 0.03% tacrolimus ointment by a local pediatrician without any improvement. On day 14, he developed many vesicles on his face. He presented to our hospital on day 16. He was afebrile and there were many vesicles and encrusted erosions on his face and neck. KVE was confirmed by detection of HSV-1 DNA by PCR from a skin lesion.^[5] Tacrolimus ointment was discontinued. Treatment with oral acyclovir (80 mg/kg) and

vidarabine ointment for ten days resulted in the resolution of vesicles. On day 30, eczema was noted on his face. Skin prick tests to egg yolk, egg white and latex were positive. The mother was advised to avoid egg-containing food and latex-containing products and his face was treated with zinc oxide, following which the baby was well.

Case 2: The second patient was a baby girl born at term gestation by spontaneous delivery. Eczema was noted on her face and neck on day 11 and she was treated with 0.03% tacrolimus ointment by a dermatologist without any improvement. On day 15, she developed many vesicles on her face and neck. She presented to our hospital on day 17. She was afebrile and there were many vesicles with crusting and oozing on her face, neck and both arms. KVE was confirmed by detection of HSV-1 DNA by PCR from a skin lesion. Tacrolimus ointment was discontinued. Treatment with oral acyclovir (80 mg/kg) and vidarabine ointment for 14 days resulted in the resolution of vesicles. On day 35, eczema was noted on her face and neck. Skin prick tests to cow's milk were positive. Her mother avoided cow's milk-containing food and her face and neck were treated with zinc oxide, following which the baby did well.

In both cases, swabs of the mothers' vagina and cervix tested negative for HSV-1 or HSV-2 DNA. Although serum IgG but not IgM were detected against HSV-1 and HSV-2 in both mothers, no increase in their IgG titers was noted. Neither mother had oral herpes, AD, HIV infection or skin infection. Moreover, none of the family members had oral herpes or any other herpes infection. Thus, the origin of HSV in these two cases remains to be elucidated. Tacrolimus is an immunosuppressive drug. Skin lesions of AD are vulnerable to infection by bacteria or viruses.^[6] It is possible that the application of tacrolimus ointment further suppresses the immunity of the lesional skin, which may result in HSV infection and may evolve into KVE in some cases. In fact, lately I have been treating more than 100 cases of KVE per month.^[7] Most of the cases were treated with steroid ointment or tacrolimus ointment. Surprisingly, many cases were not diagnosed as KVE and thus those patients visited our hospital from far off cities. As the incidence of KVE is rapidly increasing, it is possible that HSV causes KVE even in neonates especially associated with tacrolimus application.^[7] Moreover, it is not surprising to see AD in neonates in our hospital. I have previously reported a 21 day-old neonate with latex allergy.^[8] As I have been treating more than 1000 patients with AD per month, cases of neonatal AD were often encountered.

The US Food and Drug Administration (US-FDA) warns that

tacrolimus ointment should not be used in children under two years of age, but there is no such warning in Japan. These cases may indicate that tacrolimus ointment should be used with caution in young children with AD.

Hajime Kimata

Department of Allergy, Moriguchi-Keijinkai Hospital, Moriguchi City, Osaka Prefecture, Japan

Address for correspondence: Hajime Kimata, Department of Allergy, Moriguchi-Keijinkai Hospital, 2-12-47, Moriguchi City, Osaka Prefecture, 570-0021, Japan.
E-mail: kimata-keijinkai@mkc.zaq.ne.jp

REFERENCES

1. Kimata H. Selective enhancement of production of IgE, IgG4, and Th2-cell cytokine during the rebound phenomenon in atopic dermatitis and prevention by suplatast tosilate. *Ann Allergy Asthma Immunol* 1999;82:293-295.
2. Kramer SC, Thomas CJ, Tyler WB, Elston DM. Kaposi's varicelliform eruption: A case report and review of the literature. *Cutis* 2004;73:115-22.
3. Lubbe J, Pournras CC, Saurt J-H. Eczema herpticum during treatment of atopic dermatitis with 0.1% tacrolimus ointment. *Dermatology* 2000;201:249-51.
4. Ambo M. Relapsing Kaposi's varicelliform eruption and herpes simplex following facial tacrolimus treatment for atopic dermatitis. *Acta Derm Venereol* 2002;82:224-5.
5. Pelligra G, Lynch N, Miller SP, Sargen MA, Osioviich H. Brainstem involvement in neonatal herpes simplex virus type 2 encephalitis. *Pediatrics* 2007;120: e442-e6.
6. Dohli MA, Lin P, Lee J, Lucky AW, Paller AS, Eichenfield LF. The epidemiology of molluscum contagiosum in children. *J Am Acad Dermatol* 2006;54:47-54.
7. Kimata H. Rapidly increasing incidence of Kaposi's varicelliform eruption in patients with atopic dermatitis. *Indian J Dermatol Venereol Leprol* 2008;74:264-65
8. Kimata H. Wheezing caused by latex allergy in a 25-day-old infant with atopic dermatitis. *Pediatr Asthma Allergy Immunol* 2004;17:287-291.