

Kaposi's Varicelliform Eruption During Long-term Treatment of Rosacea with 0.03% Tacrolimus Ointment

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To the Editor: Kaposi's varicelliform eruption (KVE) is a distinct viral skin disease which is characterized by disseminated vesiculopustules and erosions superimposed on the preexisting dermatosis. It is mostly caused by herpes simplex virus (HSV) type 1 or 2 and rarely by vaccine-virus or Coxsackie A16 virus. The KVE is normally described in atopic dermatitis (AD), but also observed in association with papulosquamous or acantholytic dermatosis.^[1] Report about rosacea complicated with KVE is rare. On the other hand, tacrolimus ointment has been demonstrated to be an effective treatment for steroid-induced rosacea. Here, we report a case of KVE in a patient with rosacea during long-term treatment with 0.03% tacrolimus ointment.

A 52-year-old woman presented to our Dermatology Department in April 2014 due to recurrent facial erythema and pustules with flushing and burning pain for more than 1 year. Physical examination found typical changes of rosacea with erythema, pustules, and telangiectasia on bilateral cheeks. The patient was started on enteric-coated minocycline hydrochloride 100 mg/d. After the relief of the pustules, 0.03% of tacrolimus ointment was prescribed to treat the facial erythema. After a consecutive treatment for totally 7 months, the patient came back with acute febrile painful facial eruptions with multiple monomorphic, umbilicated grouped vesicular lesions on the cheeks and lower lip [Figure 1a-c]. Polymerase chain reaction examination of the blister fluid revealed a strong expression of HSV type 1 DNA. The diagnosis of KVE was made and the patient was treated with 500 mg valacyclovir and topical boric acid solution twice daily, respectively, for totally 10 days, leading to a complete clinical remission [Figure 1d].

KVE also called eczema herpeticum when it happens in patients with AD. There is a growing number of case reports of KVE related to tacrolimus use in AD.^[2] Tacrolimus, a hydrophobic macrolide lactone with potent anti-inflammatory and immunosuppressive activities, has been documented to be useful in various inflammatory dermatoses. It remains to be determined whether the facilitation of herpes simplex infection is more related to the underlying skin barrier/immune defect in atopic state or is mainly caused by the immunosuppressive effect of tacrolimus. A decreased level of interleukin-18 (IL-18) may be related to KVE since tacrolimus was shown to inhibit IL-18 production in

human peripheral blood mononuclear cells *in vitro*. On the other hand, mutation of the promoter gene in IL-18 has been found to be the susceptibility gene of AD patients treated with tacrolimus ointment,^[3] suggesting some patients under treatment with tacrolimus are inborn susceptible to suffer KVE.

However, the immunosuppressive effect caused by long-term using of tacrolimus is a susceptible factor to induce an exaggerated eruption of herpes simplex (EEHS) in patients

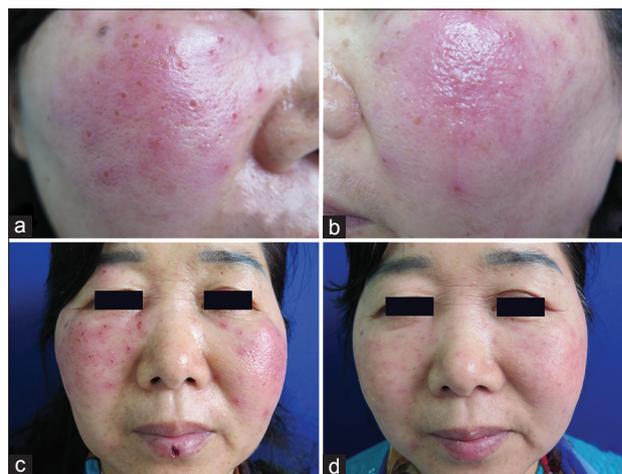


Figure 1: A febrile, painful, and acute facial eruption with multiple monomorphic, umbilicated grouped vesicular lesions on the erythema of the right cheek (a), left cheek (b), and lower lip (c). The vesicular lesions of the cheek and lower lip had totally disappeared and the erythema had been improved obviously after being treated for 10 days (d). The patient has signed the informed consent.

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who was infected before. It can present with disseminated lesion which is needed to distinguish from KVE. There are some differences between KVE and EEHS. First, KVE is characterized by monomorphic eruption of dome-shaped and umbilicated vesicles,^[1] but EEHS mainly presents with the cluster distribution of small fluid-filled vesicles with a raised erythematous. Second, the eruption of KVE is mainly based on the setting skin condition, but the rash of EEHS is diffused base on the skin or mucous membrane. Moreover, KEV only happens on the condition of various setting skin diseases but EEHS is not limited by this. This case performed as classical eruptions with multiple monomorphic, umbilicated grouped vesicular lesions based on the rosacea; it is a typical KVE, but the setting skin condition is rare.

To our knowledge, the association of KVE with rosacea has only been described once.^[4] Although tacrolimus has been demonstrated to be useful in the treatment of rosacea, continuous use of tacrolimus can paradoxically induce rosacea-like dermatitis with the question of Demodex infection.^[5] More well-controlled studies are needed to define the indication and to prove the therapeutic efficacy of calcineurin inhibitors in the treatment of rosacea. Doctors, as well as patients under long-term use of calcineurin inhibitors, should be aware of this serious complication.

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Conflicts of interest

There are no conflicts of interest.

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