# Herpes simplex virus in erythrokeratoderma variabilis

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## Abstract

We report a 48 -year-old woman with erythrokeratoderma variabilis, which is a rare hereditary disorder of keratinization, who developed new, painful, blisters within her skin lesions. The diagnosis of herpes simplex virus infection was made based on the clinical history and histopathologic features. She was successfully treated with prophylactic valacyclovir, and her herpetic outbreaks have halted. This case serves as a reminder that even among the most rare skin disorders, common secondary complications may be easily overlooked.

## Case Presentation

**PATIENT:** 48-year-old-woman
**DURATION:** Eight years
**DISTRIBUTION:** Face, neck, chest, abdomen, arms, and legs

**HISTORY:** A 48-year-old woman presented to the Skin and Cancer Unit for evaluation of an episodic burning sensation of her skin. The patient, along with her three children, had been evaluated in the distant past for erythrokeratoderma variabilis (EKV). Treatments with topical tretinoin were unsuccessful, and she had discontinued treatment due to irritation several years ago. The patient was lost to follow-up. She returned to our clinic concerned about a new development; over the past eight years, she experienced numerous, painful episodes in the EKV plaques on her left arm and left thigh. These episodes lasted several days and were associated with fevers, chills, and myalgias. The skin would ultimately develop fluid-filled blisters before resolving spontaneously.

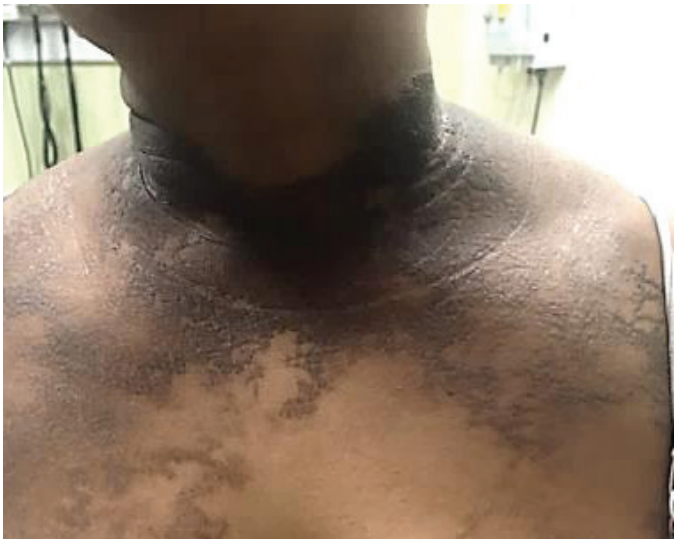

**Figure 1.** Well-demarcated, hyperpigmented, and hyperkeratotic plaques in geometric patterns were present on the neck, periorbital skin, chest, abdomen, antecubital fossa, inguinal folds, and thighs.

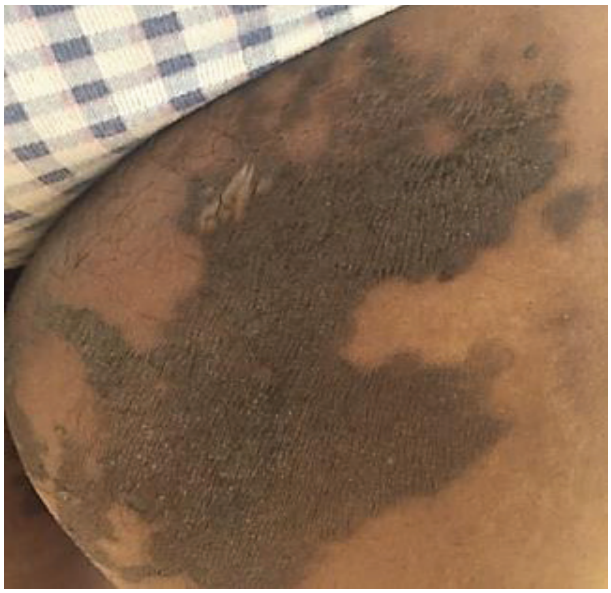

**Figure 2.** Well-demarcated, hyperpigmented, and hyperkeratotic plaques.

Past medical history was negative. A punch biopsy was obtained from an intact blister on the left thigh.

**PHYSICAL EXAMINATION:** Well-demarcated, hyperpigmented, and hyperkeratotic plaques in geometric patterns were present on the neck, periorbital skin, chest, abdomen, antecubital fossa, inguinal folds, and thighs (**Figures 1 and 2**). Along the superior aspect of one of these plaques on the left thigh was an intact blister that measured approximately 2-cm.

**LABORATORY DATA:** None.

**HISTOPATHOLOGY:** There is intraepidermal vesiculation with reticular degeneration, neutrophils, necrotic keratinocytes, and cellular debris. There is evidence of epidermal regeneration underneath the vesiculation. At the edge of the blister, the epidermis is mildly papillomatous and acanthotic (**Figure 3**). Within the superficial-to-mid dermis, there is a perivascular and interstitial, mixed infiltrate with eosinophils. A periodic acid-Schiff-diastase stain does not show fungal hyphae.

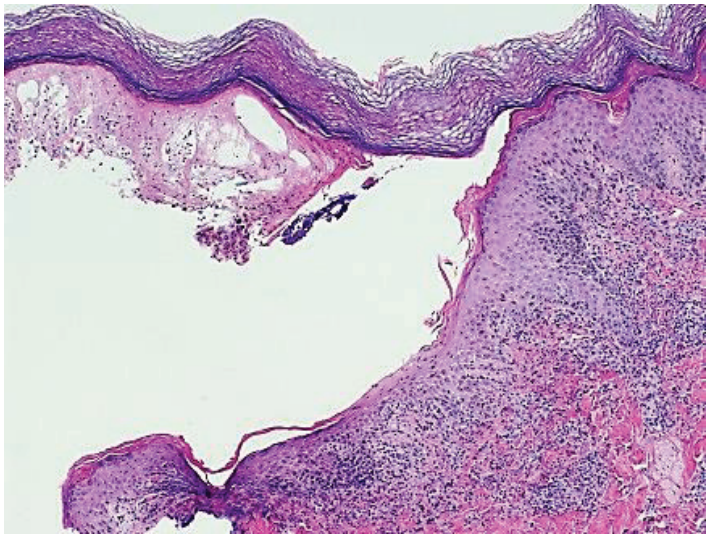

**Figure 3.** There is intraepidermal vesiculation with reticular degeneration, neutrophils, necrotic keratinocytes, and cellular debris. There is evidence of epidermal regeneration underneath the vesiculation. At the edge of the blister, the epidermis is mildly papillomatous and acanthotic

**DIAGNOSIS:** Herpes simplex virus in erythrokeratoderma variabilis

## Discussion

Erythrokeratoderma variabilis (EKV) is an uncommon, autosomal dominant disorder of keratinization. First described in 1925, EKV features two distinct morphologic skin findings: fixed hyperkeratotic plaques and transient erythema [1]. The skin findings in EKV patients first develop near birth or in early childhood, and they persist throughout life. Owing to the autosominal dominant transmission pattern, most patients have affected family members.

EKV is caused by mutations in connexin 31 or connexin 30.3 [2,3]. Connexin 31 and connexin 30.3 also are known as gap junction beta-3 protein (GJB3) and gap junction beta-4 protein (GJB4), respectively. Connexins are proteins that form gap junctions, which are specialized intercellular channels. It is theorized that disruptions in the gap junctions of keratinocytes result in dysregulated homestasis and, ultimately, the abnormal skin findings observed in these patients.

On histopathologic examination, EKV shows hyperkeratosis, acanthosis, papillomatosis, and characteristic grain-like cells in the stratum corneum [4].

Although there is no specific treatment for EKV, topical and systemic retinoids may be effective [4-6]. Keratolytics, which include salicyclic acid and alpha-hydroxy acid, also have been used although with limited success [6].

EKV is a benign disease and complications are rare. Secondary dermatophyte infections may occur, but there are no reports of serious or fatal conditions that develop in EKV [7].

Herpes simplex virus (HSV) infection is a ubiquitous skin disorder. After the initial infection, the HSV establishes latency in local neurons and may periodically become reactivated, which corresponds to the episodic outbreaks. Classically, HSV infection is characterized by grouped vesicles on erythematous bases. Burning, pain, and non-specific systemic complaints may precede or accompany outbreaks. The recurrent nature, associated symptoms, and morphology are deeply

characteristic of this infection.

To the best of our knowledge, this patient represents the first reported case of HSV arising in EKV. She was treated with a suppressive dose of valacyclovir to be taken at the first sign of an outbreak. This medication has prevented further outbreaks.

The diagnosis of HSV should be considered in any patient with a recurrent, focal, vesicobullous eruption that is associated with pain and systemic complaints. This patient's striking skin findings, which are due to EKV, are distractors from identifying this more common and easily treated viral infection. Although treatment for her EKV was not previously satisfactory, the patient has benefited from antiviral medication, which has successfully prevented further HSV outbreaks and the associated systemic symptoms.

## References

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