

Erythrokeratoderma variabilis: Two case reports

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ABSTRACT

Erythrokeratoderma variabilis (EKV) is a rare heterogeneous skin disorder. The classical EKV first described by Mendes da Costa is characterized by two types of skin lesions: (1) figurate hyperkeratotic plaques, and (2) transient erythematous areas. Herein, we report two patients presenting with erythematous and hyperkeratotic lesions that were histopathologically diagnosed with EKV.

Key words: Erythrokeratoderma variabilis, genodermatosis, transient erythema

INTRODUCTION

Erythrokeratoderma variabilis (EKV) is a rare subtype of heterogeneous group of skin diseases called the erythrokeratoderma, and presents with migratory erythema and fixed hyperkeratotic plaques.^[1] EKV lesions commonly occur in the early stage of life. The lesions are hyperkeratotic and well-marginated and have a tendency to become confluent. EKV lesions are usually distributed on the extensor surface of extremities, buttocks, and face. Erythematous lesions are transitory and show variation with stress and heat.^[2] Two patients aged 10 and 15 years were evaluated for erythematous and hyperkeratotic lesions that were clinically and histopathologically confirmed with EKV. We report these cases due to their rarity.

CASE REPORTS

Case 1

A 10-year-old boy came to our clinic for brownish and red spots that had started 5 years ago and had appeared from time to time. The red spots initially spread centrifugally and disappeared without any mark, however, the brownish lesions on the anterior part of trunk and arms did not disappear. He was seen by different physicians and was treated with various fungal treatments that were not beneficial. No similar lesions were detected in other family members. No systemic disease was detected.

The dermatological examination showed erythematous, annular plaques located on the anterior part of chest, arms, and neck; and

brownish hyperkeratotic plaques on the left shoulder and axillary region [Figure 1a and b]. No lesions were detected on the palm, sole, nail, hair, teeth, or mucosa. The histopathological examination of the hyperkeratotic plaque showed hyperkeratosis with moderate papillomatosis and acanthosis [Figure 2].

Case 2

A 15-year-old boy was admitted to our clinic for transient redness and brownish-crusty lesions. He had these lesions since age 2. He was seen by several physicians and he was treated with different treatments including salicylic acid, and corticosteroids that were ineffective. Erythematous lesions appeared from time to time that worsened with physical activities and heat, and disappeared spontaneously. However, the brownish crusty lesions did not recover. His parent was a second-degree relative. His sister had similar symptoms, but did not come to the clinic for an examination. The dermatological examination showed well-marginated, brownish hyperkeratotic lesions symmetrically distributed on the axillary regions, antecubital fossa, inguinal region, and lower extremities [Figure 3a and b].

No fungal elements were detected in potassium hydroxide preparations in both patients. The laboratory tests including complete blood count, liver function tests, lipid profile, glucose, creatinine, serum urea nitrogen, calcium, phosphate, and urinalysis were within normal limits.

The histopathological assessments of hyperkeratotic lesion showed basket-like

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Figure 1: (a) Hyperkeratotic plaques that superimposed with randomized erythematous circular plaques in the patient one, (b) Transient annular type erythematous plaques on flexor parts of forearm and arm in both sides (Case one)

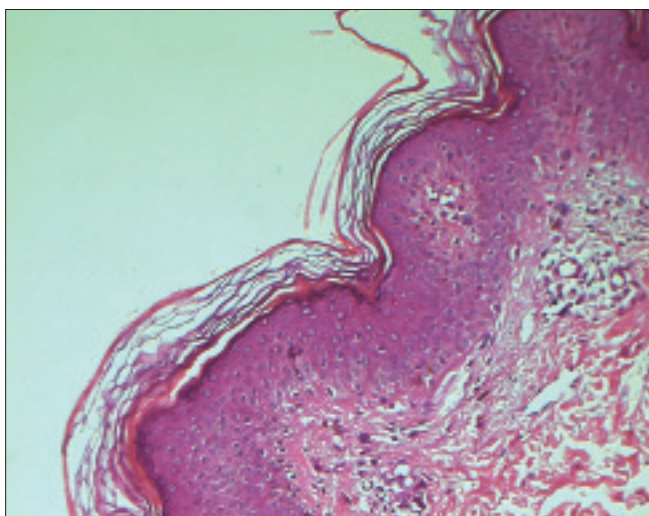


Figure 2: Hyperkeratosis with moderate papillomatosis and acanthosis are shown (H and E, ×20)

hyperkeratosis, papillomatosis, acanthosis, and perivascular lymphocytic infiltration of the dermis [Figure 4]. The clinical and histopathological findings were consistent with EKV. Systemic therapy in case one was refused by the parents; so topical corticosteroid treatment was initiated. The second patient was treated with acitretin po (25 mg/d). The lesions were regressed with mild hyperkeratosis at the end of 4 months treatment. Then the patient discontinued the treatment. During the 1 year follow-up period, he occasionally had episodes of erythema and mild degree of hyperkeratosis.

DISCUSSION

There are two major subtypes of EKV: (1) EK variabilis (Mendes da Costa),^[3] and (2) EK progressiva symmetrica (Gotttron).^[4] The classical EKV initially described by Mendes da Costa is characterized by two types of skin lesions: (a) figurate

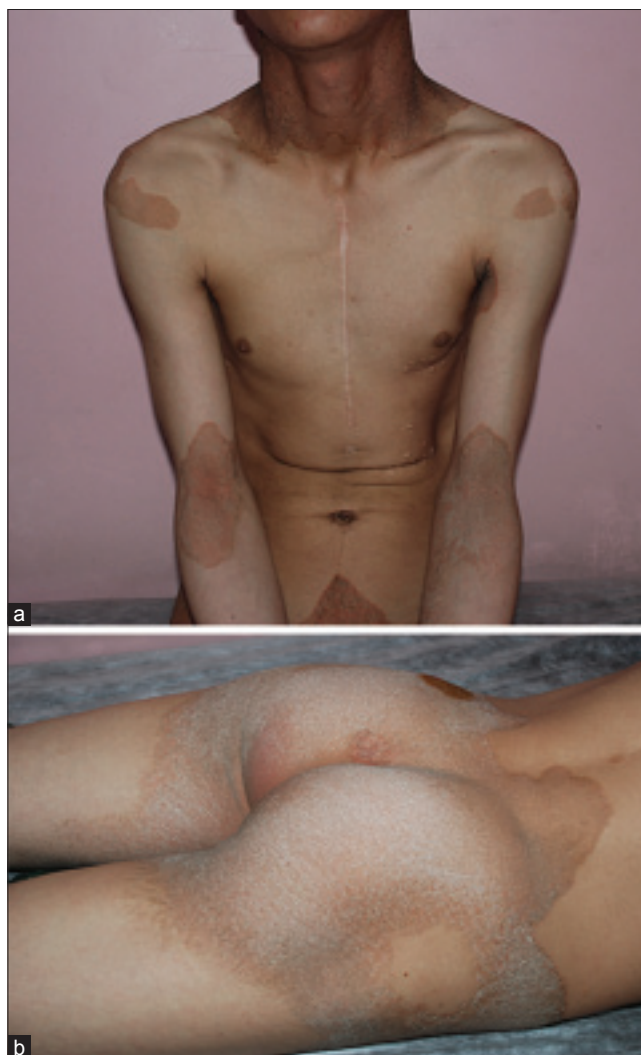


Figure 3: (a) Hyperkeratotic plaques with well-defined margin on the neck, axillary, flexor aspect of elbow, inguinal region, lateral part of shoulder in the patient two, (b) Disseminated squamous, hyperkeratotic plaques on the gluteal region (Case two)

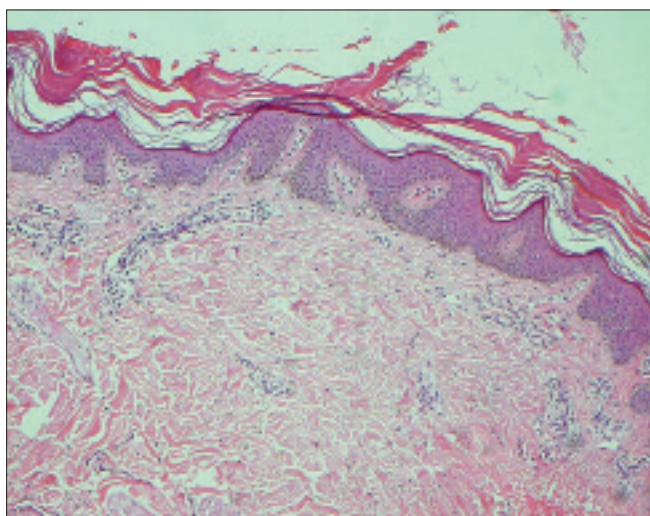


Figure 4: Hyperkeratosis with moderate papillomatosis and acanthosis are shown (H and E, $\times 10$)

hyperkeratotic plaques and (b) transient erythematous areas. These subtypes are independent, and their shapes and distribution can be changeable at any time.^[2,5] The lesions have propensity to locate on the distal extremities, buttocks, and trunk. Hyperkeratotic plaques are particularly distributed on the face, hip, and extensor aspect of the limb. In both cases, the hyperkeratotic lesions were located on the flexor areas. EKV usually presents at birth or during infancy.^[6] The case one had developed the lesions since age 5, and the case two had developed since age 2. Progressive symmetric erythrokeratoderma (PSEK) is less common among the erythrokeratoderma variants (that was initially described by Gottron in 1922).^[4] It presents as symmetrical plaques on the limbs, buttocks, and face during early childhood. The plaques progress in childhood and frequently stabilize in adolescent age.^[4] It is autosomal dominant disease, often with incomplete penetrance. There is considerable similarity between PSEK and EKV due to the presence of a symmetrically distributed, fixed or very slowly progressive erythematous, scaly plaques. PSEK differs in the absence of migratory erythematous lesions and in greater incidence of palmoplantar keratoderma.^[7] A distinctive feature of EKV from PSEK is the lack of facial involvement.^[6] Histopathological findings of PSEK are non-specific as well. The findings include loose hyperkeratotic stratum corneum, wide plugged hyperkeratotic follicular openings, acanthosis and papillomatosis, and perinuclear vacuolization and parakeratosis. The treatment of PSEK is similar to EKV. Patients with PSEK have been successfully treated with retinoids, however, the rate of recurrence is high.^[7]

Rare EKV variants include erythroderma en cocardes, known as Degos' disease,^[8] reticulate erythrokeratoderma,^[9] EKV with erythema gyratum repens-like lesions.^[1]

EKV is typically an autosomal dominant inheritance, but three cases with autosomal recessive transmission have been

reported in literature (one of recessive EKV case was of Middle Eastern origin).^[3,6] In our cases, the family member of the patient one did not have similar lesions; and the sibling of the patient two had similar lesions. However, we could not perform genetic analysis in our cases.

The gap junction proteins including connexin 31 (GJB3 gene) and connexin 30.3 (transmembrane proteins) (GJB4 gene) are mutated in EKV patients.^[2,5] Connexins come together to form hexameric aqueous channels or connexons in the cell membrane.^[4] However, connexin mutation was not detected in some EKV cases.^[5,10]

The pathogenesis of EKV is unclear. The postulated pathogenesis is systemic ectodermal vascular dysplasia and abnormal vascular dilatation that may lead to the disturbance of keratinization.^[2] Electron microscopy studies show grain-like cells at the junction of stratum granulosum and corneum, containing large amounts of clumped perinuclear tonofilaments. Unmyelinated nerve axons and Schwann cells can be seen in the superficial dermis of erythematous patches and uninvolved skin. The presence of these nerves may link to the variability of lesions that can change with temperature changes, wind and emotional stress.^[2]

Differentiation between the erythrokeratodermas is challenging and can be performed based on clinical findings and genetic analysis. Histopathology findings of hyperkeratotic plaques, and erythematous patches is usually non-specific and can demonstrate hyperkeratosis, papillomatosis, epidermal hyperplasia and a granular cell layer 2-3 layers thick. Dilated blood vessels and a mononuclear perivascular infiltrate can be seen in the dermis.^[2,11] The histopathological findings of our patients were consistent with the previous literature's findings.

No specific therapy is available for EKV. It is a genodermatosis and can express itself throughout a patient's lifetime. It often worsens until puberty, and then followed by chronic stage. It does not affect patient's life span. However, due to its disfiguring appearance, it can cause significant psychosocial consequences on the affected individual's life. The first-line treatments of PSEK include topical keratolitics, topical retinoids, tazarotene, alpha-hydroxy acid, and topical corticosteroid.^[1,2,12-16] However, some experts suggest systemic retinoids instead of topical therapies.^[16] Second-line treatments are etretinate, isotretinoin, and acitretin.^[16] In some selected cases, retinoid plus psoralen with ultraviolet A therapy was also administered.^[15] There was symptomatic relief of the pruritus associated with the erythematous component in two patients in one family with the use of an oral non-sedating H1 antihistamine.^[7]

The erythematous patches of EKV can be treated with topical corticosteroids. Hyperkeratotic lesions usually show a good

response to retinoids, however, the erythematous lesions do not respond to retinoids.^[2] However, patient's response to retinoid therapy is only limited during the therapy course. The lesions reappear during the untreated period. Medication choice should be made based on its side-effect because of its prolonged use.

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