

Erythrokeratoderma Variabilis in a 6 Year Old Child: An Uncommon Genodermatosis with Typical Presentation

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Introduction

A 6 year old male term child, born of consanguineous marriage presented with pruritic, erythematous, hyperkeratotic fixed scaly plaques along with erythematous patches showing bilaterally symmetrical distribution affecting lower abdomen, inguinal fossa, thighs, axilla and side of neck since his neonatal age (Figure 1). KOH mounting for fungus was negative. Systemic examination and developmental milestones were normal. Skin biopsy from the fixed hyperkeratotic plaque revealed orthohyperkeratosis, papillomatosis, normal granular layer and acanthosis. Based on the typical history, characteristic clinical features and histopathological findings, diagnosis of 'Erythrokeratoderma Variabilis (EKV)' was made and the child was put on topical keratolytics only with mild improvements.

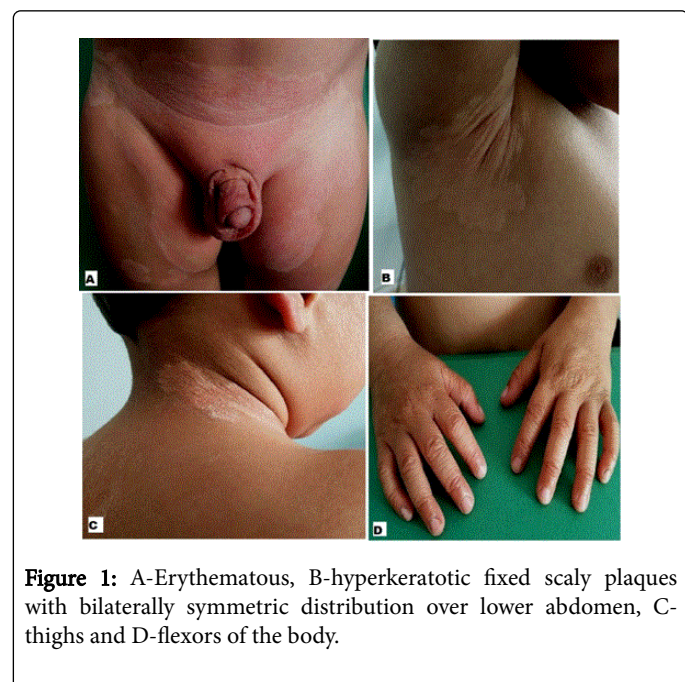


Figure 1: A-Erythematous, B-hyperkeratotic fixed scaly plaques with bilaterally symmetric distribution over lower abdomen, C-thighs and D-flexors of the body.

Initially both EKV and progressive symmetric erythrokeratoderma (PSEK) were identified as separate clinicopathologic entity. Classical EKV was first described by Mendes da Costa and Darier described PSEK in 1911 though it is named as 'Gottron's syndrome' after Gottron's article in 1922 [1,2]. Over the time, owing to the similar genetic mutations, both of these two conditions were included under a common clinical spectrum.

Erythrokeratoderma variabilis is a heterogeneous group of inherited keratinization disorders (usually autosomal dominant) often

manifesting at birth or in infancy [3]. It characteristically presents as "well-defined, persisting, erythematous, fixed, hyperkeratotic scaly plaques with irregular borders as the 'boundary lines of seacoasts'" and "migratory transient erythematous lesions" seen for only hours or days and reappear especially during physical or mental stress or in hot weather [3]. The lesions tend to involve distal extremities, buttocks, and trunk. Hyperkeratotic plaques are particularly distributed on the face, hip and extensor aspect of the limb. There are some variants of EKV which may present atypically such as EKV.

CramMevorah with erythema gyratum repens like skin lesions and Erythrokeratoderma en cocardes or Degos' syndrome characterized by annular lesions with central scaling and surrounding erythema, giving the appearance of targetoid, or "encocardes" distributed on the extremities [3].

Germline mutations in $\beta 3$ and $\beta 4$ genes that code for gap junction proteins connexin 31 and 30.3 have been held responsible for EKV [4-6]. The disease locus is at chromosome 1p34-p35 near the rhesus cluster, where several genes encode members of the connexin family of gap junction proteins [7].

The pathogenesis of EKV is yet to be explained. One hypothesis is that systemic ectodermal vascular dysplasia and abnormal vascular dilatation may lead to abnormal keratinization [8].

Histopathologically, orthohyperkeratosis or parakeratosis, with acanthosis and papillomatosis are the consistent features. On immunohistochemistry, there is an increased suprabasal staining for involucrin and perinuclear connexin 31 expression. Reduced numbers of keratinosomes are seen within the stratum granulosum [9].

The close differential diagnosis includes most importantly PSEK, non-bullous ichthyosiform erythroderma and Netherton syndrome [3,10]. Atypical variants (EKV CramMevorah and Erythrokeratoderma en cocardes) must be differentiated from subacute lupus erythematosus, erythema annulare centrifugum, and erythema multiforme [3,10,11] Being closest differential diagnosis, PSEK should always be kept as first differential but it can be ruled out by its characteristic features such as non-migratory well-demarcated, polycyclic, hyperkeratotic lesions distributed symmetrically over the elbows, knees, dorsal aspect of hands, feet and buttocks typically sparing the trunk.

There is no specific treatment. Topical keratolytic agents such as alpha hydroxyl acid, urea and corticosteroids are used in mild cases. Bath PUVA has also been effective in some cases. [12] For recurrent and recalcitrant lesions, low dose of oral retinoids such as isotretinoin, acitretin, etretinate have been found to very effective [13-15].

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