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 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 erythrokeratodermia (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.

Erythrokeratodermia 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 β3 and β4 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 welldemarcated, 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].
References

1. Mendes da Costa S (1925) Erythro-et keratodermia variabilis in a mother and a daughter. Acta Derm Venerol 6: 255-261.
2. Nazzaro V, Blanchet-Bardon C (1986) Progressive symmetric erythrokeratodermia. Histological and ultrastructural study of patient before and after treatment with etretinate. Arch Dermatol 122: 434-440.
3. Srinivas SM, Dhar S (2016) Erythrokeratodermia variabilis and erythrokeratoderma en cocardes: Case series with review of literature. Indian J Paediatr Dermatol 17: 202-205.
4. Van Steensel MAM, Oranje AP, van der Schroeff JG, Wagner A, van Geel M (2009) The missense mutation G12D in connexin30.3 can cause both erythrokeratodermia variabilis of Mendes da Costa and progressive symmetric erythrokeratodermia of Gottron. Am J Med Genet 149A: 657-661.
5. Richard G, Brown N, Rouan F (2003) Genetic heterogeneity in erythrokeratodermia variabilis: novel mutations in the connexin gene GJB4 (Cx30.3) and genotype-phenotype correlations. J Invest Derm 120: 601-609.
6. Common JE, O'Toole EA, Leigh IM, Thomas A, Griffiths WA, et al. (2005) Clinical and genetic heterogeneity of erythrokeratoderma variabilis. See comment in PubMed Commons below J Invest Dermatol 125: 920-927.
7. van der Schroeff JG, Nijenhuis LE, Meera Khan P, Bernini LF, Schreuder GM, et al. (1984) Genetic linkage between erythrokeratoderma variabilis and Rh locus. Hum Genet 68: 165-168.
8. Wesmann UN, DiDonato S, Herschkowitz NN (1975) Effect of chloroquine on cultured fibroblasts: release of lysosomal hydrolases and inhibition of their uptake. Biochem Biophys Res Commun 66: 1338-1343.
9. McFadden N, Oppedal BR, Ree K et al. Erythrokeratodermia variabilis: immunohistochemical and ultrastructural studies of the epidermis. Acta Derm Venereol (Stockh) 1987; 67: 284-288.
10. Papadavid E, Koumantaki E, Dawber RP (1998) Erythrokeratoderma variabilis: Case report and review of the literature. J Eur Acad Dermatol Venereol 11: 180-183.
11. Landau M, Cohen-Bar-Dayan M, Hohl D, Ophir J, Wolf CR, et al. (2002) Erythrokeratodermia variabilis with erythema gyratum repens-like lesions. Pediatr Dermatol 19: 285-292.
12. Heinisch S (1999) PUVA bath therapy in erythrokeratodermia figurata variabilis. Z Hautkrank 74: 445-446.
13. Singh N, Thappa DM (2010) Erythrokeratoderma variabilis responding to low-dose isotretinoin. Pediatr Dermatol 27: 111-113.
14. van de Kerkhof PC, Steijlen PM, van Dooren-Greebe RJ, Happle R (1990) Acitretin in the treatment of erythrokeratoderma variabilis. Dermatologica 181: 330-333.
15. Balci DD, Yaldiz M (2008) Erythrokeratodermia variabilis: Successful palliative treatment with acitretin. Indian J Dermatol Venereol Leprol 74: 649-650.