CASE REPORT

Adult-onset erythrokeratodermia variabilis (EKV) triggered by pregnancy and crash dieting: A rare case report

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Abstract

Erythrokeratodermia variabilis (EKV) is a rare inherited genodermatosis characterised by migratory and erythematous patches changing over the course of hours to days and fixed keratotic plaques. The disease begins mostly at birth or within the first year of life; it very rarely starts after childhood. We present here a sporadic case with adult onset EKV that was aggravated by pregnancy with spontaneous resolution, and later on, after crash diet more persistent patches and plaques appeared with no spontaneous resolution. The patient showed excellent response to systemic retinoids.

Keywords: Acitretin, Adult onset, Crash diet, Erythrokeratodermia variabilis, pregnancy, Retinoids, Sporadic.

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Introduction

Erythrokeratoderma variabilis is a rare inherited form of localised ichthyosis. It is an autosomal dominant inherited disease. Sporadic and autosomal recessive inheritance has also been reported. It was first described by Mendes da Costa in 1925. It occurs due to a mutation in GJB3, GJB4 gene located on chromosome 1p34-p35, encoding for connexin 31 and connexin 30.3 respectively.[1] Mutations in connexin genes alter the structure and function of gap junctions resulting in abnormal intercellular transport and cell-to-cell signalling. Connexin 31 and 30.3 are expressed in the stratum granulosum, and both play a role in late keratinocyte differentiation. EKV has two different types; one type is characterised by generalised, persistent hyperkeratosis, while in the other, the involvement is localised, symmetrically distributed, and sharply demarcated.[2] In more than 90% of the cases, it presents during the first year of life. Adult onset of erythrokeratoderma is rarely described with possible sporadic onset. We hereby report a case of EKV in a young lady who developed EKV at the age of 33 and responded well to systemic retinoids.

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Case Report

A 30-year-old married female, mother of two children presented to the OPD at PNS Shifa Hospital, Karachi, on April 2021 with the complaint of erythematous scaly hyperkeratotic patches and plaque on lower and upper limbs, associated with mild itching, for the last one year. The condition had developed first on the inner part of her thigh seven years ago during her first pregnancy. It resolved postpartum, responding well to oral anti allergic medication, after which she remained asymptomatic for three years. During her second pregnancy, she experienced a similar eruption that involved her inner thigh, legs, ankle, wrist, and upper arm, that resolved on its own during postpartum, and she remained asymptomatic for four years. Then she started crash dieting, restricting herself to nuts and protein for five months. She relates these new eruptions with her crash diet, and according to her these patches and plaques wax and wane and are associated with seasonal variation, exacerbating in summer and with emotional stress. On various occasions, she was managed with topical emollients, but nothing benefited her. Family history was non-significant for similar lesions.

Examination revealed bilateral, symmetric, sharply demarcated, and hyperpigmented to mildly erythematous plaques of variable sizes and shapes with geographical borders on the upper and lower extremities (Figure 1).

Palms, soles, mucous membranes, teeth, nails, and hair were normal. The remaining physical examination revealed no abnormality.

Results of a complete blood cell count, fasting blood glucose, liver function test, serum creatinine, serum urea, serum electrolytes, fasting lipid profile, serum calcium, serum phosphate concentrations, and urine detail report were within normal ranges. Scraping for fungal hyphae was done, which was non-significant.

A skin biopsy was done from a fixed lesion that showed epidermis hyperkeratosis, focal parakeratosis, irregular acanthosis, spongiosis, and exocytosis. Dermis showed oedema and mild perivascular infiltrate comprising

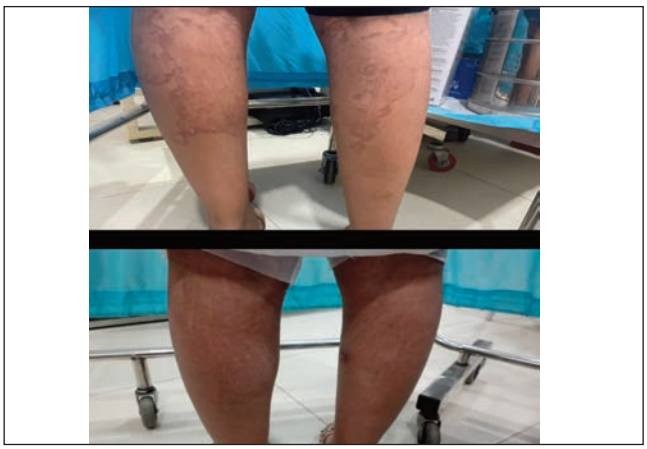

Figure-1: The picture shows bilateral, symmetric, sharply demarcated, and hyperpigmented erythematous plaques of variable sizes and shapes with geographical borders on the upper and lower extremities.

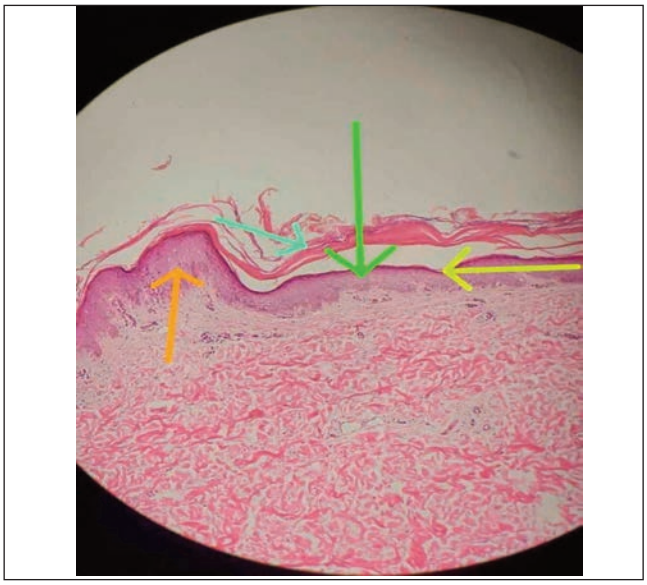

Figure-2: Light green arrow showsi irregular acanthosis, yellow arrow shows hypergranulosis, light blue arrow shows hyperkeratosis, orange arrow shows spongiosis.

lymphocytes, histiocytes, and few neutrophils. There was no evidence of granuloma or malignancy in the section. (Figure 2).

With a diagnosis of EKV, the patient was started on Isotretinoin in a dose of 60 mg/day (equivalent to 0.9 mg/kg) plus topical ointments containing 20% urea and 80% white soft paraffin for one month. At the one-month follow-up her lesions had improved, so she was continued on the same treatment for another month with the same dose; the total duration of her treatment was two months. On follow-up, after five months of stopping oral retinoids, no recurrence of similar lesions was reported. The patient was counselled about the side effects of retinoids, like skin dryness and itching. Pregnancy test was done before the start of the treatment, and strict contraception was advised to the patient during and after one month of cessation of Isotretinoin.

Discussion

EKV is an inherited disorder; adult onset of the disease is rarely described in the literature. The resolution of the symptoms is spontaneous, there can be some exacerbating factors such as temperature with seasonal variations, ultraviolet light, trauma, and emotional stress.[3] In the present case, the patches and plaques were aggravated by emotional stress and show seasonal variations, and waxed and waned spontaneously. According to the patient, the lesions persisted after a crash diet. Crash diet has many detrimental effects on different bodily functions including the skin, so this can be an identifiable provoking factor for these more persistent skin eruptions. About 50% of the affected individuals have associated patchy or diffuse glove-like palmoplantar keratoderma, with hair, nails, and mucous membranes remaining unaffected[4] but in this case, there was only cutaneous involvement of the limbs with no changes in the skin of the palms and soles. Histology of EKV is non-specific with hyperkeratosis, irregular acanthosis, papillomatosis, and mild perivascular inflammation.[5] This case has similar histopathological findings. Only a few case reports of EKV with adult-onset have been described in the literature with variable responses to systemic retinoids. Systemic retinoids are the treatment of choice for erythrokeratoderma variabilis, as they act by improving scaling. Abnormal epidermal differentiation and inflammation are the pathogenetic factors in EKV. Retinoids have been shown to interfere with the epidermal differentiation process and also with various aspects of cutaneous inflammation.[6] Hence, retinoids are considered the first line of treatment for EKV.[7] One case of adult-onset EKV has been described by Zulal et al. that was nonresponsive to systemic retinoids and there was associated severe palmoplanter discomfort.[8] But in the present case, the patient responded well to systemic retinoids (Isotretinoin), with significant improvement of scaling and erythema in just two months of treatment, and on five-month follow-up the patient was in remission, and there was no associated palmoplantar discomfort.

Limitation: Genetic testing was not done.

Conclusion

EKV is a genetically inherited condition that runs in families but a few case reports are being published on its sporadic occurrence with different triggering factors and variable response to treatment with early relapse on stopping treatment. In our case report we identify crash dieting as triggering factor, with an excellent response to systemic retinoids and no recurrence thereafter.

Consent for Publication: Written consent was obtained from the patient for publishing her case.

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Conflict of Interest: None .

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Author Contribution:

GA: Concept, drafting, final approval and accountable for all aspects of the work.
NA: Design, revision, final approval and accountable for all aspects of the work.
NJ, FZ: Analysing, drafting, final approval and accountable for all aspects of the work.