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Case Report

Beyond the usual: a case of acrodermatitis enteropathica clinically resembling erythrokeratoderma variabilis

Mohammed S. Hyder[1]*, Arisha Salam[2], Arun C. Inamadar[3]

[1]Department of Dermatology, Hairline International Hair and Skin Clinic, Bengaluru, Karnataka, India
[2]Department of Dermatology, V Care Skin and Hair Clinic, Bengaluru, Karnataka, India
[3]Department of Dermatology, Shri B. M. Patil Medical College Hospital and Research Centre, Karnataka, India

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***Correspondence:**
Dr. Mohammed S. Hyder,
E-mail: salmanhyder1996@gmail.com

ABSTRACT

Acrodermatitis enteropathica (AE) is an uncommon genetic condition marked by impaired zinc absorption, often presenting with skin and hair changes. An 18-year-old male came to our department with longstanding scaly skin lesions showing a migratory pattern, closely resembling erythrokeratoderma variabilis (EKV), along with universal hair loss. Symptoms had worsened after using traditional remedies. A family history of similar complaints in a sibling was noted. His serum zinc level measured 116 ng/ml. Treatment with oral zinc at 3 mg/kg showed limited improvement, which significantly increased after raising the dose to 5 mg/kg. Based on the periorificial involvement, alopecia, family history, and response to zinc, a diagnosis of AE was made. This case highlights an atypical presentation of AE mimicking EKV, emphasizing the need for high suspicion in unusual dermatoses and the importance of therapeutic response in guiding diagnosis.

Keywords: Acrodermatitis enteropathica, Zinc deficiency, ZIP4 transporter, Periorificial dermatitis, Alopecia, Erythrokeratoderma variabilis, Nutritional dermatosis, Zinc supplementation

INTRODUCTION

Acrodermatitis enteropathica (AE) is a rare inherited disorder caused by mutations in the SLC39A4 gene. This gene encodes ZIP4, a zinc transporter protein predominantly found in intestinal enterocytes, where it plays a crucial role in the uptake of dietary zinc.[1] Impairment of this transporter results in systemic zinc deficiency, which commonly presents with a clinical triad of periorificial and acral dermatitis, alopecia, and gastrointestinal symptoms such as diarrhea.[2] Although AE typically manifests in infancy, particularly after weaning, late-onset or atypical cases have been reported and may pose diagnostic challenges.[3] Zinc is essential for various biological functions, including skin barrier maintenance, immune regulation, and wound healing.[4] Deficiency may therefore lead to a range of cutaneous and systemic manifestations. In this report, we describe a unique case of adolescent-onset AE presenting with migratory scaly plaques resembling erythrokeratoderma variabilis, initially unresponsive to conventional therapies.

CASE REPORT

An 18-year-old male presented to our dermatology outpatient department with complaints of chronic skin lesions that had recently worsened. The patient reported a gradual onset of erythematous, scaly plaques over the past several months, with superimposed acute exacerbation in the form of increased erythema, oozing, and crusting. He also noted progressive hair loss involving the scalp, eyebrows, eyelashes, and body hair. In an attempt to manage his symptoms, he had taken native medications, following which his skin condition worsened. On further

inquiry, the patient revealed a positive family history, with a younger sibling experiencing similar cutaneous complaints during early childhood.

Cutaneous examination revealed sharply demarcated erythematous to brownish plaques with peripheral studding of crusted pustules and areas of oozing (Figure 1). The lesions were symmetrically distributed, predominantly involving the periorificial regions, neck, distal aspects of the hands and feet, groin, and perineal areas.

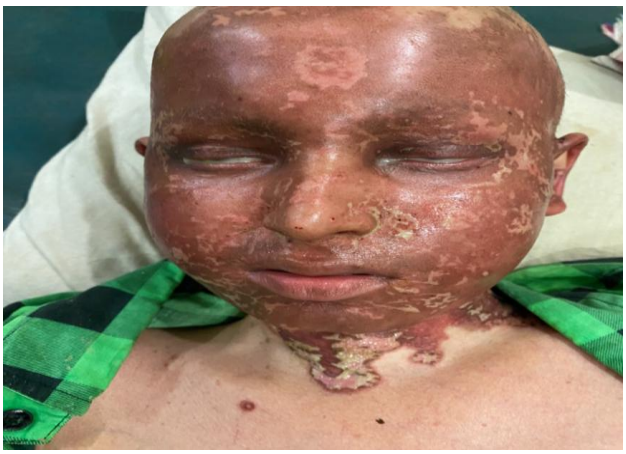

Figure 1: Sharply defined erythematous to brownish patches with peripheral studded pustules over the face.

In view of the clinical features suggestive of a nutritional dermatosis, serum zinc levels were evaluated and found to be 116 ng/ml (reference range: 70–120 ng/ml), which although within normal limits, was on the lower side. A therapeutic trial of oral elemental zinc was initiated at 3 mg/kg/day. However, clinical improvement was minimal over the subsequent two weeks. The dose was subsequently increased to 5 mg/kg/day, following which a marked reduction in inflammation, crusting, and erythema was noted. Hair regrowth was also observed over the scalp and body.

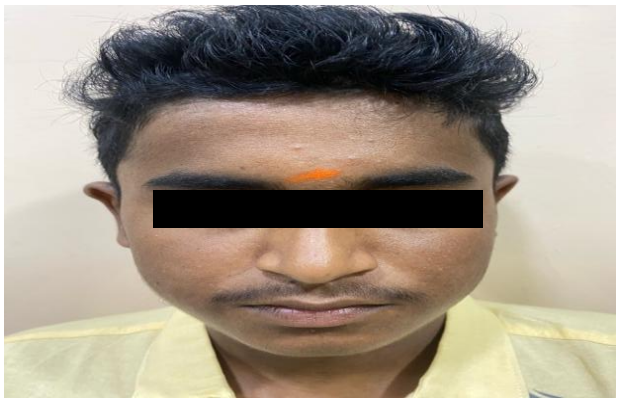

Figure 2: Significant improvement of the lesions over the face following treatment along with regrowth of hair over scalp and eyebrows.

Based on the periorificial distribution of lesions, alopecia, partial family history, and dramatic clinical response to zinc supplementation, a diagnosis of acrodermatitis enteropathica was established. At 4-month follow-up, the patient showed near-complete resolution of cutaneous lesions and significant hair regrowth (Figure 2-4). He continues to remain in clinical remission on maintenance zinc therapy.

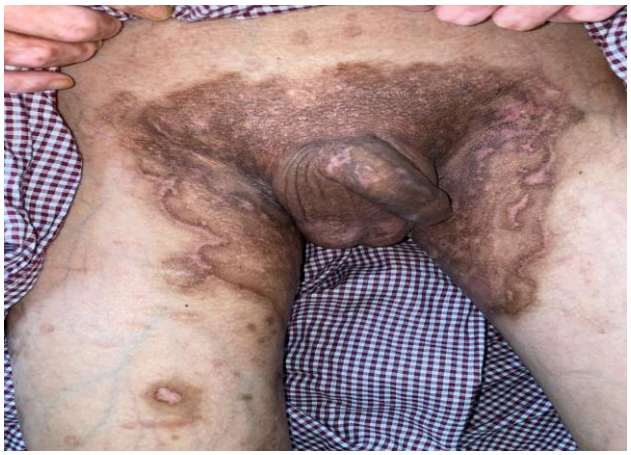

Figure 3: Significant improvement in lesions following treatment: resolution of pustules, reduction in erythema and scaling, with residual post-inflammatory hyperpigmentation over the groin.

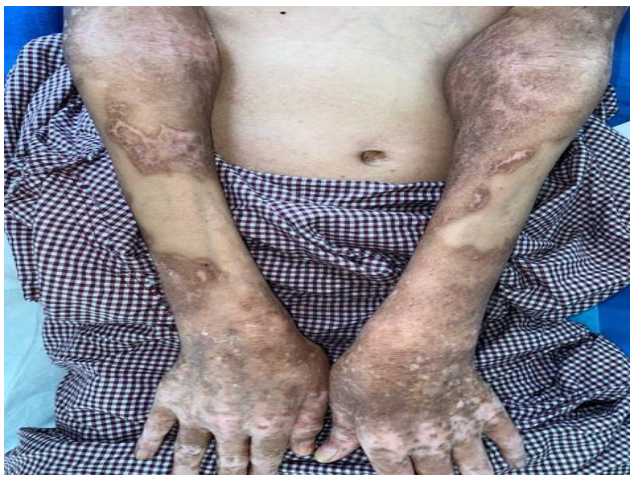

Figure 4: Significant improvement in lesions following treatment: resolution of pustules, reduction in erythema and scaling, with residual post-inflammatory hyperpigmentation over the extremities.

DISCUSSION

AE is characterized by a classic triad of periorificial and acral dermatitis, alopecia, and diarrhea. However, this complete triad is seen in only about 20% of patients.[1] In our case, although the patient exhibited extensive cutaneous involvement and significant alopecia, gastrointestinal symptoms were notably absent,

underscoring the diagnostic challenge posed by atypical presentations.

Cutaneous manifestations are often the earliest and most prominent features. Typically, they present as erythematous, scaly, or eczematous plaques, primarily affecting the periorificial and acral regions.[2] These may evolve into vesiculobullous, pustular, or psoriasiform lesions depending on the severity and chronicity of the disease. Our patient had sharply demarcated erythematous to brownish plaques with peripheral pustules and crusting involving classical sites, which closely resembled erythrokeratoderma variabilis, making the clinical differentiation more complex.

Diarrhea, although considered a hallmark extracutaneous symptom, is highly variable and may be intermittent or entirely absent, as observed in this case.[3] The absence of gastrointestinal symptoms can often delay diagnosis and lead to mismanagement.

As the disease progresses, lesions may become erosive and susceptible to secondary bacterial infections commonly by Gram-positive cocci or *Candida albicans*, further altering the clinical picture and potentially leading to systemic complications.[4] In this patient, worsening after native medication use raised suspicion of secondary infection or irritant reaction.

Diagnosis is primarily clinical, supported by serum zinc estimation and a robust therapeutic response to zinc supplementation.[5] Our patient demonstrated only marginal improvement with an initial zinc dose of 3 mg/kg/day; however, after increasing to 5 mg/kg/day, there was rapid and sustained resolution of lesions and hair regrowth, confirming the diagnosis.

Erythrokeratodermia variabilis (EKV), historically referred to as Mendes da Costa syndrome, was later found to occur in association with the features of progressive symmetric erythrokeratodermia (PSEK), a condition producing stable, symmetric, hyperkeratotic erythematous plaques.[6] Reports of families exhibiting features of both EKV and PSEK led to the suggestion that these disorders might represent different clinical expressions of the same inherited disease. This concept was reinforced by the discovery of identical gene mutations in patients with both conditions, prompting some researchers to use the unifying term erythrokeratodermia variabilis progressiva (EKVP) to describe the full spectrum of clinical presentations. In a study by Common and colleagues, genetic analysis of GJB3 and GJB4 was performed in several families and sporadic cases of EKV. Mutations in connexin 31 (Cx31) or connexin 30.3 (Cx30.3) were identified in only a subset of patients, with two being novel and one recurrent mutation.[7] No variants were detected in other connexin genes known to cause epidermal disorders, highlighting the genetic heterogeneity of EKV and confirming that individuals diagnosed clinically with this disease may harbor different connexin mutations.[8]

Lesions most often develop within the first year of life, sometimes being present at birth, though later onset in childhood or early adulthood is also reported. Two characteristic patterns are recognized. Transient erythematous patches appear as well-defined, map-like or annular areas of redness that can merge into large figurate patterns. They vary in size, shape, and distribution over hours to days, sometimes surrounded by a pale halo, and may become more prominent with temperature changes, friction, emotional stress, or sunlight. Stable hyperkeratotic plaques present as thick, scaly, yellow-brown areas that are clearly demarcated and often rest on an erythematous base, sometimes taking on a geographic configuration. In certain cases, the plaques are so thick and dark that they resemble a hystrix-like surface. Additional features such as hypertrichosis, collarette-like desquamation, or psoriasiform scaling may be observed, and while one of the two lesion types usually predominates, occasionally one may be absent altogether.[9-11]

Some patients present with atypical forms. Variants have included lesions resembling erythema gyratum repens in those with Cx30.3 mutations, circinate or gyrate erythematous patches known as erythrokeratodermia en cocarde in association with GJB4 mutations, and erythema annulare centrifugum-like patterns.[12] Lesions typically favor the extensor surfaces of the limbs, buttocks, and lateral trunk in a symmetrical distribution. In about half of patients, palmoplantar keratoderma is also present. The face, scalp, and flexural areas are usually spared, although any skin site may be involved. Hair, teeth, and nails remain unaffected, and their growth proceeds normally. A burning sensation can accompany the erythematous patches in some individuals. The disease tends to stabilize after puberty, and although lifelong, it may show gradual improvement or periods of partial remission.[9,11]

While EKV is usually confined to the skin, evaluation of systemic features is important to exclude other conditions with similar cutaneous changes. For example, keratitis-ichthyosis-deafness (KID) syndrome can mimic EKV but is also associated with keratitis, hearing impairment, alopecia, and increased susceptibility to infections.[13] Rare reports link EKV-like skin changes to neurological symptoms such as ataxia and peripheral neuropathy.[14] Treatment is generally symptomatic and guided by the extent of hyperkeratosis. Mild cases are managed with emollients, keratolytic agents, and topical retinoids, whereas extensive or severe forms may respond to systemic retinoids at doses lower than those required for other keratinization disorders, often resulting in marked improvement or even complete clearance of hyperkeratosis.[15] Erythematous lesions, however, tend to respond less favorably. Cosmetic camouflage may help patients with persistent redness, and preventive measures such as avoiding sudden temperature changes, mechanical friction, and skin irritation are advised to reduce exacerbations.[13,15]

CONCLUSION

We report a rare case of AE that remained undiagnosed until early adulthood, resulting in significant morbidity and compromised quality of life. The patient endured progressive skin lesions, alopecia, and social isolation, culminating in poor educational attainment and psychosocial distress. This case highlights the importance of early recognition of atypical presentations of AE, especially in patients with suggestive cutaneous findings and a positive family history. Prompt diagnosis and appropriate zinc therapy can prevent severe cutaneous manifestations, life-threatening infections, and long-term psychosocial sequelae.

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