Kindler syndrome with palmoplantar hyperhidrosis and blonde hair

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ABSTRACT

Kindler syndrome (KS) is a very rare genodermatosis characterized by acral blistering starting in infancy along with photosensitivity, progressive poikiloderma, cutaneous atrophy, and a variable degree of mucosal involvement. A large number of other cutaneous and extracutaneous features have been described, which aid in diagnosing it. Generally KS has been found to be associated with hypohidrosis/anhidrosis. We herein present a rare case of KS with unique features.

Key words: Hyperhidrosis, Kindler syndrome, poikiloderma

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INTRODUCTION

Kindler syndrome (KS) is a very rare disorder characterized by acral blistering in infancy followed by photosensitivity, progressive poikiloderma, cutaneous atrophy, and various forms of mucosal involvement. Theresa Kindler originally described the syndrome in 1954. Autosomal recessive mode of inheritance is most common in KS, but dominant transmission and sporadic cases have also been reported.[1] Associated findings include a variable degree of ophthalmological involvement, syndactyly, and hypohidrosis/anhidrosis[2]. Only a hundred and odd cases of KS have been reported in the literature.

CASE REPORT

A 12-year-old female, born of non-consanguineous marriage presented to us with a history of formation of multiple blisters, predominantly over the acral sites since birth. The patient also complained of photosensitivity.

Dermatological examination revealed a well-defined hemorrhagic flaccid bulla over dorsolateral aspect of the left foot of size 2 × 2 cm [Figure 1]. Multiple hypopigmented scars with cigarette paper wrinkling were present over the dorsa of feet, hands, and elbows [Figure 2]. She also had erythema, hypopigmented and hyperpigmented macules with telangiectasia, and atrophic scars over the face with angular cheilitis [Figure 3]. The patient also had blonde hair. Similar clinical features were present in her younger sister. No other siblings and close relatives had such complaints.

The patient was found to have hyperhidrosis of her palms and soles that was confirmed by starch iodine test. Examination revealed webbing of some interdigital web spaces [Figure 2]. There was no complaint of dysphagia or difficulty in urination or defecation. Eye examination was within normal limits. Punch biopsy of skin over hand showed focal hyperkeratosis and thinning of epidermis with an area of focal elongation of rete-ridges. Superficial dermis showed focal sparse chronic inflammatory infiltrate.

A clinical diagnosis of KS was made based on the criteria proposed by Angelo-Fischer *et al*.[2] Our patients fulfilled four major criteria [Table 1]. Genetic mapping could not be done in our patients due to financial constraints and local nonavailability.

Counseling was offered to the patient and her guardian about the various aspects and prognosis of disease. The patient was advised to use sun protective measures and was prescribed sunscreens. She was also advised to observe precautions against trauma in her daily activities.

DISCUSSION

KS results from pathogenic mutations in the FERMT1 (formerly KIND1 or C20orf42) gene that

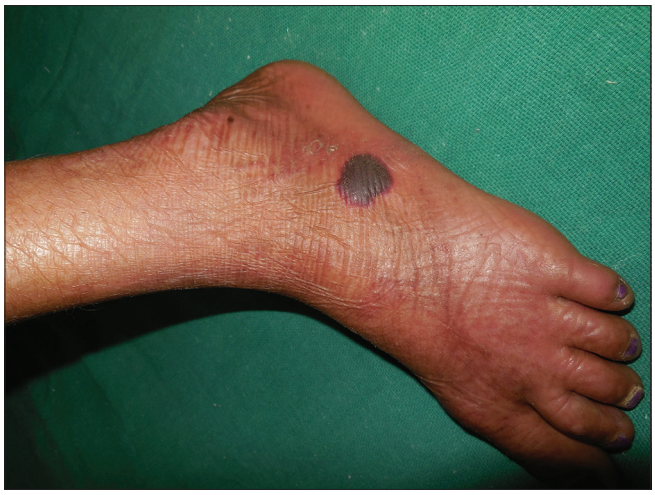

Figure 1: Hemorrhagic bullae over the leg

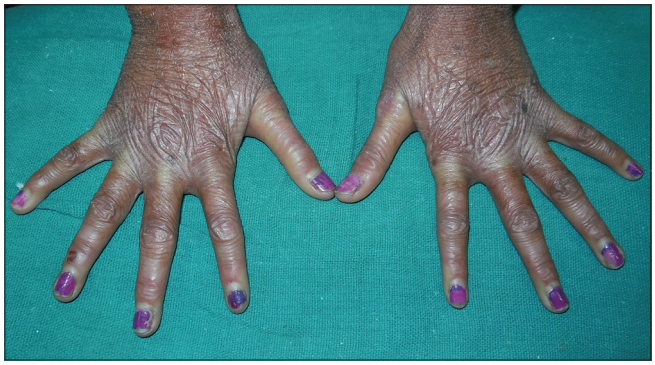

Figure 2: Cigarette paper atrophy of hands with webbing of interdigital spaces

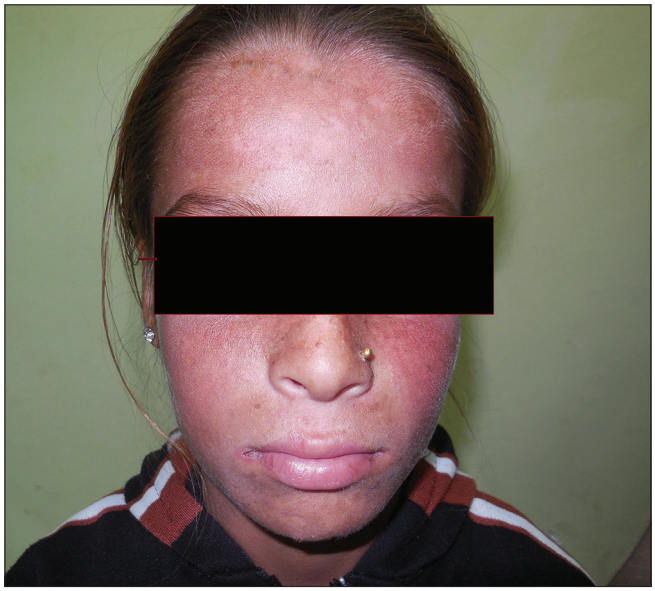

Figure 3: Hypopigmented and hyperpigmented macules with scarring and blonde hair

encodes fermitin family homolog-1 (FFH1) (formerly kindlin-1 or kindlerin), an actin cytoskeleton and focal adhesion-associated molecule mapped to chromosome 20p12.3. FERMT1 (formerly kindlin-1) is located in basal epidermal keratinocytes in a polar fashion, close to the cell surface facing the basement membrane, in the areas between the hemidesmosomes. There are two forms of kindlin-1 in the keratinocytes, with apparent molecular masses of 78 and 74 kDa, which correspond to phosphorylated and dephosphorylated forms of the protein. Kindlin-1 plays a role in keratinocyte adhesion, polarization, proliferation, and migration. It is involved in the organization and anchorage of the actin cytoskeleton to integrin-associated signaling platforms.[3] Atrophy of skin in patients of KS is due to reduced proliferation of interfollicular keratinocytes. In oral mucosa, kindlin-1 co-localizes with migfilin and paxillin in the basal epithelial cells and in cultured keratinocytes. The kindlin-1 deficient oral mucosal tissue from a patient with KS showed a complete lack of paxillin and reduced migfilin immunostaining in the basal keratinocytes leading to periodonitis.[4] Kindlerin may mediate TGF-β signaling in tumor progression via integrin-dependent cellular functioning.

Table 1: Criteria for Kindler syndrome

Major	Acral blistering in childhood
	Progressive poikiloderma
	Skin atrophy
	Abnormal photosensitivity
	Gingival hyperplasia and/or swelling
Minor	Syndactyly
	Mucosal involvement:
	Urethral, anal, laryngeal and esophageal stenosis
Associated findings	Nail dystrophy
	Palmoplantar keratoderma
	Pseudoainhum
	Ectoprion of lower lid
	Leukokeratosis of lip
	Anhidrosis/hypohidrosis
	Skeletal abnormalities
	Poor dentition/dental caries/periodonitis
	Squamous cell carcinoma

Criteria for diagnosing a case of Kindler's syndrome: 4 major - Certain, 3 major and 2 minor - Probable, 2 major and 2 minor or associated findings - Likely

Clinical findings in KS are increased skin fragility, acral blistering, photosensitivity, atrophy, and poikiloderma. The photosensitivity usually decreases over time, coinciding with decreased blister formation by 10-12 years of age, although some degree of photosensitivity usually persists even after that age. Poikiloderma and atrophy generally occur at sun-exposed sites, but it can also present at non-exposed sites.[5]

Less common findings in patients of KS include webbing of spaces, palmoplantar keratoderma, leukokeratosis of lips and oral mucosa, pseudoainhum, xerostomia, phimosis, dental caries, periodonitis, or actinic keratoses. Squamous cell carcinoma of the hard palate, lower lip, hand, bladder, larynx

can be associated with it.[6,7] Cutaneous malignant lesions usually develop after the fourth or fifth decade of life.

The patient may have eye involvement in the form of ectropion, keratoconjunctivitis or conjunctival scarring. There may be associated syndactyly, hypermobility of joint,[8] a dome-shaped skull, and bifid or missing ribs.[9] Mucosal involvement is quite common and can be in the form of esophageal, urethral, and anal stenosis.[10]

Hypohidrosis/ anhidrosis[2] is generally found to be associated with KS but our patient had hyperhidrosis. It may be a coincidental finding or an association of KS. As it was also present in her younger sister, this likely represents a new association of KS. Similarly, blonde hair was present in both sisters but was absent in both parents and close relatives. This may also be an associated finding or a coincidence; further case studies are required for confirmation.

Treatment encompasses protective measures that include sun protection and care of acral bullae/wounds by appropriate topical and systemic antibiotic treatment.

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