

Case Report

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Kindler syndrome: A rare case report

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Abstract

Kindler Syndrome (KS) is a rare hereditary disorder characterized by acral blistering of infancy and childhood, photosensitivity, progressive poikiloderma, and cutaneous atrophy. We report this case of KS in a 4 year old female child on account of its rarity.

Keywords: Kindler syndrome; acral blistering; pokiloderma; photosensitivity.

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Introduction

KS is an autosomal recessive genodermatosis, a subtype of Epidermolysisbullosa (EB). While the levels of cleft in simplex, junctional and dystrophic types of EB are established, KS may have multiple cleft levels. Clinically, the child presents with acral blistering of infancy and childhood, photosensitivity, progressive poikiloderma, and cutaneous atrophy. Less than 250 cases have been reported in literature since Theresa Kindler's original description 1954.

Case presentation

A 4 year old female child born out of a non-consanguineous marriage was brought by her parents with history of fluid filled lesions over hands and feet, followed by discoloration and thin skin over hands and feet since birth. On enquiry, she had history of multiple episodes of these fluid filled lesions without any antecedent trauma, and this tendency to form blistering had reduced with age. She also complained of redness and burning sensation over exposed areas on sun exposure. There

was no history of difficulty in deglutition, micturation, or vision. There was no history of similar complaints in family members. On cutaneous examination, there were few intact vesicles on the dorsum of hands and feet overlying severely atrophic cigarette paper like skin (Figures 1,2a,b,3a,b). Diffuse poikiloderma predominantly affecting face was noted (Figure 4a,b). Scalp hair were normal in colour, thickness and growth pattern. On oral examination, calculi and mild gingival inflammation on upper and lower anterior region were present. Nails were normal. Ocular and external genital examination and rest cutaneous examination were unremarkable.

On the basis of history and clinical examination, differential diagnoses of KS, EB with mottled pigmentation and porphyriacutaneatarda were considered.

Complete blood counts and urine analysis were normal. Radiological screening was unremarkable. Urine porphyrin levels were within normal limits. Parents of the child did not consent for skin biopsy, Transmission Electron Microscopy (TEM) and genetic analysis. Patient was treated symptomatically. She was

prescribed a broad spectrum sunscreen, topical antibiotics and emollients and was explained about trauma avoidance and blister care. Unfortunately, she was lost to follow up due to the ongoing COVID-19 pandemic.



Figure 1: Figure showing dorsa of bilateral hands and feet. Black circle shows cigarette paper atrophy, yellow circle shows vesicle



Figure 2a,b: Bilateral dorsum of feet showing vesicles and atrophy.



Figure 3a,b: Bilateral dorsum of hands showing vesicles and atrophy

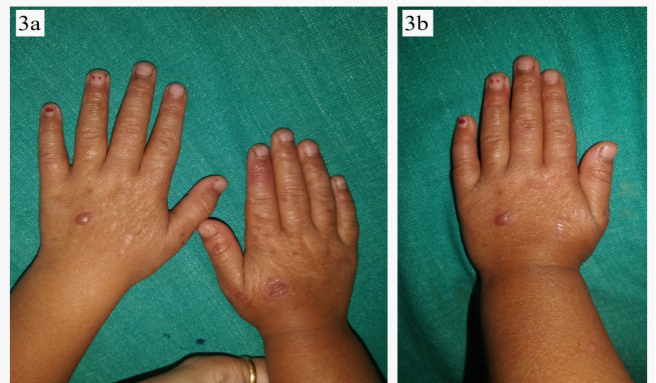


Figure 4: Poikilodermatous changes over face.

Table 1: Diagnostic criteria for Kindler syndrome as put forth by Angelova-Fischer, et al.

Major findings	Minor findings	Associated findings
Acral blistering in infancy and childhood	Syndactyly	Nail dystrophy
Progressive poikiloderma	Mucosal involvement	Ectropion of lower lid
Skin atrophy		Palmoplantarkeratoderma
Abnormal photosensitivity		Pseudoainhum
Gingival fragility and/or swelling		Leukokeratosis of lips
		Squamous cell carcinoma
		Anhidrosis/hypohidrosis
		Skeletal abnormalities
		Poor dentition/dental caries/periodontosis

CRITERIA: Certain= 4 major
 Probable= 3 major + 2 minor
 Likely= 2 major + 2 minor / associated findings

Table 2: Summarization of differential diagnoses of Kindler syndrome.

Disorder	Acral blistering	Photosensitivity	Poikiloderma	Skin atrophy	Comments
Other forms of Epidermolysisbullosa (EB)	Present	Absent	Present	Present	Blistering will be trauma induced and persistent. Findings will differ according to type of EB- simplex, dystrophic, junctional; localized/generalized involvement; systemic involvement
Porphyria cutanea tarda	Present	Present	Absent	Present	Pseudosclerodermatous scarring, polycythemic facial plethora, non virilising hypertrichosis
Weary Kindler syndrome	Absent	Absent	Present (flexural)	Present	Sclerotic bands, poor dentition, and, occasionally, calcinosis
Xeroderma pigmentosum	Absent	Present	Present	Present	early-onset skin cancers and multiple neurologic abnormalities
Bloom syndrome	Absent	Present	Absent	Absent	Telangiectasias, Short stature, recurrent infections, and increased frequency of hematological malignancies
Rothmund Thompson syndrome		Present	Present		Short stature, sparse scalp hair, sparse or reduced eyelashes and eyebrows, hypogonadism, premature aging, and juvenile cataracts
Dyskeratosis congenita	Absent	Absent	Absent	Absent	Reticulated hyperpigmentation (not true poikiloderma), nail dystrophy, and leukoplakia

Discussion

KS was first described by Theresa Kindler in 1954, presenting as simultaneous occurrence of poikiloderma congenitale and hereditary epidermolysis bullosa [1]. In 1971, Weary P, et al reported a widespread eczematous and acral blistering disorders of infancy and childhood with subsequent development of poikiloderma and various acral keratoses, which he called hereditary acrokeratotic poikiloderma [2]. It had been a matter of widespread debate whether these two entities were separate or belonged to the same spectrum, until recently, when the genetic basis and molecular mechanisms underlying KS were discovered. In 2003, the genetic defect of the syndrome was first localised to loss-of-function mutations in the gene KIND1 mapped to chromosome 20p12.3 [3]. It codes for kindlin-1 protein, expressed particularly in the basal keratinocytes, loss of which results in defects in actin-extracellular matrix linkages and abnormal skin fragility [4]. The largest cluster of KS has been reported from the Ngobe Bugle tribe in the Bocas Del Toro province of Panama, comprising of 26 cases [5].

The typical clinical findings of KS include:

- Acral blistering tendency is usually the earliest feature, manifesting at birth or early days of life, which subsides as child grows up. It occurs unprovoked or secondary to trivial trauma.
- Severe photosensitivity in response to minimal sun exposure.
- Diffuse skin atrophy with cigarette paper consistency, typically pronounced over the dorsum of hands, and feet and abdomen, mostly occurring during adolescence but have also been observed in infants as young as 3 months.
- Progressive poikiloderma, prominent over lateral side of face and neck.

All the 4 above mentioned findings were present in our case. Apart from these, KS may also present with variable mucosal involvement, ranging from xerostomia, angular cheilitis to laryngeal, esophageal, and anal swelling and stenosis [6]. Dental caries, periodontal disease, glandular cheilitis, and leukokeratosis of lips could be present upon oral examination [7]. Our case

had gingival inflammation and calculi. Syndactyly, sclerotic wrist bands, nail dystrophy, palmoplantar keratoderma, pseudoainhum may be present [8]. On ocular examination, corneal opacities, ectropion, thickened corneal nerves may be present [9]. Examination of external genitalia may show phimosis in males and labial agglutination in females [10]. Skeletal examination may reveal a dome shaped skull and bifid ribs [9].

Angelova-Fischer, et al devised a diagnostic criteria in 2005 which has been addressed in Table 1 [11]. As can be surmised from the table, our case fulfills all 5 major criteria, making the diagnosis of KS certain. Diagnosis is mainly clinical and differential diagnoses of KS have been summarized in Table 2. Light microscopic findings include epidermal atrophy, vacuolar alteration with cleft formation, and colloid bodies. TEM of vesicular specimen will show various planes of cleavage at the basement membrane zone with reduplication of lamina densa. Immunostaining with anti-kindlin-1 antibody shows decreased epidermal staining. Skin ultrastructure study shows cleavage planes in variable locations, mostly localized to the lowermost portion of the basal keratinocyte layer. This phenotype correlates with genotype as the mutation results in structural defects in anchoring of actin filaments in the lowermost portion of keratinocytes [12].

Treatment of KS is mainly symptomatic. Medical care includes prevention of skin trauma which will bring down new blister formation, proper wound care and dressings to hasten healing and prevent of infections, use of appropriate sunscreens, good nutrition, surveillance for extracutaneous complications, psychosocial support and genetic counselling. Antioxidants and flavinoid luteolin which reduce UV-B induced keratinocyte apoptosis may be upcoming therapies [13]. Telangiectasias can be treated with vascular lasers. Surgical correction of urethral, anal, or esophageal stenosis may be done as and when required.

The treatment is multidisciplinary and consultations with various departments, primarily paediatrics, dentistry, ophthalmology, gastroenterology, urology, gynecology, and psychiatry should be made when needed.

Conclusion

We report this case because it's rare and also needs to be differentiated from a plethora of similar disorders. Due to its wide

spectrum of features, KS is associated with significant morbidity and mortality. As there is no definitive treatment, management is mainly directed towards reducing morbidity and improving the quality of life.

References

1. Kindler T. Congenital poikiloderma with traumatic bulla formation and progressive cutaneous atrophy. *Br J Dermatol.* 1954; 66: 104–11.
2. Weary P, Manley WJr, Graham G. Hereditary acrokeratoticpoikiloderma. *Arch Dermatol.* 1971; 103: 409–22.
3. Siegel DH, Ashton GH, Penagos HG, Lee JV, Feiler HS, Wilhelmsen KC, et al. Loss of kindlin-1, a human homolog of the *Caenorhabditiselegans* actin-extracellularmatrix linker protein UNC-112, causes Kindler syndrome. *Am J Human Genet.* 2003; 73: 174-87.
4. Martignago BC, Lai-Cheong JE, Liu L, McGrath JA, Cestari TF. Recurrent KINDIN1 (C20orf42) gene mutation, c.676insC, in Brazilian pedigree with Kindler syndrome. *Br J Dermatol.* 2007; 157: 1281-4.
5. Penagos H, Jaen M, Sancho M et al. Kindler syndrome in native Americans from Panama. *Arch Dermatol* 2004; 140: 939–44.
6. Ohashi A, Kiniwa Y, Okuyama R, Kosho T, Suga T, Has C, et al. A case of Kindler syndrome with severe esophagealstenosis. *Int J Dermatol.* 2015; 54: e106-8.
7. Barbosa NM, Visioli F, Martins MD, Martins MA, Munerato MC. Oral manifestations in Kindler syndrome: case report and discussion of literature findings. *Spec Care Dentist.* 2016; 36: 223-30.
8. Al Aboud K, Al Hawsawi K, Al Aboud D, Al Githami A. Kindler syndrome in a Saudi kindred. *Clin Exp Dermatol.* 2002; 27: 673–6.
9. Sharma R, Mahajan V, Sharma N, Sharma A. Kindler syndrome. *Int J Dermatol.* 2003; 42: 727–32.
10. Krishna CV, Parmar NV, Has C. Kindler syndrome with severe mucosal involvement in childhood. *Clin Exp Dermatol.* 2014; 39: 340-3.
11. I. Angelova-Fischer, J. Kazandjieva, S. Vassileva, A. Dourmishev. Kindler syndrome: a case report and proposal for clinical diagnostic criteria. *ActaDermatoven APA.* 2005; 14: 2.
12. Burch JM, Fassihi H, Jones CA, Mengshol SC, Fitzpatrick JE, et al. Kindler syndrome: A new mutation and new diagnostic possibilities. *Arch Dermatol.* 2006; 142: 620-4.
13. Maier K, He Y, Wolfe U, Esser PR, Brummer T, Schempp C, et al. UVB induced cutaneous inflammation and prospects for antioxidant treatment in Kindler syndrome. *Hum Mol Genet.* 2016.