

Kindler's syndrome: A rare case report

NEELAM SUMAN, SIMRAT KAUR, SUPREET KAUR¹, VANDANA SARANGAL¹

Abstract

Kindler syndrome is a rare hereditary disorder, associated with skin fragility. The syndrome involves the skin and mucous membrane with radiological changes. The genetic defect has been identified on the short arm of chromosome 20. This report describes a 16-year-old patient with classical features like blistering and photosensitivity in childhood and the subsequent development of poikiloderma.

Keywords: Desquamative gingivitis, photosensitivity, poikiloderma, skin blisters

Introduction

Kindler syndrome (KS) is a rare autosomal recessive genodermatosis, which was first described in a 14-year-old girl in 1954 by Kindler and later by Forman *et al.* in 1989.^[1,2] More than 120 cases have been reported since the original report by Kindler; the largest series being a cluster of 26 patients identified within a tribe in the Bocas del Toro province on the Northwestern Caribbean coast of Panama.^[3] The syndrome is a combination of features of inherited blistering skin disorders (e.g., dystrophic epidermolysis bullosa) and congenital poikilodermas (e.g., Rothmund-Thompson syndrome) and should be differentiated due to clinical overlap with hereditary acrokeratotic poikiloderma (HAP) and dystrophic epidermolysis bullosa.^[4] Apart from the skin changes, changes in the oral and conjunctival mucosa, phimosis and radiological changes, namely a dome-shaped skull (turriccephaly), rib and mandibular abnormalities have been reported.^[5] Other features that vary between cases include acral hyperkeratosis, nail dystrophy, webbing and contractures of the fingers and toes, alopecia, actinic changes, pigmentation of lips and onchodystrophy.^[6-9] The association of aggressive periodontitis with KS was based on a single case in 1996 and later confirmed with a larger population of patients.^[10,11]

Departments of Prosthodontics, and ¹Periodontics, SGRD Institute of Dental Sciences and Research, Amritsar, Punjab, India

Correspondence: Dr. Neelam Suman, Department of Prosthodontics, SGRD Institute of Dental Sciences and Research, Amritsar, Punjab, India.
E-mail: docneelam5@yahoo.com

A number of oral features have been described, such as gingival swelling, advanced periodontal bone loss, mild-to-severe gingivitis, dental caries, and leukokeratosis of buccal mucosa.^[6] Dental findings had been briefly reported for Kindler patients in dermatologic and pediatric publications including oral lesions, atrophy of buccal mucosa, limited oral opening, malocclusion, dystrophic teeth, ankyloglossia, bleeding gums, lip erosions and geographic tongue, atrophy of gingiva, erosion of the hard palate, gingival swelling and desquamative gingivitis.^[9,12]

Case Report

Chief complaint and medical history

A 16-year-old female patient presented with the chief complaint of bleeding gums, ulcerations of buccal mucosa, missing teeth and difficulty in swallowing. Patient's mother reported that she had two children; one was healthy physically and mentally. Both of her pregnancies and deliveries were normal, but history of the affected child revealed skin blisters beginning at the age of 3 months. Some blisters were spontaneous, whereas others were due to friction or pressure. These blisters were filled with clear fluid and left scars after their rupture, and occurred until the age of 1 year.

Skin

Cutaneous examination revealed multiple hypopigmented and a few hyperpigmented macules of variable sizes, distributed over his face, neck, trunk, and limbs [Figure 1]. Poikilodermatous skin changes were present. The overall texture of the skin was xerotic with marked cutaneous atrophy. The palms showed hyperkeratosis with diminution of palmar creases [Figure 2]. Skin over the hands and neck was dry, atrophic and photosensitive to the sunlight. The patient was short stature. Hyperkeratotic plaques were seen on the flexures [Figure 3]. The scalp hair was normal in color and growth pattern. Keratoconjunctivitis and conjunctival scarring was also reported. The patient complained of frequent constipation and urinary output was low. Scarring of genitalia was also reported.

Access this article online	
Quick Response Code: 	Website: www.contempclindent.org
	DOI: 10.4103/0976-237X.132342

Oral manifestations

Scarring was evident on the soft tissues of the buccal mucosa and tongue. Tongue showed reduced mobility and was quite hard due to fibrosis [Figure 4]. Retained deciduous teeth exhibited marked mobility. Mamelons were still present in the permanent teeth at the age of 16. The gingival condition was of particular interest. Marginal gingivae were swollen, and erythematous. Deep pockets with marked bleeding on minimal probing were present around the teeth. In certain areas, erythema extended to mucogingival junction; resulting in appearance of desquamative gingivitis [Figure 5]. Xerostomia was quite evident. The oral opening was restricted due to fibrosis [Figure 6].

Radiographic examination

Orthopantomograph showed areas of moderate bone loss around all the teeth present. Multiple congenitally missing teeth, and retained deciduous teeth were reported [Figure 7].

Histopathology

Histopathologic examination of atrophic skin lesions in patients with KS reveals nonspecific features of poikiloderma. The epidermis is flattened and atrophic; edema is present at the dermoepidermal junction, and the basal layer shows focal vacuolization with basal cell degeneration. Other histologic features include a prominence of dermal capillaries, pigmentary incontinence, and possibly, perivascular lymphocytic infiltrate.

Discussion

In 2003, Siegel *et al.* mapped the disease locus to band 20p12.3 by using linkage and homozygosity analysis in an isolated cohort of patients with KS.^[13] Loss-of-function mutations were identified in the candidate gene *FLJ20116*, which was renamed kindlin-1 (*KIND1*). This gene encodes a 677-amino acid protein, *KIND1*, which is thought to play a regulatory role in inhibiting oversecretion of basement membrane components by basal keratinocytes at the dermoepidermal junction. An autosomal recessive pattern of transmission is usual, but sporadic cases are not uncommon. In KS, there is an unusual interruption and reduplication of the basement membrane and a broad reticular pattern of type VII collagen staining deep into the connective tissue beneath the basement membrane. It has also been suggested that KS and Weary's HAP are variants of the same disease. However, the mode of inheritance, onset of blistering, photosensitivity and presence of eczema is different in these two syndromes. The level of ultrastructural cleavage for blistering appears to be junctional in KS and intraepidermal in HAP.^[2] The dominant cutaneous findings in KS are increased skin fragility, acral blistering, photosensitivity, atrophy, and poikiloderma. Although increased skin fragility may be explained by the weakening of basal keratinocyte-extracellular matrix adhesion, the pathomechanisms of other features such as photosensitivity

and skin atrophy remain unclear. Mucosal involvement is very common and may lead to urethral, anal and esophageal stenosis. Our patient presented with acral blisters in the neonatal period and childhood, diffuse poikiloderma, skin fragility and atrophic changes, which were more prominent on skin exposed areas. The histopathology was consistent with poikilodermatous changes. Other clinical dental and oral findings have been found in KS. Shimamoto *et al.* suggested that Kindler patients have defective dentitions, and Ban *et al.* referred to fragile teeth susceptible to fractures. In the present case the major finding was that of aggressive periodontitis at an early age. A set of clinical diagnostic criteria has recently been proposed for this condition to facilitate clinical diagnosis. The major criteria are acral blistering in infancy and childhood, progressive poikiloderma, skin atrophy, photosensitivity, and gingival fragility, and/or swelling. The minor criteria proposed were syndactyly and involvement of other mucosal sites. The additional features of these criteria are nail dystrophy, ectropion, palmoplantar keratoderma, leukokeratosis of lips, squamous cell carcinoma, anhidrosis, skeletal abnormalities, and dental problems. According to the proposed criteria, the presence of four major criteria makes the diagnosis certain, the presence of three major and two minor criteria makes the diagnosis probable, and diagnosis is considered to be likely if two major and two minor/additional features are present. According to these criteria a definitive diagnosis of KS was made. Genetic mapping could not be done in our patient due to financial constraints. Several conditions that can cause blistering, cutaneous atrophy, and/or poikilodermatous skin changes must be differentiated from KS. KS might be difficult to differentiate from variants of epidermolysis bullosa in newborns. Progressive improvement of blistering, photosensitivity, poikilodermatous changes, and cutaneous atrophy with age help to differentiate KS from epidermolysis bullosa. In dystrophic epidermolysis bullosa, there is a mutation in the gene encoding type VII collagen (COL7A1) distinguishing it from KS. Rothmund-Thomson syndrome shows poikiloderma and photosensitivity like KS, but additional features like sparse hair, hypogonadism, and cataracts in the former condition distinguish it from KS. Bloom's syndrome is characterized by telangiectasia and photosensitivity with the presence of erythema on the face and other sun-exposed areas without showing true poikiloderma. Short stature, recurrent infections, and increased frequency of hematological malignancies are also features of this disease. Patients with Cockayne's syndrome develop erythema in photo-distributed areas, atrophy, and hyperpigmentation. The associated features of dwarfism, cachexia, progressive pigmentary retinopathy, deafness, and birdlike faces differentiate Cockayne's syndrome from KS. Reticulated hyperpigmentation, nail dystrophy, and leukoplakia are characteristic features of dyskeratosis congenita. Unlike KS, the pigmentary changes are not truly poikilodermatous and bullae are not an important feature of this rare genodermatosis. Management of KS is essentially



Figure 1: Areas of hyper- and hypo-pigmentation on face



Figure 2: Absence of palmar creases



Figure 3: Hyperkeratotic plaques on the flexures



Figure 4: Fibrosed tongue



Figure 5: Desquamative gingivitis



Figure 6: Restricted mouth opening due to fibrosed commissures

preventive and symptomatic. Good wound care including the use of topical and systemic antibiotics for infected bullous lesions and ulcerations might reduce the morbidity. Traditional nonsurgical treatment had been found beneficial in recent studies. Patient should be advised to avoid

trauma, which helps to prevent blister formation. Patients usually have a normal life span, but significant morbidity may be caused by secondary infections of congenital blisters; mucosal involvement leading to urethral, anal and



Figure 7: Orthopantomograph showing retained deciduous and congenitally missing permanent teeth

esophageal stenosis; aggressive periodontitis, and ocular complications.

References

1. Kindler T. Congenital poikiloderma with traumatic bulla formation and progressive cutaneous atrophy. *Br J Dermatol* 1954;66:104-11.
2. Forman AB, Prendiville JS, Esterly NB, Hebert AA, Duvic M, Horiguchi Y, *et al.* Kindler syndrome: Report of two cases and review of the literature. *Pediatr Dermatol* 1989;6:91-101.
3. Penagos H, Jaen M, Sancho MT, Saborio MR, Fallas VG, Siegel DH, *et al.* Kindler syndrome in native Americans from Panama: Report of 26 cases. *Arch Dermatol* 2004;140:939-44.
4. Ashton GH. Kindler syndrome. *Clin Exp Dermatol* 2004;29:116-21.
5. Sharma RC, Mahajan V, Sharma NL, Sharma AK. Kindler syndrome. *Int J Dermatol* 2003;42:727-32.
6. Hacham-Zadeh S, Garfunkel AA. Kindler syndrome in two related Kurdish families. *Am J Med Genet* 1985;20:43-8.
7. Bordas X, Palou J, Capdevila JM, Mascaro JM. Kindler's syndrome. Report of a case. *J Am Acad Dermatol* 1982;6:263-5.
8. Kapasi AY, Khopkar U, Raj S, Wadhwa SL. Weary-Kindler syndrome with multiple seborrheic keratoses. *Int J Dermatol* 1993;32:444-5.
9. Shimizu H, Sato M, Ban M, Kitajima Y, Ishizaki S, Harada T, *et al.* Immunohistochemical, ultrastructural, and molecular features of Kindler syndrome distinguish it from dystrophic epidermolysis bullosa. *Arch Dermatol* 1997;133:1111-7.
10. Wiebe CB, Silver JG, Larjava HS. Early-onset periodontitis associated with Weary-Kindler syndrome: A case report. *J Periodontol* 1996;67:1004-10.
11. Wiebe CB, Penagos H, Luong N, Slots J, Epstein E Jr, Siegel D, *et al.* Clinical and microbiologic study of periodontitis associated with Kindler syndrome. *J Periodontol* 2003;74:25-31.
12. Ricketts DN, Morgan CL, McGregor JM, Morgan PR. Kindler syndrome: A rare cause of desquamative lesions of the gingiva. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 1997;84:488-91.
13. Siegel DH, Ashton GH, Penagos HG, Lee JV, Feiler HS, Wilhelmsen KC, *et al.* Loss of kindlin-1, a human homolog of the *Caenorhabditis elegans* actin-extracellular-matrix linker protein UNC-112, causes Kindler syndrome. *Am J Hum Genet* 2003;73:174-87.

How to cite this article: Suman N, Kaur S, Kaur S, Sarangal V. Kindler's syndrome: A rare case report. *Contemp Clin Dent* 2014;5:217-20.

Source of Support: Nil. **Conflict of Interest:** None declared.