Kindler Syndrome: A case Report from Iran

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Abstract

Kindler syndrome (KS) is a rare, autosomal recessive genodermatosis characterized by skin blistering and photosensitivity in infancy, progressive poikiloderma, and diffuse cutaneous atrophy. It affects the skin, mucous membranes, and oral cavity and is caused by mutations in the KIND1 gene on 20p12.3. The first case of KS associated with periodontitis was reported in 1996, and have been infrequently reported since. Here we present a case of KS with classic clinical presentations involving skin, mucous membranes, and the periodontium in a patient from Iran.

Key words: Case report, genodermatosis, Kindler Syndrome.

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Introduction

Kindler syndrome (KS) is a rare, autosomal recessive disorder that was first described in 1954 and less than 150 cases have been reported worldwide till today (1). Symptoms of KS include congenital acralblisters and photosensitivity, which improve considerably with age, followed by progressive poikiloderma usually developing in childhood, and diffuse cutaneous atrophy (2,3). Acral blisters and bullae are more frequent in trauma-prone areas of the body. Cutaneous alterations including skin fragility and atrophic changes (cigarette paper-like wrinkled appearance of the skin) are more common in sun-exposed areas, especially on the dorsal surfaces of the hands and feet (4). Mucosal involvement may lead to stenosis of urethral, anal, esophageal, and oral commissures (5,6). Ophthalmic abnormalities such as ectropion, keratoconjunctivitis, and conjunctival scarring, have also been reported (7). Less common symptoms include pitted or punctuate palmoplantar hyperkeratosis, webbing and joint contractures of fingers and toes, nail dystrophy, alopecia, and actinic changes of the skin (2). Skeletal malformations including dome-shaped skull (turricephaly) and mandible and rib abnormalities have been described in one case and transitional cell carcinomas of the bladder have been reported (3).

The histological features of KS are a disorganization of basal layer cells and disruption and reduplication of the lamina densa. These observations differentiate KS from dystrophic epidermolysis bullosa and other genodermatoses (8). Histopathologic examination of skin lesions in patients with KS reveals non-specific

features of poikiloderma. The epidermis is flattened and atrophic. Edema is present at the dermoepidermal junction, and the basal layer has focal vacuolization with basal cell degeneration (8,9). Other histologic features can include a prominence of dermal capillaries, pigmentary incontinence, and prevascular lymphocytic infiltration (3).

There have been few reports of oral lesions in patients with KS since the original report in 1954. When oral lesions occur in KS, they are most often gingivitis, white patches on oral mucosa, atrophy and erosion of the mucosa, and lip pigmentation (8). In some cases, early development of actinic keratosis as well as squamous cell carcinoma of the lower lip and hard palate has been reported (3).

Since desquamative gingivitis is indicative of mucocutaneous disease, differential diagnosis includes pemphigus, pemphigoid, and lichen planus. In KS, the marginal gingival tissue appears reddened and inflamed as a result of its fragility and susceptibility to inflammation induced by bacterial plaque. Poor oral hygiene found in most patients with KS is explained by significant bleeding and pain in the hands and oral soft tissues during tooth brushing (10). Wiebe et al. (10) described a case of a female with Weary-Kindler syndrome who presented early exfoliation of the deciduous dentition and severe juvenile periodontitis around the permanent teeth, with fragile and bleeding gingiva. The periodontal disease in this weary-kindler case treated with conventional periodontal therapy, without any surgery or chemotherapeutic agents.

Because of the rarity of reports of KS with oral manifestations; here we present a case of sporadic KS with classical clinical presentations involving skin and mucous membranes and oral involvement.

Case Report

A 25-year-old female was referred to the Mashhad Faculty of Dentistry with complaints of dry mouth and gingival pain during brushing, which had occurred for 6 years. The patient history was consistent with KS, having generalized poikiloderma, (multiple hypo- and hyperpigmentation patches over the face, neck, and lips), acral blisters, progressive skin atrophy and photosensitivity (Fig. 1). The dorsal aspect of the hands and feet showed atrophic scarring with shiny cigarette paper-like wrinkling (Fig. 2). At presentation, the patient had one missing in mandibular teeth, some dental caries, and limited localized plaque and calculus but with significant spontaneous bleeding and bleeding on probing. The gingiva was thin and fragile and the epithelium was sloughed with minor trauma. The depth of pockets was less than 2 mm but localized areas of recession of 3 mm were observed (Fig. 3).

Scaling, root planning, and regular periodontal maintenance procedures were initiated, and resulted in significant improvement in the appearance of the gingiva and general oral comfort. After a four-month follow up, the number of sites with bleeding on probing was decreased and the gingiva appeared healthy.

Histopathological examination of a biopsy taken from a plaque on her skin revealed hyperkeratosis with flattened rete ridges, epidermal atrophy, fibrosis in papillary and reticular dermis, and capillary formation in the form of network (Fig. 4). The dermis showed a mild lymphohistiocytic infiltration and pigmentary incontinence and hydropic degeneration of basal layer. Diagnosis of KS was made on the basis of clinical and histopathological examination.

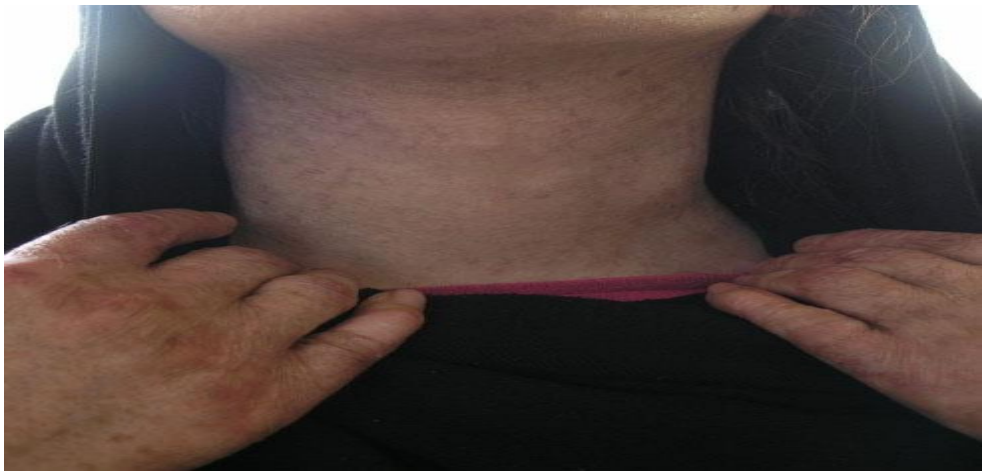

Figure 1. Multiple hypo- and hyperpigmentation patches over the neck

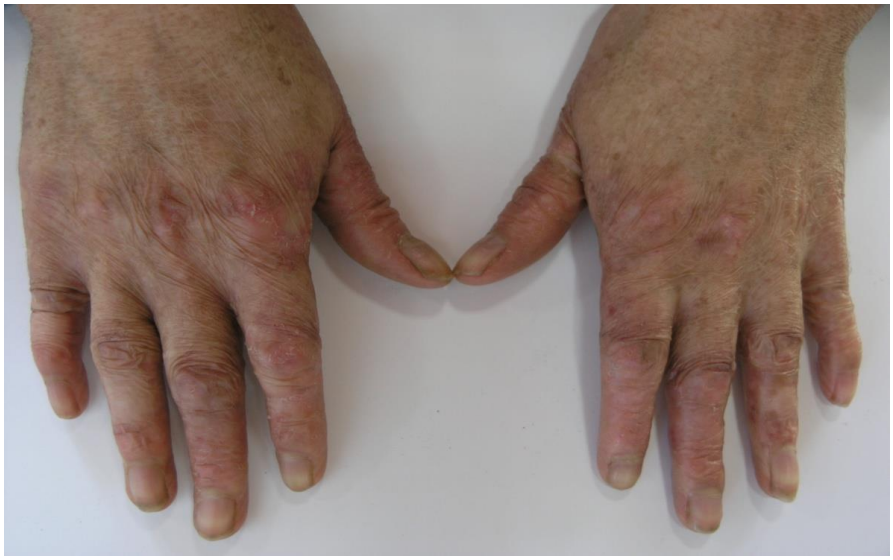

Figure 2. Dorsal side of hands showing atrophic scarring and cigarette paper-like wrinkling

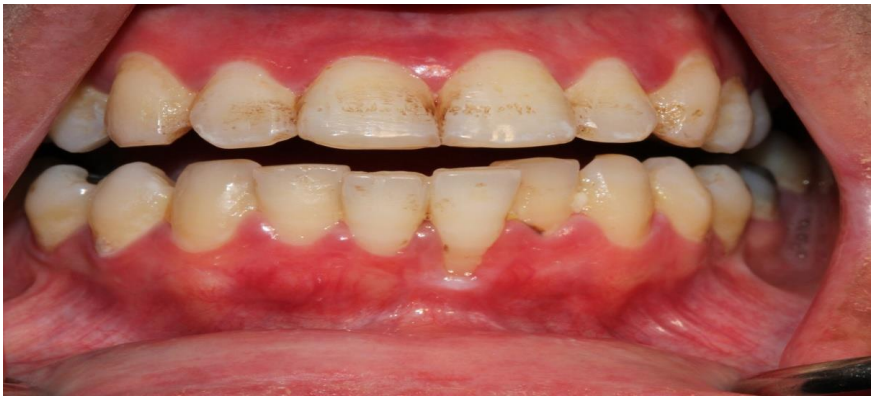

Figure 3. The gingiva was thin and fragile with limited localized plaque and calculus. Pocket depth was generally less than 2 mm

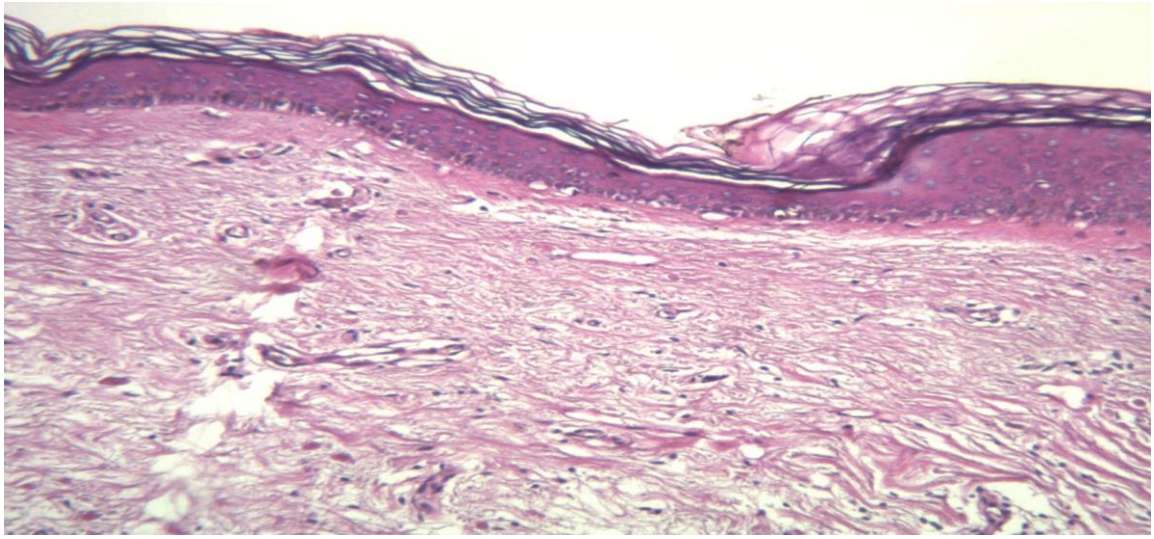

Figure 4. Histological examination of biopsy tissue taken from a plaque on the patient's skin showing hyperkeratosis with epidermal atrophy, papillary fibrosis, and reticular dermis (H & E staining). The dermis had mild lymphohistiocytic infiltration and hydropic degeneration of the basal layer

Discussion

Congenital poikiloderma is a rare finding and has been reported in association with several different syndromes (10,11). Although an autosomal recessive pattern of inheritance has been suggested, sporadic cases have been reported, with many originating in consanguineous families (8,12). The case presented here seems to be sporadic. Weary syndrome was thought to have features like KS (acral blisters and poikiloderma) but absence of photosensitivity and cutaneous atrophyand presence of acral keratotic papules are the main distinguishing features from KS. Wiebe et al. (10) described a case of a female with Weary-Kindler syndrome who presented early exfoliation of the deciduous dentition and severe juvenile periodontitis around the permanent teeth, with fragile and bleeding gingiva. The periodontal disease in this weary-kindler case treated with conventional periodontal therapy, without any surgery or chemotherapeutic agents.

The clinical manifestation of periodontal disease in patients with KS may show considerable variations, as is seen for other clinical symptoms, even with the same type of mutations (2).

Desquamative gingivitis is sometimes observed, that should be differentiated from pemphigus, pemphigoid and lichen planus in diagnosis. The marginal gingiva appears reddened and inflamed as a result of its fragility and susceptibility to inflammation induced by bacterial plaque (13). Because many patients with this syndrome also having periodontal problems may gounreported, clinician should pay more attention to this clinical manifestation of the illness. This case report provides some hope for these patients that their periodontal disease can be arrested, at least in part, with maintenance therapy.

Improving photosensitivity and blisters followed by the appearance of reticular pigmentation in KS are key signs used to differentiate KS from epidermolysis bullosa. Moreover mutations in the gene encoding type VII collagen (COLA7A1) are seen in dystrophic epidermolysis bullosa but not in KS (3).

Poikiloderma and photosensitivity are clinical presentations of Rothmund-Thompson syndrome which are similar to those observed in Kindler syndrome, but they are also accompanied by short stature, sparse hair, hypogonadism, and cataracts, which are not seen in Kindler syndrome (14).

The KIND1 gene, mapped to chromosome 20p12.3, is implicated in KS (2,3,15,16). It encodes the protein kindlin-I, which is a factor of focal contact in keratinocytes expressed in the epidermis and is involved in connecting the actin cytoskeleton to the extracellular matrix.

Histopathological examination using electron microscopy shows disruption of the lamina densa with attached anchoring fibrils along the dermoepidermal junction and cleft formation in the lamina lucida, suggesting continual remodeling of the basement membrane zone (3,10). Immunostaining with anti-kindlin-1 antibody is a new and valuable diagnostic test in the diagnosis of KS (12), but may be most helpful in young children with inadequate clinical features for definitive diagnosis.

The hallmark features of KS are acral blisters and photosensitivity that occur in infancy and childhood and improve with age, progressive poikiloderma that begins in childhood, and cutaneous atrophy (3,7). Recurrent trauma-induced blister formation occurs primarily on hands and feet, and often results in an incorrect diagnosis of epidermolysis bullosa. More variable features of KS include sclerodermatous changes in the fingers and nails, which did occur in this patient (12). Webbing of the fingers and joint contractures did not occur in our patient. Histologic findings suggest that because the junctional epithelium is abnormal, patients are susceptible to periodontal disease. The oral problems experienced by our patient were consistent with other (7,11). Typically, attachment loss progresses around the teeth and prognosis is poor. However, studies have reported that the periodontium can be maintained with proper treatment (2).

Diffuse poikiloderma, skin fragility, and atrophic changes such as cigarette paper-like wrinkled appearance of the skin are most prominent in sun-exposed areas, and are more common on the dorsal surfaces of the hands and feet (3,7).

Treatment of KS is symptomatic with emphasis on sun damage prevention. Sun protection may postpone the onset and progression of poikiloderma. Periodontal treatment includes scaling, root planning, and maintenance procedures (2,3). Our patient management included scaling and root planning for mild periodontitis and the dermatologist advised her for sun avoidance and photoprotection for skin lesions.

Conclusions

Diagnosis of KS is made based on clinical features but can be verified using immunostaining with kindlin-1 antibody (for sporadic cases) or by KIND1 mutation analysis (for familial cases). Periodontitis in KS responds to conservation therapy, but the gingiva and oral mucosa may still have an abnormal appearance with white patches. As individuals with Kindler syndrome grows, their problems related with blisters and photosensitivity diminish. However, pigment changes and thinning of the skin become more serious.

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