Section A -Research paper
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Kindler Syndrome with a severe form of periodontal manifestation: A Case Report

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Introduction
Kindler Syndrome (KS) is an extremely rare genodermatosis characterized by - acral blistering, photosensitivity, progressive poikiloderma, skin atrophy, and diverse forms of mucosal involvement since childhood. An array of dermal and extra dermal features has also been described. We present a 17-year-old patient whose main complaint was about swollen gums that existed for the past 1 year. Intraoral examination revealed pale oral mucosa and a depapillated tongue without significant ankyloglossia. A detailed periodontal charting was performed. The Gingival (GI) and Plaque Index (PI) scores were both 3 and the Oral Hygiene Index - Simplified score was poor. Gingival enlargement (grades 2 and 3) was documented for the upper and lower anterior teeth. The average Probing Pocket Depth (PPD) was approximately 10 mm (deep infra-bony and supra-bony pockets). Clinical Attachment Loss (CAL) was >4 mm. Full mouth extractions were performed as all the teeth were grade 3 mobile. Therefore, young patients with Kindler syndrome and severe periodontal disease must undergo a detailed intraoral examination and receive appropriate periodontal treatment at the earliest.

Keywords: Kindler syndrome, oral manifestation, chronic periodontitis, severe periodontitis, Epidermolysis Bullosa

Introduction

Theresa Kindler in the year 1954 first described Kindler syndrome (KS), it is a rare vesiculobullous dermatological disease characterized by acral blisters and generalized progressive poikiloderma. Oral mucosa and the gastrointestinal tract mucosa can also be

affected. KS is a rare subtype of Epidermolysis Bullosa (EB). To date, 100 cases of KS have been reported since 1954 and this association of aggressive periodontitis with KS was based on only one case published in 1996 and subsequent case series with 18 patients [1, 2]. In this report, we describe a case of KS with severe periodontitis.

Case Report

A 17-year-old patient presented to the Department of Dentistry, JSS Medical College & Hospital, JSSAHER, with a major complaint of swollen gums that had been evident for about 1 year. The patients' parents reported that they had a consanguineous marriage and that this was their first visit to the dentist. A depapillated tongue was observed on intraoral examination. A detailed periodontal charting was performed (Fig. 1). Inflamed and enlarged gingiva intraorally was observed (Fig. 2). Extraoral features are poikiloderma and blistering of the neck and hands skin (Fig. 3 a & b).

Figure1: Clinical Parameters Recorded

Clinical Charting					
Gingival Index (Loe & Silness, 1963)	Plaque Index (Silness & Loe, 1964)	OHI-S (Greene & Vermillion, 1964)	Gingival enlargement 2-3 grading (Bokenkamp 1994)	PPD >10mm Infrabony pockets	CAL >4mm

Figure 2: Red and enlarged gingiva, representing a combination of true and pseudo pockets.

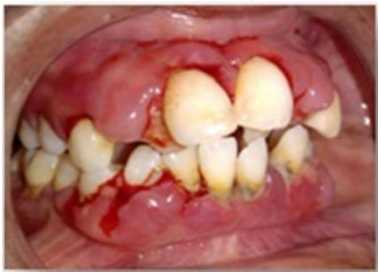
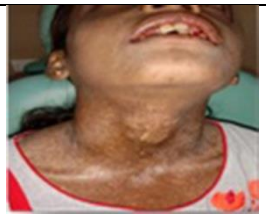
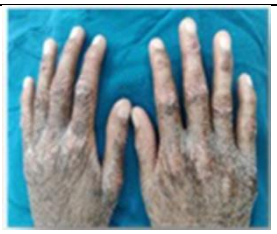


Figure 3 a & b: Poikiloderma of neck and hands



(a)



(b)

Histopathology:

At the time of extraction, a biopsy was taken from the left upper first molar region and sent for histopathological examination. The hematoxylin and eosin staining showed epithelial atrophy with orthokeratosis. Vascular degeneration was observed on the basement membrane and the upper dermis exhibited melanin incontinence with sparse lymphocytic infiltrates (Figures 4 & 5). Genetic analysis and electron microscopy could not be performed due to a lack of adequate facilities and financial constraints.

Clinical management included full mouth extraction as all the teeth were grade 3 mobile.

Figure 4: Hematoxylin and eosin staining of a tissue section, showing atrophic epithelium with flattened rete ridges and lymphocytic infiltration around the blood vessels (100X)

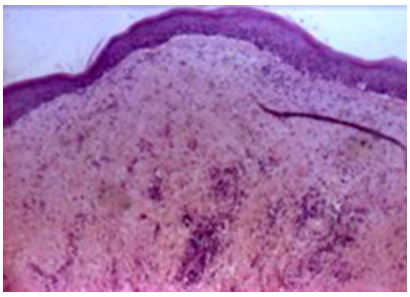
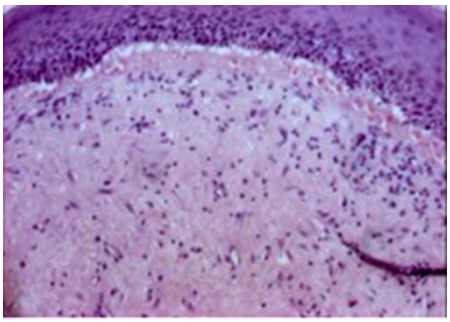


Figure 5: Hematoxylin and eosin staining of a tissue section, showing vascular degeneration at the basal cell layer and pigmentary incontinence (400X)



Discussion:

KS is a rare autosomal recessive disorder characterized by trauma-induced blistering of the skin leading to fragility, progressive poikiloderma (dorsal aspects of the hands and feet are most susceptible), skin atrophy, mucosal inflammation, and varying degrees of photosensitivity [3, 4]. In this report, we presented a case of KS with a very rare and severe form of periodontitis.

Recently, it was shown that the underlying molecular basis of KS contains mutations with loss of function in the KIND1 gene, which is mapped on chromosome 20p12.3. KIND1 was originally called FLJ20116Gen. The encoded protein, kindlin-1, is an actin extracellular matrix (ECM) linked protein and a human homolog of the Caenorhabditis elegans UNC-112 protein. UNC-112 is a membrane-associated structural / signaling protein that is responsible for connecting the actin cytoskeleton to the ECM. KS is the first known skin fragility disorder caused by a deficiency in the actin-ECM linkage rather than the keratin-ECM linkage[5].

While an autosomal recessive pattern of transmission is often observed in the majority of KS cases, sporadic cases are not uncommon. Indeed, environmental factors, such as trauma to the oral cavity and sun exposure, have been linked to the etiology of KS. Age, which is an important factor with different clinical characteristics, is associated with the phenotypic diversity of KS. Ethnic and geographical factors can also influence the clinical heterogeneity of KS [3].

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The predominant dermal or cutaneous findings in KS are increased skin fragility (delicate skin membrane), acral blistering (peripheral body parts, such as fingers, toes, and ears), photosensitivity (ocular response to light), atrophy (degeneration of cells), and poikiloderma (netlike appearance and/or reddish-brown pigmentation of the skin). Although increased skin fragility or delicateness may be explained by the weakening of the basal keratinocyte ECM adhesion, the pathological mechanisms of other characteristics (e.g., photosensitivity, and skin atrophy) remain unclear[5]. Poikiloderma and atrophy are often progressive, and the development in those areas not exposed to light may suggest that it is not caused exclusively by photodamage only. Nail plate thinning (angel-wing deformity) and nail plate separation from supporting tissues (onycholysis) have also been documented in patients diagnosed with KS. Palmar hyperkeratosis, i.e., thickening of the stratum corneum often has a glassy appearance and obscures the dermatoglyphic patterns on the palm [4, 6].

Mucosal involvement is quite common, especially in the oral cavity. Gingival fragility and rapidly progressing early periodontitis (aggressive periodontitis) were observed in this present case, as well as in other previously published cases of KS [2, 3, 7]. Wiebe et al reported the lack of an epithelial seal (i.e., junctional epithelium) between the gingival tissues and the tooth surface, as well as of pocket epithelium in extracted teeth [1]. This can be attributed to the loss-of-function mutations in Kindlin-1, which normally mediates the adhesion of epithelial cells to the tooth surface [3, 7]. Thus, the evidence suggests that periodontal disease in patients with KS is caused by bacterial access and infection of the connective tissues, similar to open chronic wounds[7, 8].

No histopathological features are specifically diagnostic of KS. The oral epithelium is often atrophic with flattened rete ridges and the basal layer is usually edematous. Vascular degeneration can also be observed. Other histological descriptions include observable prominent capillaries, pigment incontinence, and a scarce perivascular lymphocytic infiltrate[9]. Although these histological features are not specific to KS, they can facilitate the differentiation of KS from dystrophic EB. Before the identification of the KIND1 mutation as the main cause of KS, ultrastructural duplication of the lamina densa was one of the key features in the diagnosis of KS. Desmosomes, hemidesmosomes, tonofilaments, anchoring filaments, and fibrils appear normal[9]. A previous immunofluorescence study showed a normal appearance (except for fractures) concerning the distribution of the basement membrane zone components. In addition, type VII collagen is often established in abnormal locations deep in the connective tissue stroma. However, the molecular mechanisms by which defective kindlin-1 causes replication of the basement membrane and the irregular distribution of type VII collagen are not yet known [5].

The major clinical diagnostic criteria for the diagnosis of KS are acral blistering in infancy and childhood, progressive poikiloderma, skin atrophy, photosensitivity, and gingival fragility (and/or swelling)[5]. The minor criteria include syndactyly intrusion into other mucosal sites. Other features include nail dystrophy, ectropion, palmoplantar keratoderma, pseudoainhum, leukokeratosis of the lips, squamous cell carcinoma, anhidrosis, skeletal abnormalities, and dental problems[9]. A KS diagnosis is confirmed if four of the five main criteria are met; a probable diagnosis is indicated when three main and two minor criteria are

met, while a diagnosis of KS is considered probable when 2 major and 2 minor/ additional criteria are met[3, 11].

Conclusion:

Patients with KS usually have a normal life expectancy but have significant morbidity. Secondary infections of congenital blisters and mucosal involvement are common, leading to urethral, anal, and esophageal stenosis, as well as accelerated periodontitis and ocular complications. Correct diagnosis of KS requires an in-depth extraoral examination by a dermatologist. Dental treatment for KS patients should include screening and diagnosis of aggressive periodontitis, as well as adequate periodontal treatment that must be carried out in a timely and long-term manner.

Conflicts of Interest: The authors do not believe that there is a conflict of interest that could potentially be construed to affect the material contained in the manuscript that is being submitted to the Journal.

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