

Kindler's Syndrome – A Rare Case Report.

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Abstract: Kindler syndrome, a rare autosomal recessive disorder which is associated with skin fragility. It was characterized by blistering in infancy, photosensitivity and progressive poikiloderma. The syndrome is characterized by involvement of the skin and mucous membrane with radiological changes. The genetic defect have been identified on the short arm of chromosome 20. This report describes a 20-year-old patient with classical features of poikiloderma who presented with as oral mucosal pigmentation.

Keywords: poikiloderma, photosensitivity, blister.

I. Introduction

Kindler syndrome (KS), a rare hereditary disorder, which was described first by Kindler in 1954.¹ The cutaneous manifestations in KS are increased skin fragility, acral blistering, photosensitivity, atrophy, and poikiloderma.² Apart from the skin changes, changes also occur in oral and conjunctival mucosa, phimosis and radiological changes, namely a dome-shaped skull (turricephaly), rib and mandibular abnormalities have been reported³.

Recently it has been reported that the loss of kindlin-1, a human homolog of the Caenorhabditiselegansactin-extracellular matrix linker protein UNC-112, causes Kindler syndrome and the gene was localized to chromosome 20p12.3⁴. This syndrome was a combination of features of both hereditary blistering skin disorders (e.g. epidermolysis bullosa dystrophica) and congenital poikiloderma (e.g. Rothmund-Thompson syndrome)⁵. We report a case of 14 year old patient with kindler syndrome with familial history of parental consanguinity.

II. Case Report

A 20 year old male reported to the Department of Oral Medicine and Radiology with the chief complaints of decayed upper front tooth region and also complaints of pigmentation in his mouth. His past medical and surgical history were non-contributory. No similar familial history. Family history revealed parental consanguinity. Patient revealed history of bulla formation 5 years back. No history of itching and photosensitivity was elicited.

On extra-oral examination, patient was moderately nourished with sparse and blond hair, skull was dome shaped, generalised brown and black pigmentation seen all over the body with dystrophic nails and atrophy of skin over lower lip. (fig 1,2,3,4,5)



Fig 1. Frontal view



fig 2. Dorsum surface of hand



fig 3. Low extremities



Fig 4. Upper half of Body



fig 5. Blond and sparse hair



fig 6. Hard palate

Intra – oral examination revealed diffuse area of black pigmentations seen on right and left buccal mucosa and dorsum of tongue, palate with multiple root stump and decayed tooth.(fig 6,7,8,9)



Fig 7. Left buccal mucosa



fig 8. Right buccal mucosa



fig 9. Dorsum of tongue

OPG revealed evidence of dental caries in 11,12,14,21,22,17,27,43,44,45,46,32,33,35 and root stump in 47 and 36,37. Disto-angularly placed 18, 28. Periapical radiolucency present in 31,36. Evidence of crown of 38 within the tooth follicle with incomplete root formation. (fig 10)



Fig 10. OPG shows multiple dental caries

With the above findings, case was provisionally diagnosed as Xerodermapigmentosum with differential diagnosis kindler syndrome and then the patient was referred to the Department of Dermatology, RGGH, Chennai for further opinion and management.

In Dermatology department, case was diagnosed as Kindler Syndrome and biopsy was taken from his leg to confirm. His histopathology report revealed flaky hyperkeratosis, acanthosis, spongiosis in some area. Sub epidermal separation seen. Pigment incontinence seen in some areas in upper dermis. Inflammatory infiltrate in dermis seen mainly around blood vessels. Lab investigation of urine porphyrin was found to be negative. And ENT examination, wood's lamp test was normal. And they also advised oral biopsy. Case was referred back to Tamil Nadu Government dental college for the favour of lip biopsy. Here we took biopsy on right buccal mucosa and histopathology report was with clinical correlation. (fig 11)

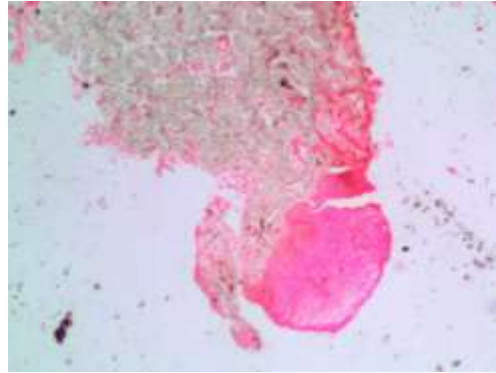


Fig 11 shows melanin incontinence in superficial connective tissue

III. Discussion

Kindler's syndrome is an autosomal recessive genodermatosis, but sporadic cases are also common, with many originating in consanguineous families⁶. More than 120 cases have been reported since the original report by Kindler⁷. Any race can be affected and no sex predilection has been reported⁸. In the present case, patient was born to the parents of consanguineous marriage. The disorder results in loss of function mutations of the KIND-1 gene which encodes the protein kindlin-1. Its results in abnormal fragility due to loss of basal keratinocytes with defects in actin-extracellular matrix linkage⁹

The clinical characteristics of KS include congenital skin blistering, photosensitivity, improves with age, and progressive poikiloderma with extensive atrophy. Other features include webbing of the fingers, palmoplantar keratoderma, nail abnormalities, involvement of the oral cavity with periodontitis, loss of teeth, gum hypertrophy, esophageal and urethral

strictures. Involvement of esophageal and genitourinary mucosa is common, and clearly increases with age. Early development of actinic keratoses, squamous cell carcinoma of the lips and transitional cell carcinoma of the bladder have also been reported. In addition, recurrent colitis is also described¹⁰. In this paper, patient present with poikiloderma, nail abnormalities and multiple dental caries.

Clinical diagnostic criteria were proposed by Angelova-Fischer. He divided clinical manifestations of the disease into three groups which includes major, minor and associated findings. The diagnosis was made by the presence of 4 major criteria. The presence of three major and two minor criteria makes the probable diagnosis. Major criteria comprised of acral blistering, progressive poikiloderma, skin atrophy, increased photosensitivity and gingival involvement. The minor criteria included syndactyly and urethral, anal, esophageal or laryngeal mucosal involvement. Associated finding includes nail dystrophy, ectropion of the lower lid, keratoderma, pseudoainhum, leucokeratosis of the lips, squamous cell carcinoma, anhidrosis, skeletal abnormalities, dental caries and periodontitis¹¹. In the present case, patient had poikiloderma, nail dystrophy, and dental caries. Histopathological examination shows features of poikiloderma like epidermal atrophy, hyper- and hypopigmentation and telangiectasia with hyperkeratosis, areas of cleavage at or near the dermoepidermal junction may be present¹².

Treatment is mainly symptomatic which emphasis on prevention of the sun damage. Sun avoidance and photo-protection may cause delay in the onset of poikiloderma. In this report, our patient is asymptomatic, but patient was under treatment for prevention of sun damage with sun protection lotion.

Differential diagnosis includes idiopathic melanin pigmentation, Peutz-Jegher's syndrome, Laugier-Hunziker syndrome, complex of myxomas, Spotty pigmentation, endocrine overactivity, Carney syndrome, Leopard syndrome, Lentiginosis profusa, drug-induced pigmentation, Addison's disease, Albright's syndrome, Acanthosis nigricans, Pregnancy, Hyperthyroidism, Generalised Neurofibromatosis, Incontinentia pigmenti, Hemochromatosis, Whipple's disease, Wilson's disease, Gaucher's disease¹³. Drug-induced pigmentation may be diffuse or localized, and it can be multifocal. The pigmentation is macular and may or may not be uniformly colored. Addison's disease manifests as diffuse mucocutaneous pigmentation. In the oral cavity, it usually presents as diffuse but patchy melanosis of multiple mucosal surfaces. Peutz-Jegher Syndrome highly distinctive pattern of oral, perioral, and acral macular pigmentation represents one of the earliest clinical manifestations of this disease. The macular pigmentation usually mimics dark freckling but without the reliance of sun exposure to increase or diminish color intensity. Laugier-Hunziker pigmentation is typically characterized by multifocal pigmentation of mouth, perioral skin, and other anatomic areas, including the esophagus, genitalia, and conjunctiva, may also be seen. LEOPARD syndrome may exhibit numerous black or dark brown "freckle-like" spots on the skin (multiple lentiginos) and may appear anywhere on the skin of the

body. Carney syndrome is rare genetic disorder characterised by abnormalities in skin coloring with spotty appearance to affected area.

Kindler syndrome is a chronic, severe syndrome for which treatment is mainly symptomatic. It is a relatively rare syndrome associated with oral mucosal and cutaneous pigmentation along with other manifestations. Only above 120 cases reported in literature so far. this syndrome has to be included in differential diagnosis of patient with diffuse oral mucosal and cutaneous pigmentation.

References

- [1]. Kindler T. Congenital poikiloderma with traumatic bulla formation and progressive cutaneous atrophy. *Br J Dermatol* 1954;66:104-11.
- [2]. Freiman A. Kindler syndrome. *E-medicine*. [accessed on 2.05.08]
- [3]. Sharma RC, Mahajan V, Sharma NL, Sharma AK. Kindler syndrome. *Int J Dermatol* 2003;42:727-32.
- [4]. Jobard F, Bouadjar B, Caux F et al. Identification of mutations in a new gene encoding a FERM family protein with a pleckstrin homology domain in Kindler syndrome. *Hum Mol Genet* 2003; 12: 925–35.
- [5]. Case Report Kindler's syndrome: a case report :IkramUllah Khan, ShafiaFazal : *Journal of Pakistan Association of Dermatologists* 2008; 18: 49-52.
- [6]. Case Report Kindler's syndrome: a case report :IkramUllah Khan, ShafiaFazal : *Journal of Pakistan Association of Dermatologists* 2008; 18: 49-52) . Any race can be affected and no sex predilection.(Ashton GH. Kindler syndrome. *ClinExpDermatol*2004; 29: 116-21
- [7]. Penagos HG, Jaen M, Sancho MT et al. Kindler syndrome in native Americans from Panama. A report of 26 cases. *Arch Dermatol*2004; 140: 939-44.
- [8]. Thappa DM, Jeevan Kumar B et al. Kindler syndrome: A case report. *Indian J PediatrDermatol*2000; 3: 19-23.
- [9]. Has C, Bruckner-Tuderman L. A novel nonsense mutation in Kindler syndrome. *J InvestigatDermatol*2004; 122:84-6.
- [10]. Yasukawa K, Sato-Matsumura KC, McMillan J, Tsuchiya K, Shimizu H. Exclusion of COL7A1 mutation in Kindler syndrome. *J Am AcadDermatol*2002; 46:447-50
- [11]. Fischer A, Kazandjieva J, Vassileva S, Dourmishev A. Kindler syndrome: a case report and proposal for clinical diagnostic criteria. *ActaDermatovenerolAlp PanonicaAdriat*2005;14:61-7.
- [12]. Hovnanian A, Blanchet-Bardon C, deProst Y. Poikiloderma of Theresa Kindler: report of a case with ultra structural study and review of literature. *PediatrDermatol* 1989;6:82-90.
- [13]. Cicek Y, Ertas U: the normal and pathologic pigmentation of oral mucous membrane: a review: *Journal of contemporary dental practice*, 2003: 4(3)