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Case Report

Kindler's syndrome: a case report

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Abstract Kindler syndrome is one of the rare autosomal recessive disorders associated with skin fragility and is characterized by blistering in infancy, photosensitivity and progressive poikiloderma. It involves the skin and mucous membranes with radiological changes. The genetic defect has been identified on the short arm of chromosome 20. This report describes a 48-year-old patient with classical features like blistering and photosensitivity since childhood and the subsequent development of poikiloderma. The differential diagnosis of Kindler's syndrome includes diseases like Bloom syndrome, Cockayne syndrome, dyskeratosis congenita, epidermolysis bullosa, Rothmund-Thomson syndrome and xeroderma pigmentosum. Our patient had classical cutaneous features of Kindler syndrome with dysphagia as a complication. Her two children, two brothers, one sister and two daughters of another sister are also suffering from the same problem.

Key words
Kindler's syndrome

Introduction

Kindler syndrome is a rare autosomal recessive disorder, and was first described in a 14-year-old girl by Kindler in 1954.[1,.2] She had unusual blistering on the hands, arms, feet and legs and later on she developed photosensitivity and pigmentary changes.[2] More than 120 cases have been reported since the original report by Kindler.[3] Clinical overlap occurs with hereditary acrokeratotic poikiloderma and dystrophic epidermolysis bullosa which causes confusion in its diagnosis.[4] Apart from the skin changes, there are changes in the oral and conjunctival mucosa, phimosis and radiological changes like a dome-shaped skull (turricephaly), mandibular and rib abnormalities also occur.[5]

This syndrome is a combination of features of hereditary blistering skin disorders (e.g. epidermolysis bullosa dystrophica) and congenital poikiloderma (e.g. Rothmund-Thompson syndrome).[6]

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Case report

A 48-year-old female presented with a history of hypopigmented patches and photosensitivity since childhood. There was a history of acral blisters, which started on the 3rd day of the neonatal period and persisted till 20 years of age. The patient had a history of oral ulcers with halitosis. She had also history of dysphagia. She also noticed generalized loss of sweating. She was born to consanguineous parents. Her two children and two brothers and one sister are also suffering from the same problem and also two daughters of another sister.

On clinical examination, the patient weighed 50 kg and was short-statured. Her IQ was normal. Cutaneous examination revealed multiple hypopigmented and hyperpigmented patches over the face (**Figure 1**), neck, trunk and limbs. The

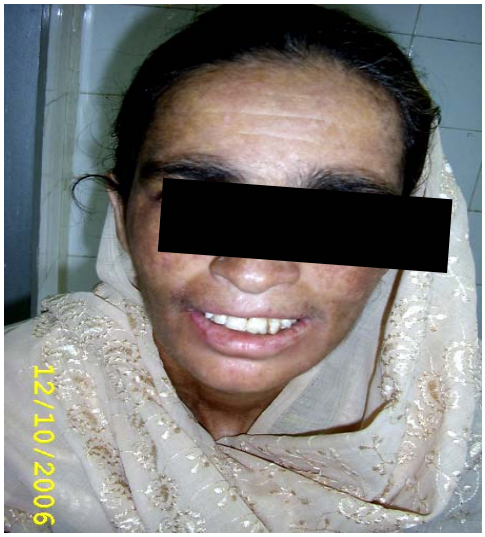

Figure 1 Hypo- and hyperpigmented patches over the face

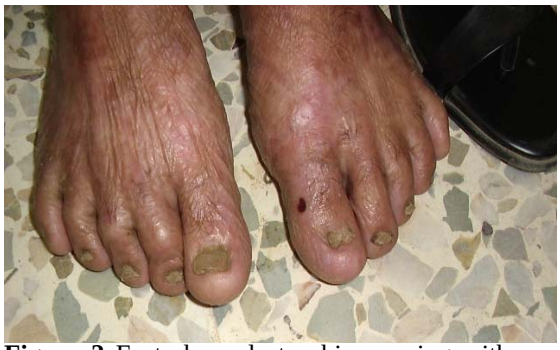

Figure 2 Feet showed atrophic scarring with shiny cigarette paper-like wrinkling.

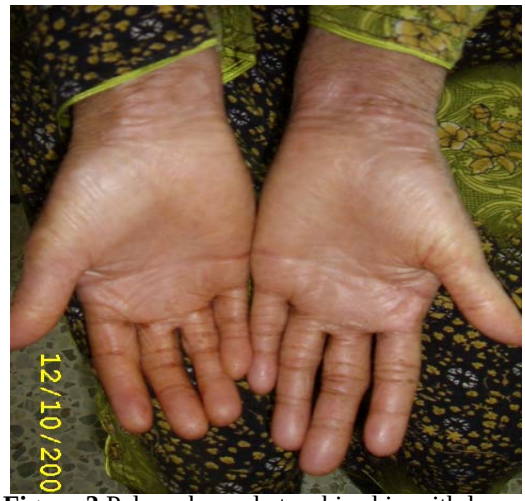

Figure 3 Palms showed atrophic skin with loss of palmar creases

trunk showed telangiectasia. The dorsal aspect of the hands and feet showed atrophic scarring with shiny cigarette paper-like wrinkling (**Figure 2**). The palms showed atrophic skin with loss of

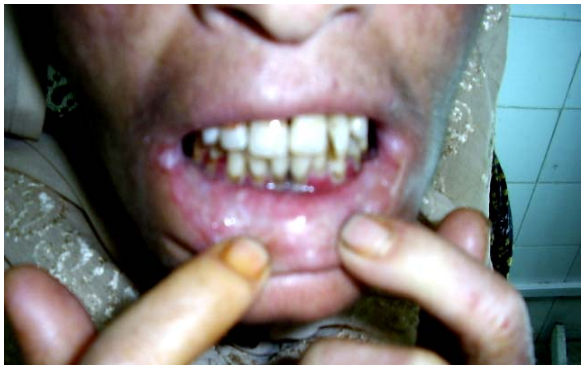

Figure 4 Oral mucosa showing oral ulcers.

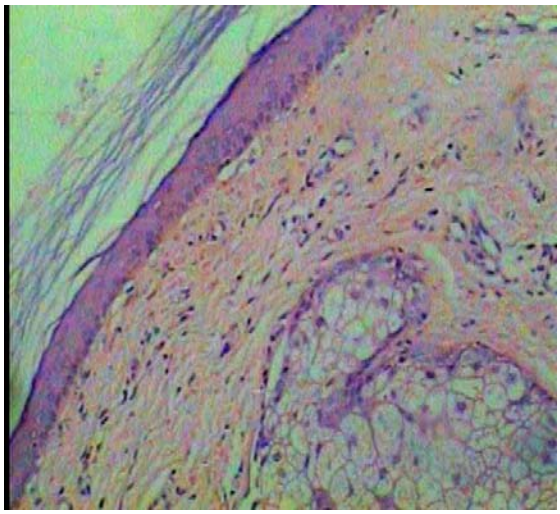

Figure 5 Hyperkeratosis with flattened rate ridges.

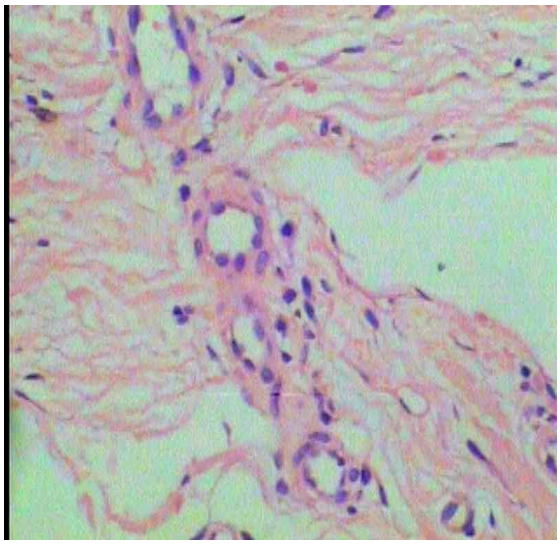

Figure 6 Network of dilated dermal capillaries.

palmar creases **(Figure 3).** Hyperkeratotic plaques were seen on the flexures. The scalp hairs were normal in color and growth pattern. Oral mucosa revealed leukoplakia with few oral ulcers **(Figure**

4). Radiological screening revealed delayed epiphyseal fusion.

Histopathological examination from a plaque revealed hyperkeratosis with flattened rete ridges **(Figure 5)** and keratotic plugging and capillaries formation in the form of network i.e. telangiectasia (**Figure 6**). The dermis showed a lymphohistiocytic infiltrate in addition to macrophages and pigmentary incontinence.

Diagnosis was made on the basis of clinical as well as histological examination as Kindler's syndrome.

Discussion

Congenital poikiloderma is an uncommon hereditary disorder and has been reported in association with various syndromes.[9] An autosomal recessive pattern of inheritance has been suggested, but sporadic cases are also common, with many originating in consanguineous families.[6]

The gene *KIND I* is involved in the pathogenesis of Kindler's syndrome. It encodes a specific protein kindlin-I. This protein is involved in connecting the actin-cytoskeleton to the extracellular matrix.[6] To differentiate Kindler's syndrome from dystrophic epidermolysis bullosa mutations in the gene encoding type VII collagen (*COLA7A1*) have been excluded.[6]

Clinically, blistering and photosensitivity begin in infancy or early childhood and improve markedly with age and poikiloderma appears gradually and becoming more prominent in later years of life. Some patients also develop sclerodermatous changes in the fingers and nails,[6] like our patient. Primarily recurrent trauma-induced blister formation occurs on hands and feet, which may impact an incorrect diagnosis of epidermolysis bullosa.[6.] There is variable presence of palmoplantar keratoderma and nail abnormalities; as well as webbing of the fingers and contractures may occur.[11] Common oral problems are gingival fragility, poor dentition and rapidly progressive periodontitis.[11,12] advanced periodontal bone loss, mild-to-severe gingivitis, dental caries, and leukokeratosis of buccal mucosa.[6] Other mucous membranes e.g. urethral, anal, oesophageal, and genital mucosa, may be involved and result in stenosis of the respective organs.[11.12.]Ophthalmic abnormalities including ectropion, keratoconjunctivitis and conjunctival scarring have also been diagnosed in some patients.[6] Diffuse poikiloderma (reticular telangiectasia, patchy hypopigmentation and hyperpigmentation, epidermal atrophy), skin fragility, and atrophic changes i.e. is cigarette paper-like wrinkled appearance of the skin are most prominent in sun-exposed areas, and are mostly present on the dorsal surfaces of the hands and feet.[6] Early development of actinic keratoses as well as squamous cell carcinoma of the lower lip and hard palate and transitional cell carcinoma of the bladder have also been reported. [6,11,12]

Histology of the atrophic skin lesions in patients with Kindler's syndrome shows nonspecific features of poikiloderma-like epidermal atrophy, hyper- and hypopigmentation and telangiectasia with hyperkeratosis and the epidermis is flattened and atrophic, edema is present at the dermoepidermal junction, and the basal layer shows focal vacuolization with basal cell degeneration.[6,12] Other findings include prominence of dermal capillaries, pigmentary incontinence, and mild perivascular lymphocytic infiltrate.[6,12]

Areas of cleavage at or near the dermoepidermal junction may be present.[7,8]

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.[6] An ultrastructural study of bullae of affected persons demonstrated a coexistence of 3 levels of abnormal cleavage: (1) within or just above the basal layer of epidermis (intraepidermal), (2) within the lamina lucida (junctional), and (3) below the lamina densa.[6]

Immunostaining with anti-kindlin-1 antibody is a new and useful diagnostic test in the diagnosis of Kindler's syndrome and shows decreased staining of the epidermis of patients with Kindler's syndrome as compared with controls.[6]

Treatment is mainly symptomatic with an emphasis on prevention of the sun damage. Sun avoidance and photo-protection may cause delay in the onset of poikiloderma.[1]

References

1. http://www.ijdvl.com/article.asp?issn=0378-6323;year=2005;volume=71;issue=5;spage=348;epage=350;aulast=Kaviarasan
2. Kindler T. Congenital poikiloderma with traumatic bulla formation and progressive cutaneous atrophy. *Br J Dermatol* 1954; **66**:104-11.
3. 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.
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. http://www.emedicine.com/derm/topic943.htm
7. Hovnanian A, Blanchet-Bardon C, de Prost Y. Poikiloderma of Theresa Kindler: report of a case with ultra structural study and review of literature. *Pediatr Dermatol* 1989; **6**: 82-90.
8. Lanschuetzer CM, Muss WH, Emberger M *et al*. Gene symbol: Kind 1 disease: Kindler syndrome. *Hum Genet* 2004; **115**: 175.
9. Chishti AH, Kim AC, Marfatia SM *et al* The FERM domain: a unique module involved in the linkage of cytoplasmic proteins to the membrane. *Trends Biochem Sci* 1998 **23**: 281-2.
10. http://digilander.libero.it/camdic/KINDLER.html
11. http://www.nature.com/jid/journal/v122/n1/full/5602126a.html
12. http://www.netzwerk-eb.de/e14/e310/e205/index_eng.html