CASE REPORT

Kindler syndrome - report of two cases *

Síndrome de Kindler - relato de dois casos

Luciana Mendes[1]
Virginia Vilasboas[1]
Sinésio Talhari[4]
Lisiane Nogueira[2]
Carolina Talhari[3]
Mônica Santos[5]

Abstract: Kindler syndrome is a rare autosomal recessive genodermatosis characterized by trauma-induced blisters, progressive poikiloderma and varying degrees of photosensitivity. In 2003, loss-of-function mutations were identified in the gene KIND1 mapped to chromosome 20p12.3. In this paper, we report Kindler syndrome in two children born to consanguineous parents presenting acral blistering, photosensitivity, poikiloderma, cutaneous atrophy and periodontitis.
Keywords: Clinical diagnosis; Epidermolysis bullosa; Photosensitivity disorders; Signs and symptoms

Resumo: A síndrome de Kindler é uma genodermatose rara, autossômica recessiva, caracterizada pela presença de bolhas induzidas por traumas, fotossensibilidade, atrofia cutânea e poiquilodermia progressiva. A alteração genética da síndrome foi descrita em 2003, com a identificação de mutação no gene KINDIN1, localizado no cromossomo 20p12.3. Nesse trabalho relata-se a presença da síndrome de Kindler em irmãos, filhos de pais consangüíneos, que apresentavam, desde a infância, fotossensibilidade, bolhas após pequenos traumas, poiquilodermia, atrofia cutânea e periodontite.
Palavras-chave: Diagnóstico clínico; Epidermólise bolhosa; Sinais e sintomas; Transtornos de fotossensibilidade

INTRODUCTION

Kindler syndrome (KS) is a rare autosomal recessive genodermatosis, characterized by the presence of trauma-induced blisters, progressive poikiloderma, varying degrees of photosensitivity, diffuse cutaneous atrophy, abnormal pigmentation, and skin fragility. The disease was first described in 1954 by Theresa Kindler in a 14-year-old girl with acral blistering since childhood who subsequently developed poikiloderma and photosensitivity. [1]

The genetic basis of the syndrome was first described in 2003, with the identification of loss-of-function mutations in the gene KIND1 mapped to chromosome 20p12.3. [2] Currently, there have been more than 25 mutations described in this gene which encodes kindlin-1 protein, a component of focal contacts in keratinocytes expressed in the epidermis, particularly in the basal keratinocytes. Loss of this protein results in abnormal skin fragility with defects in actin-extracellular matrix linkage. [3,4] In 2007, during the Third International Consensus Meeting on Diagnosis and Classification of Epidermolysis Bullosa (EB), KS was included within the EB spectrum based on the presence of epidermal separation and mechanical fragility at sites of trauma. According to this new classification, the group of EB includes four subtypes: EB simplex, junctional EB, dystrophic EB and KS.[5]

Received on 19.06.2011.
Approved by the Advisory Board and accepted for publication on 20.09.2011.
* Study carried out at theTropical Medicine Foundation of the Amazonas (Fundação de Medicina Tropical do Amazonas - FMTAM) – Manaus (AM), Brazil.
Conflict of interest: None
Financial funding: None

[1] M. D. Dermatologist of the Tropical Medicine Foundation of the Amazonas (Fundação de Medicina Tropical do Amazonas - FMTAM) – Manaus (AM), Brazil.
[2] Substitute Professor of Dermatology of the Federal University of the Amazonas (Universidade Federal do Amazonas - UFAM) – Manaus (AM), Brazil.
[3] PhD in Tropical Medicine – Professor of dermatology at the State University of the Amazonas (Universidade do Estado do Amazonas - UEA) – Manaus (AM), Brazil.
[4] PhD in dermatology - Professor of dermatology at Nilton Lins University – Manaus (AM), Brazil.
[5] PhD in Tropical Medicine - Dermatologist of the Tropical Medicine Foundation of the Amazonas (Fundação de Medicina Tropical do Amazonas - FMTAM) – Manaus (AM), Brazil. Professor of dermatology at the State University of the Amazonas (Universidade do Estado do Amazonas - UEA) – Manaus (AM), Brazil.

CASE REPORT

Two siblings, a 4-year-old male and a 2-year-old female, born to consanguineous parents, presented with recurrent blistering over the hands and feet, with spontaneous healing without scarring since early neonatal period. Subsequently, progressive photosensitivity with burns at the slightest exposure to sunlight, abnormal pigmentation of skin and skin fragility, with ulcerations to minor trauma developed. On physical examination, both patients presented with poikiloderma mainly on the face, neck and upper chest; erythematous scaly lesions on sun-exposed areas; hyperpigmentation; xeroderma and diffuse cutaneous atrophy mainly on the back of the hands and feet. Examination of the oral cavity showed poor preservation of teeth and severe periodontitis, with easy bleeding, more severe in the male patient who also had phimosis (Figures 1 and 2). Routine blood examinations were within normal range. Histopathological examination of a cutaneous biopsy showed epidermal atrophy, dilatation of blood vessels in the upper dermis, focal vacuolar degeneration of basal layer with subepidermal cleft, and presence of pigmentary incontinence (Figure 3). Symptomatic treatment was given to the patient with an advice to avoid trauma and direct exposure to sunlight.

DISCUSSION

KS is clinically characterized by the presence of minor trauma-induced blisters usually arising within the first days of life. Photosensitivity, poikiloderma and diffuse cutaneous atrophy with the characteristic cigarette paper-like wrinkled skin tend to appear subsequently. Mucous membranes involvement such as hemorrhagic gingivitis, cheilitis, leukoplakia and periodontitis are also common. Due to the periodontitis, difficulty in cleaning up the oral cavity and easy bleeding, cavities and premature teeth loss are common in KS patients. Other less frequent clinical manifestations are hyperkeratosis, pseudosyndactyly, nail dystrophy, finger webbing, ectropion, hypohidrosis, squamous cell carcinoma, and anal, laryngeal and esophageal stenosis. [6]

The appearance of blisters and photosensitivity tend to improve with age, but the atrophy and poikiloderma are persistent. The patients with extensive mucous membranes involvement (severe oral lesions and/or stenosis of the esophagus, larynx, or anus) have a worse prognosis. [7] Our patients had poorly preserved teeth, periodontitis and gingival bleeding after minimal trauma. The male patient also had phimosis, a rare complication of KS.

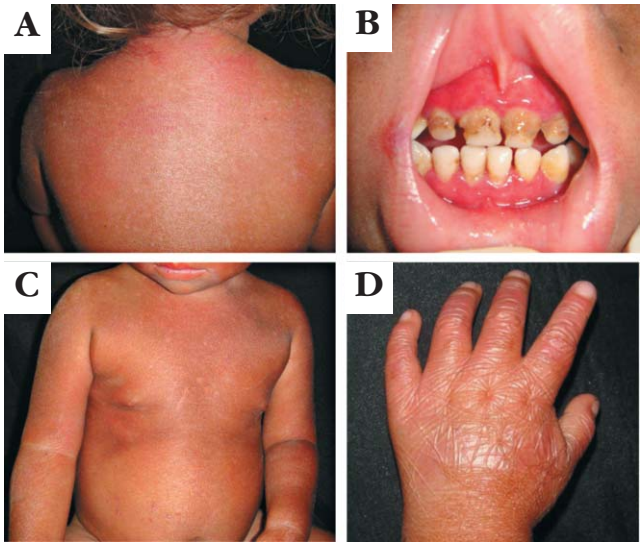

Figure 1: Xeroderma, diffuse cutaneous atrophy, mainly on the back of the hands and feet; poor preservation of teeth and severe periodontitis

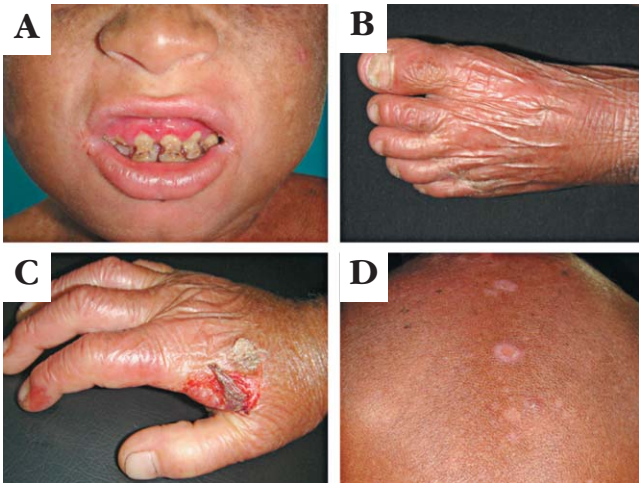

Figure 2: Erythematous scaly lesions on sun-exposed areas, hyperpigmentation, xeroderma, diffuse cutaneous atrophy and periodontitis

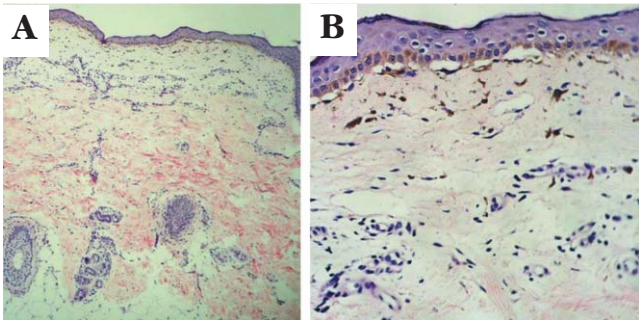

Figure 3: Epidermal atrophy, dilatation of blood vessels in the upper dermis, focal vacuolar degeneration of basal layer with subepidermal cleft, and presence of pigmentary incontinence

The diagnosis is essentially clinical and the following histological findings are suggestive of KS: epidermal atrophy, dilatation of blood vessels in the papillary dermis, vacuolar degeneration of basal layer, presence of cracks in the dermo-epidermal and pigmentary incontinence. Transmission electron microscopy of KS skin often shows major disorganization of the basement membrane with extensive reduplication of the lamina densa, focal widening of the lamina lucida, and multiple planes of cleavage (intraepidermal, within the lamina lucida and sublamina densa). Immunofluorescence microscopy labeling of KS skin can reveal abnormal labeling patterns for several basement membrane proteins, including a6b4 integrin, type XVII collagen, laminin-332, and types IV and VII collagens, reflecting the basement membrane disruption. A marked reduction or complete absence of immunostaining with antibodies to kindlin-1/fermitin family homolog 1 can also be useful diagnostically, although the availability of robust and reliable antibodies to the protein is currently limited. [8]

In 2005, Angelova-Fischer et al proposed diagnostic criteria for the syndrome, describing major and minor criteria, as well as any findings. The major criteria are acral blistering in infancy and childhood, progressive poikiloderma, skin atrophy, abnormal photosensitivity, gingival fragility and/or swelling. The minor criteria are syndactyly and mucosal involvement (anal, esophageal, urethral, laryngeal stenosis). A number of associated findings have been observed in these patients: nail dystrophy, ectropion, palmoplantar keratoderma, leukoplakia, squamous cell carcinomas, skeletal abnormalities, periodontitis and tooth decay. The presence of four major criteria makes the diagnosis of KS certain. The presence of 3 major and 2 minor criteria makes the diagnosis probable and the presence of 2 major criteria and 2 minor criteria or associated symptoms renders the diagnosis likely.[9] Our patients had all five major criteria, periodontitis and poorly preserved teeth.

KS must be differentiated from dystrophic EB, Rothmund-Thomson syndrome, hereditary sclerosing poikiloderma and Weary syndrome. Since its description in 1971, hereditary acrokeratotic poikiloderma or Weary syndrome has been the main differential diagnosis of KS and some cases have even been published as Kindler-Weary syndrome. However there are significant differences between KS and Weary syndrome. Photosensitivity, pronounced in KS, is usually absent in patients with Weary syndrome and blisters are not present shortly after birth but rather appear within the first 6 months of life. Skin atrophy, if present, is not as pronounced as in KS. [10] In this paper, we report the presence of the Kindler syndrome in sibling children of consanguineous parents, with the presence of acral blistering, photosensitivity, poikiloderma, cutaneous atrophy and periodontitis. ❑

REFERENCES

1. Kindler T. Congenital poikiloderma with traumatic bulla formation and progressive cutaneous atrophy. Br J Dermatol. 1954;66:104-11.
2. Siegel DH, Ashton GH, Penagos HG, Lee JV, Feiler HS, Wilhelmsen KC, et al. Loss of kindlin-1, a human homolog of the Caenorrhabditis elegans actin-extracellular-matrix linker protein UNC-112, causes Kindler syndrome. Am J Human Genet. 2003;73:174-87.
3. Martignago BC, Lai-Cheong JE, Liu L, McGrath JA, Cestari TF. Recurrent KINDIN1(C20orf42) gene mutation, c.676insC, in Brazilian pedigree with Kindler syndrome. Br J Dermatol. 2007; 157: 1281-4.
4. Lai-Cheong JE, Liu L, Sethuraman G, Kumar R, Sharma VK, Reddy SV, et al. Five new homozygous mutations in the KIND1 gene in Kindler syndrome. J Invest Dermatol. 2007;127:2268-70.
5. Fine JD, Eady RA, Bauer EA, Bauer JW, Bruckner-Tuderman L, Heagerty A, et al. The classification of inherited epidermolysis bullosa (EB): Report of the Third International Consensus Meeting on Diagnosis and Classification of EB. J Am Acad Dermatol. 2008;58:931-50.
6. Penagos H, Jaen M, Sancho MT, Saborio MR, Fallas VG, Siegel DH, et al. Kindler Syndrome in Native Americans from Panama. Arch Dermatol. 2004;140:939-44.
7. Nofal E, Assaj M, Elmosalany K. Kindler Syndrome: a study of Egyptian cases with evaluation of severity. Int J Dermatol. 2008;47:658-62.
8. Forman AB, Prendiville JS, Esterly NB, Hebert AA, Duvic M, Horiguchi Y, et al. Kindler syndrome: report of two cases and review of literature. Pediatr Dermatol. 1989;6:91-101.
9. Angelova-Fischer I, Kazandjieva J, Vassileva S, Dourmishev A. Kindler syndrome: a case report and proposal for clinical diagnostic criteria. Acta Dermatovenerol Alp Panonica Adriat. 2005;14:61-7.
10. Marques SA, Pereira FP, Stolf HO. Você conhece esta síndrome? Síndrome de Rothmund-Thomson (poikiloderma congenitale). An Bras Dermatol. 2008;83:476-9.

MAILING ADDRESS:
Mônica Santos
Avenida Pedro Texeira, 25, Dom Pedro
69040-000 Manaus, AM
E-mail: m.n.souza.santos@gmail.com

How to cite this article: Mendes L, Nogueira L, Vilasboas V, Talhari C, Talhari S, Santos M. Kindler syndrome - report of two cases. An Bras Dermatol. 2012;87(5):779-81.