

Kindler syndrome: Case Report.

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ABSTRACT:

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Kindler syndrome (KS, OMIM 173650) is a rare autosomal recessive disorder characterized by trauma-induced blister, progressive poikiloderma, skin atrophy, mucosal inflammation and varying degrees of photosensitivity¹. Sporadic cases are common, with many originating in consanguineous family². The pathogenesis of Kindler syndrome caused by a defect in the actin-extracellular matrix linkage, known as protein fermitin family homologue 1 (previously known as kindling-1 or kindlerin)^{4,5}, encoded by the gene FERMT1.

We are hereby reporting a patient with classical cutaneous features of Kindler syndrome. A 8 year- old boy presented with a history of recurrent trauma-induced acral blistering, which started on the neonatal period and persisted until now. The acral blistering improved with age but pigmentary changing and skin atrophy appear gradually. He present as sporadic case, his parents are remote related from north-eastern Thailand. Because of the rarity of the syndrome and to emphasize the importance of considering this condition in the differential diagnosis of disorders that can cause blistering, cutaneous atrophy, and/or poikilodermatous skin changes.

Key words: Kindler syndrome, KS

บทคัดย่อ :

ทราย ทศเกตุ มนัสลักษ์ อริยะชัยพานิชย์ วิวัฒน์ ก่อกิจ รายงานผู้ป่วยโรคไคเลอร์ วารสารโรคผิวหนัง 2554; 27: 312-316.

หน่วยผิวหนัง ภาควิชาอายุรศาสตร์ คณะแพทยศาสตร์ จุฬาลงกรณ์มหาวิทยาลัย

โรคไคเลอร์ เป็นโรคทางพันธุกรรมที่ถ่ายทอดแบบลักษณะด้อย หรือเกิดขึ้นเองจากการแต่งงานระหว่างเครือญาติ โดยจะมีผื่นผิวหนังเป็นตุ่มน้ำในบริเวณที่ได้รับบาดเจ็บ ผื่นหนังฝ่อ การอักเสบบริเวณเข่า และภาวะไวต่อแสง เชื่อว่าความผิดปกติทางพันธุกรรมของโรคนี้เกิดจากการเสียการทำงานของยีนเอฟอีอาร์เอ็มทีวัน

รายงานฉบับนี้เป็นการนำเสนอผู้ป่วย เด็กชายอายุ 8 ปี มาตรวจรักษาด้วยประวัติ คุ่มน้ำบริเวณแขนขา ตั้งแต่แรกเกิดจนถึงปัจจุบัน ร่วมกับมีสีผิวผิดปกติและผิวหนังบาง ตรวจเพิ่มเติมมีอาการฟันผุและถ่ายเป็นเลือด จากประวัติและการตรวจร่างกายบ่งชี้ถึงโรคโกลเลอร์

คำสำคัญ: โรคโคเลอร่า

Introduction

Kindler syndrome (KS, OMIM 173650) is a rare autosomal recessive disorder characterized by trauma-induced blister, progressive poikiloderma, skin atrophy, mucosal inflammation and varying degrees of photosensitivity¹. Sporadic cases are common, with many originating in consanguineous family². The pathogenesis of Kindler syndrome caused by a defect in the actin-extracellular matrix linkage, known as protein fermitin family homologue 1 (previously known as kindling-1 or kindlerin)^{4,5}, encoded by the gene FERMT1 that is mapped to chromosome 20p12.3⁴.



Figure 1 Physical examination reveals multiple patchy hypopigmentation and hyperpigmentation with epidermal atrophy resembling cigarette paper-like wrinkle prominent on acral area.



Figure 2 The poikiloderma is prominent on his neck and sun-exposed areas of both extremities. His right hand revealed trauma-induced acral blistering.

Case report

A 8 year- old boy, from consanguineous family, presented with a history of recurrent trauma-induced acral blistering, which started on the third day of the neonatal period and persisted until now. His parents brought him to the hospital since he was 3 year-old and epidermolysis bullosa was diagnosed. Since then he had never come to see the doctor with this problem again.

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The acral blistering improved with age but pigmentary changing and skin atrophy appear gradually.

On clinical examination, he was short-statured but his IQ was normal. Cutaneous examination revealed multiple patchy hypopigmentation and hyperpigmentation with epidermal atrophy resembling cigarette paper-like wrinkle (Figure 1). The poikiloderma is prominent on his neck and sun-exposed areas of both extremities but spare the face (Figure 2). Neither freckles nor café au lait macules were observed. Oral mucosa have erosions and severe gingivitis. He also has poor dentition causing dental caries of the deciduous teeth. He occasionally had light bloody diarrhea and constipation without history of hemorrhoid that spontaneous recovery without any treatment.

The diagnosis was based on clinical manifestation. Genetic analysis is currently on process.

Discussion

Kindler syndrome is a rare genodermatosis, which was first described in a 14-year-old girl by Kindler in 1954. Since then, more than 100 cases compatible with Kindler syndrome have been reported worldwide.

In our case, the patient, from consanguineous family, had trauma-induced acral blistering begin in infancy and improve significantly with age but pigmentary changing and skin atrophy appears gradually and becomes more prominent later on his neck and sun-exposed areas of both extremities.

Our patient demonstrates the classic clinical features of Kindler syndrome. Previous reported cases share the

major clinical findings: acral blister formation following minor trauma, progressive poikiloderma, diffuse and severe skin atrophy giving cigarette paper-like appearance, and photosensitivity. Additional presentations have been observed in these patients such as palmoplantar keratoderma, webbing of the fingers and contractures, pseudosyndactyly, squamous cell carcinoma and nail dystrophy. The pseudosyndactyly may resemble that seen in dystrophic EB⁸. Gingival fragility, poor dentition, as well as early and rapidly progressive periodontitis are common features⁹. Other mucous membranes such as urethral, anal, oesophageal, and genital mucosae, may be involved¹⁰. The lesions can lead to stenosis of the organs as well as phimosis⁷. Corneal erosions caused pain and discomfort but did not affect visual acuity¹¹. Gastrointestinal tract involvement is frequently found, as presented in our patient with history of light bloody diarrhea that should be closely observe for complications such as severe colitis and perianal erosions¹¹. In patient with colitis-like symptoms may develop iron-deficiency anemia¹².

The differential diagnosis of Kindler syndrome includes epidermolysis bullosa simplex with mottled pigmentation (EBS-MP), Bloom syndrome, Cockayne syndrome, dyskeratosis congenita, Rothmund-Thomson syndrome and xeroderma pigmentosum. In neonates and infants, Kindler syndrome can be difficult to diagnose because of the clinical overlap with other disease. The spontaneous reduction in blisters and photosensitivity followed by progressive skin atrophy

and poikiloderma may point to the diagnosis of Kindler syndrome later in life as in our patient. Recent reports have suggested that gene sequencing of the FERMT1 gene remains the gold standard for diagnosing Kindler syndrome¹.

Siegel et al have mapped the gene locus to chromosome 20 p 12.3 by using linkage and homozygosity analysis in patients with Kindler syndrome⁵. Loss-of-function mutations were identified in a actin cytoskeleton-associated protein, known as fermitin family homologue 1. This gene encodes a protein, Kindlin I, which plays a regulatory role in inhibiting over-secretion of basement membrane components by basal keratinocytes at the dermo-epidermal junction. Kindler syndrome is suggested as the first skin fragility disorder caused by a defect in the actin-extracellular matrix (ECM) linkage rather than the keratin-ECM linkage.

Morbidity and mortality are mostly related to secondary infection from cutaneous bullae and cosmetic disfigurement. Patients usually have normal intelligence and normal life span². Squamous cell carcinoma of the hard palate, lip and a transitional cell carcinoma of the urinary bladder have been reported as complications of this syndrome.

Treatment is largely symptomatic. The skin in Kindler syndrome is often dry and pruritus¹. Telangiectasias can be treated with pulsed-dye laser². Sun avoidance and UV protection may prevent or retard progression of poikiloderma. Wound care includes the

use of topical and systemic antibiotics for infected bullae. The annual checks for premalignant keratoses and early squamous cell carcinoma are indicated, especially hands and feet seem to be more susceptible sites. Regular dental care such as scaling and root planing and careful regular hygienist attention are advised¹³. Surgical correction of urethral, anal, or esophageal stenosis may be needed.

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