KINDLER'S SYNDROME: THE FIRST REPORT OF FOUR SIBLINGS WITH NEW FINDINGS

H. Ghaninejad, K. Balighi, A. Ehsani* and M. Hoseini

Department of Dermatology, Razi Hospital, School of Medicine, Tehran University of Medical Sciences, Tehran, Iran

Abstract- Kindler's syndrome is a rare entity of unknown cause characterized by acral blisters early in life followed by progressive diffuse poikiloderma and cutaneous atrophy. The inheritance pattern of this syndrome is not clear. We report four Iranian siblings (three boys and one girl) with this syndrome, who were the result of a consanguineous marriage. In addition to the usual manifestations of the syndrome, corneal epithelial punctate defects were detected in all four, and segmental chorioretinal atrophy in one case. This is the first report of the affliction of four siblings, and also the first report of the association of the above ophthalmologic findings with Kindler's syndrome.

Acta Medica Iranica, 42(2): 146-148; 2004

Key words: Kindler's syndrome, eye

INTRODUCION

Kindler's syndrome is a rare entity of unknown cause characterized by acral blisters early in life followed by progressive diffuse poikiloderma and cutaneous atrophy later on (1-4).

Poikiloderma, reticular telangectasia, hypopigmentation and hyperpigmentation with epidermal atrophy begins in early childhood (4).

The inheritance patterns of this syndrome are not clear (5).

Ultra structural studies of the damaged skin in Kindler's syndrome show separation of the sub-basal lamina (5). Colloid bodies which show IgM deposition on direct immunofluorescence have been described (5).

Case Reports

Four Iranian siblings, three boys aged 10,15,20 years, and one 8 year-old girl (Fig 1), presented to our center for evaluation of their dermatologic disorder. They were the result of a consanguineous marriage and were living in Khoozestan, a southern province of Iran. The patients were normal at birth but gradually developed bullous lesions at the sites of trauma to their extremities. The bullae healed with scarring but without the formation of miliae (Fig. 2). All patients developed poikilodermatous alterations first on exposed areas, followed by unexposed sites, especially the trunk. Skin dyschromia was present in all except the 8 year-old girl. They also had periodontitis, poor dentition, photosensitivity and photophobia. Ophthalmologic examination revealed the presence of papillary conjunctival reaction and corneal epithelial punctate defects in all four patients. Hair examination and trichogram were normal, as were the patients' physical and mental growth. In addition to the presence of poikilodermatous changes in the biopsy specimens, subcorneal blisters with dense band-like infiltration of inflammatory cells were present in the superficial dermis of the 10 year-old patient. Direct immunoflourescent examination revealed numerous colloid body deposits of IgM in the papillary dermis. Iron deficiency anemia was detected in the three younger siblings. In addition to the shared features described above, the following manifestations were specifically seen in each patient:

- The 8 year-old girl was suffering from dysphagia

Received: 7 Nov. 2002, Revised: 26 May. 2003, Accepted: 23 Jul. 2003

***Corresponding Author:**
A. Ehsani, Department of Dermatology, Razi Hospital, School of Medicine, Tehran University of Medical Sciences, Tehran, Iran
Tel: +98 21 5609952, Fax: +98 21 5609953
E-mail: ehsania2000@yahoo.com

to solid food.

- The 10 year-old boy had meatal stricture and web on urologic examination.
- The 15 year-old boy had contracture deformities of the 4th and 5th fingers of both hands.

On radiological examination, osteopenia and flexion deformity of the proximal interphalangeal joints of these fingers were noted. The patient had also dystrophy of the finger and toe nails and leukoplakia of the lip and oral mucosa. Urologic examination showed the presence of meatal stricture and web. He was also suffering from bilateral ectropion and segmental chorioretinal atrophy in the superior part of his globes.

- The 20 year-old sibling had leukoplakia of the lip and oral mucosa (Fig. 3).
-

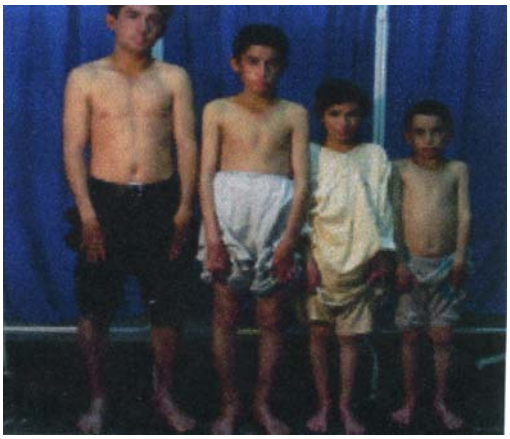

Fig. 1. The four siblings afflicted with Kindler's syndrome

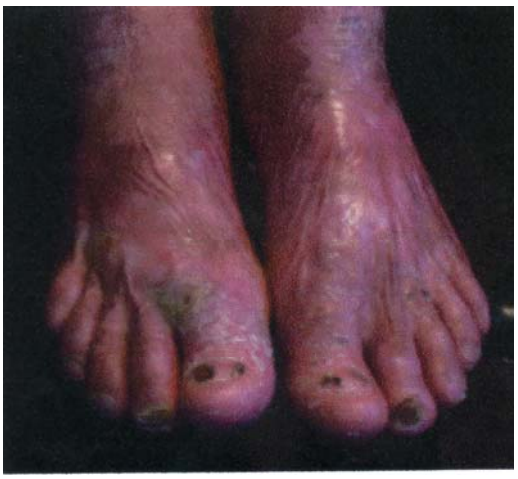

Fig. 2. Scars on the extremities following healing of bullae

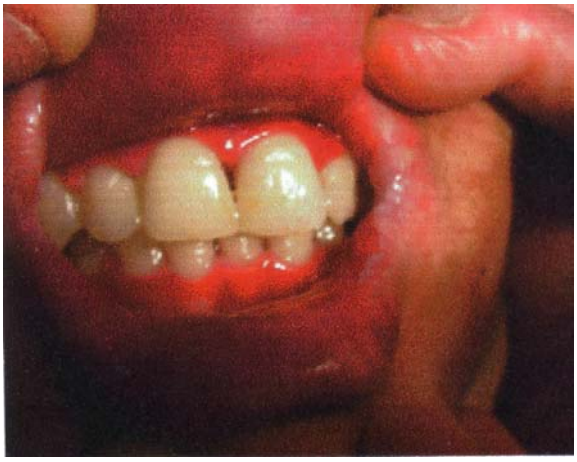

Fig. 3. Leukoplakia of the lip in the 20 years old sibling

DISCUSSION

Kindler syndrome was first described by Theresa Kindler in 1954 (l). The main features of this rare entity are acral blister formation in early life and the later development of progressive diffuse poikiloderma and cutaneous atrophy (2-4). Blisters begin in infancy on the hands and feet, in response to little or no trauma, and improve in adult life. This may be the only symptom for the first few years and may falsely lead to the diagnosis of epidermolysis bullosa (4).

Poikiloderma-reticular telangiectasia, hypopigmentation, and hyperpigmentation with epidermal atrophy begin in early childhood. It is most marked in sun-exposed areas (4). Poikiloderma is progressive, resulting in thin, wrinkled skin without surface markings (5). There is fine cigarette paper-like wrinkling of the skin over the hands and elsewhere (4). Photosensitivity is common and, like other cutaneous features, tends to improve with time (5,6). However, recurrent acral blisters have been described in a 46-year-old Japanese male (7).

Palmoplantar hyprekeratosis is generally mild and occurs in about 65% of individuals (4). Acrokeratoses resembling flat warts and punctate keratoses on the palms and soles were described by Weary *et al* (8). Gingivitis and/or leukokeratosis has been reported in a few reports (4). Mild onychodystrophy with ridging, grooving, and atrophy may occur. Blisters can occasionally occur in the oral mucosa. There are several case reports of esophageal,

urethral, rectal, and/or conjunctival scarring (4,9).

Other reported findings include eczema, dermatitis, xerosis, milia around blisters and webbing of the fingers and toes (3,4,10). However, corneal epithelial punctate defects which were present in all of our cases and segmental chorioretinal atrophy which was detected in one of them have not been reported previously. Ultrastructural studies of the damaged skin in Kindler's syndrome show separation of the sub-basal lamina. Activated fibroblasts are present in the subepidermal region, suggesting a transient mechanobullous dermatosis, and enabling distinction from epidermolysis bullosa (5,11,12) Colloid bodies which show IgM deposition on direct immunofluorescene have been described (5,10,13). The inheritance pattern of Kindler's syndrome is not clear. Although familial types of the syndrome are reported (9,13-14), affliction of four siblings has not been previously reported. Conclusively, we presented the first report of the affliction of four siblings with Kindler's syndrome associated with previously unreported ophthalmologic findings.

REFERENCES

1. Kindler T. Congenital poikiloderma with traumatic bulla formation and progressive cutaneous atrophy. Br J Dermatol 1954; 66: 104-111.

2. Hovanian A, BlancherBardon C, de Prost Y. Poikiloderma of Theresa Kindler: Report of a case with ultrastructural study and a review of the literature. Pediatr Dermatol 1989; 6: 82-90.

3. Forman AB, Prendiville 1S, Esterley NB, *et al.* Kindler syndrome: Report of two cases and review of the literature. Pediatr Dermatol 1989; 6: 91-101.

4. Sentur N, Usubutun A, Sahin A, *et al.* Kindler Syndrom: absence of definite ultrastructural feature. Am Acad Dermatol 1999; 40:335-337.

5. Sybert VP. Genetic Skin Disorders. 1st ed. New York. Oxford University Press; 1997. p. 579-581.

6. Burton JL, Lovell CR. Disorders of Connective tissue In: Champion RH, Burton JL, Burns DA and Breathnach SM. Textbook of Dermatology. 6th ed. Vol 3. Oxford: Bluckwell Scientific Publications; 1998.p. 2018.

7. Ban M, Hosoe H, Yamada T, *et al.* Kindler's syndrome with recurrence of bullae In the fifth decade. Br J Dermatol 1996; 135: 503-504.

8. Weary PE, Manley WF and Graham GF. Hereditary acrokeratotic poikyloderma. Arch Dermatol 1971; 13: 409-422.

9. Al Aboud K, Al Githami A. Kidler Syndrome In a Saudi kindred. Clin Exp Dermatol 2002; 27:673-676

10. Alper JC, Baden HP, Goldsmith LA. Kindler's Syndrome. Arch Dermatol 1978; 114: 457-459.

11. Patrizi A, Pauluzzi P, Neri I, *et al.* Kindler Syndrome: report of a case with ultrastructural study and review of the literature. Pediatr Dermatol 1996; 13: 394-402.

12 Shimizu H, Sato M, BanM, *et al*. Immuno-histochemical, ultrastructural, and molecular features of Kindler syndrome distinguish it from dystrophic epidermolysis bullosa. Arch Dermatol 1997; 133(9): 1111-1117

13. Larregue M, Prignet F, Lorette G, Canuel C and Ramdenee P. Acrokeratose poikilodermique bulleuse et herditaire de Weary-Kindler. Ann Dermatol Venereol 1981; 108: 69-76.

14. Haber RM, Hanna WM. Kindler Syndrome. Clinical and ultrastructural findings. Arch Dermatol 1996; 132(12): 1487-1490.