

## Annular epidermolytic ichthyosis: A rare phenotypic variant of bullous congenital ichthyosiform erythroderma

Sir,

Bullous congenital ichthyosiform erythroderma of Brocq is a rare mechanobullous eruption first described by Brocq in 1902. This autosomal dominant disorder is characterized by blistering and erythroderma in early life with many similarities to epidermolysis bullosa simplex. However, these patients subsequently develop ichthyosis and hyperkeratosis. Epidermolytic hyperkeratosis is the hallmark feature on light and electron microscopy. Annular epidermolytic ichthyosis is a distinct phenotypic variant of bullous congenital ichthyosiform erythroderma characterized by intermittent development of polycyclic, erythematous, scaly plaques on the trunk and proximal extremities.<sup>[1]</sup> Histological features are similar to those of classical epidermolytic hyperkeratosis, and keratin K10 or K1 mutations, similar to those of bullous congenital ichthyosiform erythroderma, have been identified in annular epidermolytic ichthyosis.<sup>[2-4]</sup>

A 26-year-old female, born of a non-consanguineous marriage, presented to the dermatology outpatient of Vardhaman Mahavir Medical College and Safdarjung Hospital, New Delhi, India, with a history of generalized recurrent blistering since birth. She had begun to develop hyperkeratotic plaques all over the body since early infancy and by 8 years of age, the lesions had cleared from most areas and had localized to the flexures (neck, cubital fossae, elbows, and wrist) [Figure 1a]. For the past 3 years, she was also developing recurrent episodes of erythematous annular plaques with scaling over the trunk, thighs, and inframammary areas. These lesions increased in size over a period of 8–10 days and later developed peripheral desquamation giving them an annular appearance [Figure 2a and b]. She had given birth to a boy with erythroderma with subsequent development of rippled hyperkeratosis of the flexures [Figure 3a and b]. There was no history of neonatal blistering in the child. Examination of the child revealed polycyclic, psoriasiform, scaly plaques on the trunk and extremities. Clinically, the hair, teeth, and nails were normal. With the provisional differential

diagnoses of bullous congenital ichthyosiform erythroderma (BCIE) occurring alone, in combination with erythrokeratoderma, or in combination with psoriasis, a skin biopsy was taken from the annular plaque and a hyperkeratotic lesion that represented the two main clinical aspects of the disease. Light microscopy of the specimens revealed hyperkeratosis, acanthosis, and degeneration of granular layer with dispersion of keratohyalin granules. Vacuolar changes were evident in the keratinocytes of the stratum spinosum [Figure 4]. These findings were consistent with the diagnosis of epidermolytic hyperkeratosis. A complete blood count, liver and kidney function tests, and serum electrolytes were normal. Skin scrapings from the scaly plaques were negative for fungi.

She was initially started on emollients and ciclosporin 3.5 mg/kg body weight because of the presumptive differential diagnosis of psoriasis for the annular plaques. Retinoids were not considered at this point because she was breastfeeding. The erythematous,

annular plaques improved moderately after 6 weeks of treatment. The plaques remained stable for 1 month after which she had a flare of the annular plaques. She was then started on acitretin 0.5 mg/kg/day after detailed counselling regarding contraception. Four weeks later, all the annular plaques disappeared and there was a remarkable improvement in the flexural as well as the annular plaques [Figure 1b]. No recurrence was noted after 2 months. We plan to re-institute acitretin in the event of a relapse. The child was treated with emollients in view of the milder phenotype and the potential side effect profile of acitretin.

The distinct phenotype seen in our patient has only been described in eight families thus far in the literature and we were unable to find any previous cases reported from India [Table 1]. It was first reported in a young female by Sahn *et al.* in 1992 who also coined the term annular epidermolytic ichthyosis.<sup>[1]</sup> She had bullous and ichthyosiform skin lesions since the age of 8 months. Later, she developed numerous annular and polycyclic, erythematous, hyperkeratotic plaques on the trunk and extremities, which were pruritic, enlarged slowly, and then resolved. Histopathology of the annular plaques revealed



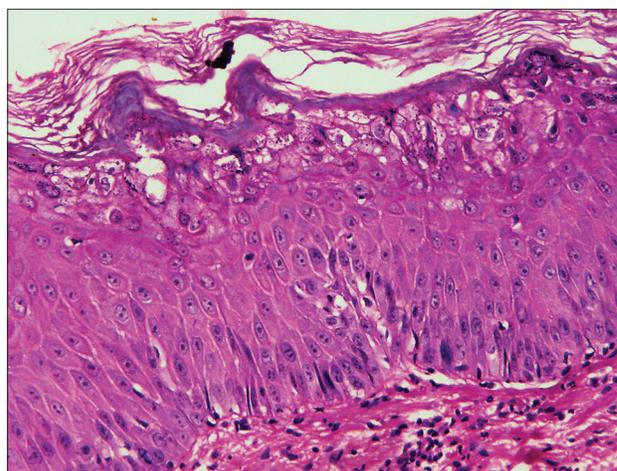
**Figure 1:** (a) Annular psoriasiform plaques over the trunk and extremities and ribbed hyperkeratosis over the flexures. (b) Considerable improvement after treatment with acitretin



**Figure 2:** (a) Erythematous polycyclic plaques over the trunk with exfoliation starting from the center. (b) Exfoliation extending toward the periphery giving an annular appearance



**Figure 3:** (a) Diffuse erythema and creamy white scaling in the child. (b) Peeling of the skin over the soles in the child



**Figure 4:** Hyperkeratosis, epidermal acanthosis with granular layer degeneration and vacuolar alteration in keratinocytes (H and E, x400)

**Table 1: Summary of previously reported cases of annular epidermolytic ichthyosis**

Authors	Case number	Age/sex	Age at presentation and clinical features	Additional features	Mutation analysis
Sahn <i>et al.</i> , 1992	1	30/F	27 years of age Trunk and extremities: Annular and polycyclic, erythematous, hyperkeratotic plaques Itchy, migratory, self-resolving	Bullous and ichthyosiform lesions since 8 months of age Bullous lesions stopped at puberty Ichthyosiform lesions persisted	Not available
Joh <i>et al.</i> , 1997	2 (father)	33/M	31 years of age Trunk and proximal extremities Numerous migrating, annular, polycyclic erythematous plaques with scaling borders, along with very superficial erosions within these plaques	Bullous and ichthyosiform lesions since birth Bullous lesions stopped at 16 years of age	Novel dinucleotide mutation (CG to CA) within 2B segment of keratin 10 in the case and his daughter
	3 (daughter of 2)	2 months/F	2 months of age Around the groin and inner side of legs Some coin-sized sharply demarcated erosions	Generalised bullous lesions and moderate erythema since birth	
Suga <i>et al.</i> , 1998	4	11/M	Trunk and proximal extremities Intermittent episodes of erythematous, scaly, annular, and serpiginous plaques	Ridged keratotic plaques in the flexures No blistering at any point of time	Novel mutation within the 2B segment of K10, codon 446
Sybert <i>et al.</i> , 1999	5 6 7 (aunt of case 6)	3/M 18/M NA/F	3 years of age for case 5 and 6 Data for case 7 not available Episodic flares of annular, polycyclic erythematous plaques with scaling Flares last weeks to months	Erythema and superficial erosions at birth, which improved during the first few months of life Palmoplantar hyperkeratosis	Both families revealed heterozygous mutations in K1 codon 479
Michael <i>et al.</i> , 1999	8, 9, 10, 11 (members of one family)	NA	Trunk: Non-migratory psoriasiform erythematous plaques Intermittent episodes	Transient blistering at birth Palmoplantar keratoderma	Heterozygous mutations in the 2B segment of K1 gene
Yoneda K <i>et al.</i> , 1999	12, 13 (mother and son)	48/F 18/M	Trunk and proximal extremities: Numerous migrating, annular, and polycyclic erythematous hyperkeratotic plaques by 4 years of age	Extensive blistering at birth	Mutation in K10 gene (1A rod domain)
Naik <i>et al.</i> , 2003	12	21/F	1 year of age Trunk and extremities: Episodic, slowly migratory red patches with scaling	Thickened, dirty brown, corrugated plaques over the knees, elbows, and ankles Palmoplantar keratoderma	Not done

M: Male, F: Female, CG: Cytosine guanine, CA: Cytosine adenine

epidermolytic hyperkeratosis. Our case also had a similar presentation. Subsequently, Joh *et al.* reported a similar condition in a family with two generations being affected. Histological examination showed typical features of epidermolytic hyperkeratosis and molecular analysis revealed a novel dinucleotide mutation within the 2B segment of the keratin 10 gene that was passed on to offspring.<sup>[2]</sup> Similar cases were reported by Suga *et al.* in 1998<sup>[3]</sup> and Sybert *et al.* in 1999.<sup>[4]</sup> Molecular analysis of these families revealed mutations in keratin 10 and keratin 1 genes, respectively. Naik reported episodic flares of polycyclic psoriasiform patches in a young woman with a life-long history of palmoplantar keratoderma with histological features of epidermolytic hyperkeratosis.<sup>[5]</sup>

The molecular mechanisms underlying this particular phenotype of epidermolytic ichthyosis caused by mutations in K1 and K10 are unclear. We were not able to perform the mutation analysis in our patient because the facility was not available in our setting.

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