Bullous icthyosiform erythroderma with rickets in child of a parent with naevus unius lateralis

Sir,

Bullous congenital icthyosiform erythroderma (BCIE), also known as epidermolytic hyperkeratosis (EHK), is a rare autosomal dominant disorder of cornification[1] that presents as bullous disease of the newborn followed by an icthyotic skin disorder throughout life. The prevalence is 1 in 200,000 to 300,000 with both genders equally affected. BCIE is caused by heterozygous mutation in the genes encoding keratin 1(KRT 1) and keratin 10(KRT 10) localized on chromosomes 12q13.3 and 17q 2.2, respectively.[2]

EHK is classified into PS types (with severe palm/sole hyperkeratosis) and NPS types (without severe palm/sole hyperkeratosis).[1] Morbidities include recurrent infection, sepsis and electrolyte imbalance during neonatal period. The association of icthyosis and rickets is rare[3-5] but well known. Similarly, the association between epidermolytic verrucous epidermal naevus (VEN) in either of the parents and bullous icthyosis in the offspring or vice versa is well known. However, both these associations are rare.

A 12-year-old boy, product of consanguineous marriage, third in birth order with two normal sibs and neonatal death in one sib, presented with a limping gait, skeletal deformity and pigmented scales over the whole body. There was no history of collodion membrane; the patient, bright red in color at birth, developed blisters during the neonatal period, which progressed till eight years. The bullae appeared at the sites of friction leading to erosions, peeling and widespread areas of denuded skin without any scarring. In subsequent years, bullae and erythroderma subsided but the skin became thick and scaly with pungent body odor and recurrent skin infections. On examination, thick, waxy, pigmented scales were seen on scalp, forehead, neck, trunk and limbs with prominent hyperkeratotic ridges over neck, elbows, knees and ankles. Mucosae, teeth and hair were normal and central face, palms and soles were spared. The patient had severe skeletal deformities in the form of genu valgum of left knee, palmar convexity of lower third of right forearm, marked widening of wrists and ankles and beading of the ribs [Figure 1]. The boy's father had an asymptomatic hyperkeratotic naevoid lesion found incidentally on examination, extending from right axilla to cubital fossa. Routine investigations were normal. Serum calcium, phosphate and 25-hydroxy-vitamin D levels were low but the serum alkaline phosphatase and parathormone levels were high. Radiographs showed rachitic changes in the form of valgus deformity of left knee with splaying of the metaphyseal ends, thinned out cortex and osteoporosis of both tibia and fibula, cupping of the metaphysis of the radius and ulna with dorsal convexity of the radius and widening of the physis of the wrist [Figure 2]. Histopathological findings were dense orthokeratotic hyperkeratosis, acanthosis, vacuolar degeneration of suprabasal layers with cleft formation and dermis showed a scanty perivascular lymphocytic infiltrate [Figure 3]. The skin biopsy of naevoid lesion of patient's father showed similar features.

Since our patient had a positive history of blistering and abnormal gait, generalized icthyotic skin with

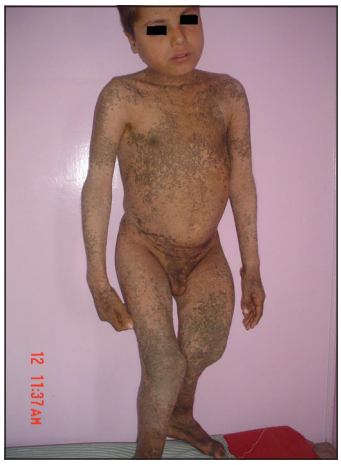

Figure 1: Generalized icthyotic scales, thickened epidermal ridges in flexures with superficial peeling and skeletal deformity.

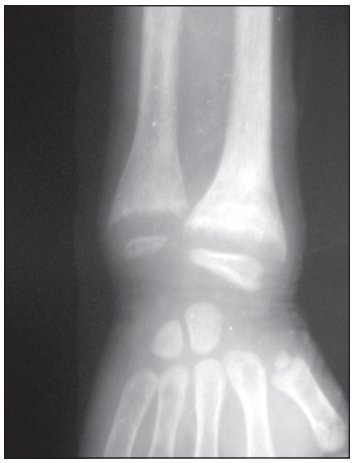

Figure 2: AP radiograph of the hand demonstrates widening of physis and metaphyseal cupping

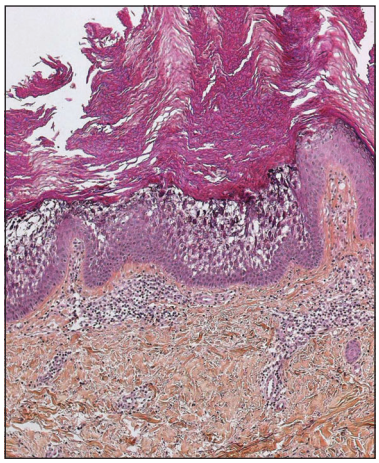

Figure 3: Orthokeratotic hyperkeratosis, acanthosis, vacuolar degeneration of suprabasal layers with cleft formation (H and E, staining, × 50).

hyperkeratotic ridges in flexural areas, normal palmoplantar surfaces and naevoid epidermolytic hyperkeratosis in a parent, diagnosis of NPS-1 epidermolytic hyperkeratosis with nutritional rickets was made. Epidermolytic hyperkeratosis includes a spectrum comprising- linear epidermal verrucous naevus, icthyosis hystrix, icthyosis bullosa of Siemens and BCIE. Bullous congenital icthyosiform erythroderma is a chronic and disfiguring disease which has a tremendous impact on family and social life. An underlying genetic defect of keratin synthesis or degradation involving keratin K1 and/or keratin 10 has been suggested.[2,6] Mutations perturb keratin alignment, oligomerization and filament assembly, weakening the cytoskeleton compromising mechanical strength and cellular integrity of the epidermis, and leading to cytolysis and blistering.[6] The barrier function of the skin is markedly disturbed, leading to increased transepidermal water loss and bacterial colonization of the stratum corneum.[7] The mosaic form of BCIE is characterized by unilateral or bilateral streaks of hyperkeratosis that follow the lines of Blaschko.[8] A patient with an epidermolytic verrucous epidermal naevus is likely to have gonadal mosaicism as well as cutaneous mosaicism, and can therefore produce offspring with generalized BIE.[9] Our patient's father had an epidermolytic verrucous epidermal naevus on right arm, indicating mosaic form of BCIE, leading to full-blown generalized disease in the child.

There are several reports of an association between icthyosis and rickets, based mainly on the causative relationship through the impaired ability of icthyotic skin to synthesize vitamin D and a defect in vitamin D receptor.[3,5,10] Other contributing factors may be alteration in cholesterol metabolism involving vitamin D3 receptors, increased keratinocyte proliferation resulting in poor or no penetration of skin by sunlight, associated vitamin D dependent rickets and limited sun exposure as patients avoid sun in summer.[5]

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