Bilateral Systematised Epidermolytic Epidermal Nevus
A case report

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Abstract: Verrucous epidermal nevi (VEN) are benign congenital hamartomas consisting of keratinocytes. Histological examination mostly exhibits hyperkeratosis, acanthosis, papillomatosis and, rarely, the features of epidermolytic hyperkeratosis (EHK). We report a case of a 6-year-old boy who presented at Aga Khan University Hospital, Karachi, Pakistan with bilaterally symmetrical linear epidermal nevi following Blaschko's lines and showing epidermolytic hyperkeratosis on histology. The patient was treated with topical keratolytics and emollients which led to considerable improvement. To the best of the authors’ knowledge, this is the first report of VEN from Pakistan.

Keywords: Verrucous Epidermal Nevus; Mosaicism; Epidermolytic Hyperkeratoses; Hamartoma; Case Report; Pakistan.

Case Report

A 6-year-old boy presented to the dermatology clinic in Karachi, Pakistan with a warty eruption involving his axillae, genitalia, hands and legs but sparing the face, scalp, palms and soles. He was born healthy, full-term and via vaginal delivery from a non-consanguineous marriage. There was no history of collodion membrane, erythroderma or blistering at birth. He had four other siblings, none of whom were affected. He had no hearing loss or other developmental delay. After two months, he developed lesions initially involving only one knee and it progressively spread to other parts of the body during a span of six years.

On examination, thick, dry, adherent, hyperpigmented verrucous scaly plaques were present on his neck, axilla, dorsum of hands and ankles, cubital fossa, flexural and extensor surfaces of elbows and knees [Figures 1 and 2]. The rash had a bilaterally symmetrical distribution. The lesion was more prominent on the left lower half of the anterior trunk extending along the mid-line of the genitalia. At all sites, the lesions followed Blaschko’s lines. The palms, soles, face, hair and nails were normal. There was no history of mental retardation or any skeletal abnormalities. A biopsy of the...
plaque from the area below the knee showed marked hyperkeratosis, focal coronoid lamella and papillomatosis of the epidermis. The upper layers of the epidermis showed a prominent granular layer, perinuclear vacuolisation and abundant keratohyalin granules in the cytoplasm of keratinocytes. The nuclei were basophilic while the deeper part of the epidermis had usual lining and scattered melanocytes at the basal layer. However, the dermis was unremarkable [Figure 3].

Based on the above constellation of clinical features and histopathologic findings, a diagnosis of ichthyosis hystrix type of epidermal nevus (systematised type of epidermal nevus) was made. The presence of focal coronoid lamella, previously thought to be specific for porokeratosis, has also been reported in linear epidermal nevus. The patient was prescribed topical keratolytics in combination with emollients that led to considerable improvement. Prior consent was obtained from the patient’s father for publication of this case.

Discussion

Epidermal nevi may be sebaceous, apocrine, eccrine, follicular or keratinocytic. All epidermal nevi are the expressions of a somatic mutation in the genes that regulate cell growth and division. Approximately 60% of the epidermal nevi are linear VEN, also called keratinocytic nevi. The term systematised linear epidermal nevus is used for linear nevi present on more than one body part.

Recently, keratinocytic epidermal nevi are subclassified, based on histology, into epidermolytic and non-epidermolytic. The term epidermolytic hyperkeratosis, or granular degeneration of the epidermis, refers to a distinctive pattern of compact hyperkeratosis, perinuclear vacuolisation of keratinocytes of the upper layers of epidermis and coarse keratohyalin granules. This histologic pattern was seen in several congenital and acquired clinical disorders. The congenital conditions include bullous congenital ichthyosiform erythroderma of Brocq, ichthyosis bullosa of Siemens, epidermolytic palmoplantar keratoderma of Vörner and epithelial nevi. EHK is present in about 5–10% of epidermal nevi and tends to be more warty.

VEN may occur as part of an epidermal nevus syndrome that includes central nervous system and skeletal abnormalities; however, a literature review showed that the epidermolytic variant of epidermal nevus does not have any extracutaneous features. Mishra et al. reported epidermolytic epidermal nevus in a 3-year-old boy who had no history of blistering at birth and had no extracutaneous features. Similar findings were evident in the current case.

Paller et al. found mutations in the $K10$ gene in lesional skin of patients with epidermolytic epidermal nevus.
neuvs, while their offspring who had generalised EHK also had this mutation in 50% of all cell types examined. Tsubota et al. reported K1 gene mutation in a Japanese boy with extensive epidermal nevi with EHK. These findings led to the idea that a post-zygotic mutation in one of the BIE genes, keratin 1 or keratin 10, occurs in a clone of cells in VEN. Mutation analysis was not available at the hospital where the patient presented and therefore was not performed.

BIE is a rare autosomal dominant disorder of keratinisation which is characterised by blisters and erythroderma at birth. As the child grows, these are gradually replaced by hyperkeratotic pigmented plaques mostly on the joints, scalp and neck. Despite their histologic likeness to BIE, patients with epidermolytic VEN do not have blistering at birth, which was also evident in the current case. Patients with this type of epidermal nevus may have offspring that have features of classic BIE.

The clinical features of epidermolytic VEN resemble non-epidermolytic VEN, the verrucous stage of incontinentia pigmenti, ichthyosis bullosa of Siemens and ichthyosis hystrix of Curth and Macklin. The lesions of incontinentia pigmenti follow Blaschko’s lines and progress through four different clinical stages (i.e. bullous, verrucous, hyperpigmentation and hypopigmentation). It shows eosinophilic spongiosis on histology. Ichthyosis bullosa of Siemens is a rare hyperkeratotic blistering condition caused by a mutation in the keratin 2e gene. It is a mild variant of BIE and especially involves the flexural sites. Areas of skin peeling showing the “mauserung phenomenon” is typical.

Ichthyosis hystrix of Curth and Macklin exhibits extensive spiky hyperkeratosis with palmoplantar keratoderma and the histology shows hyperkeratosis, binucleate keratinocytes and papillomatosis without epidermolysis.

Treatment of systematised epidermal nevus is largely symptomatic. Topical therapies with corticosteroids, retinoic acid, 5-fluorouracil, calcipotriol and podophyllin have been reported. Abdel Aal and Happle et al. studied the effect of oral retinoids in systematised VEN and found improvement with etretinate within a month and complete regression in 80 days. Surgical excision, carbon dioxide laser and cryotherapy treatment have shown recurrences.

Conclusion
We reported a rare case of bilateral symmetrical VEN with epidermolytic hyperkeratosis on histology. The nevi are always sporadic and not transmitted to the next generation; however, if the mutation occurs in gonadal cells, the offspring of patients with VEN can develop bullous ichthyosiform erythroderma. Therefore, the patient should be counselled at an appropriate age. Extensive skin involvement is also associated with an increased risk of germ-line transmission.

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