Sultan Qaboos University Med J, February 2021, Vol. 21, Iss. 1, pp. e124–126, Epub. 15 Mar 21
Submitted 16 Apr 20
Revision Req. 3 Jun 20; Revision Recd. 25 Jun 20
Accepted 7 Jul 20
https://doi.org/10.18295/squmj.2021.21.01.018

CASE REPORT

Bilateral Systematised Epidermolytic Epidermal *Nevus*

A case report

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وحمة بشروية التنظيم وثنائية الجانب

تقرير حالة

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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 emolients 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.

الملخص: لوحمات البشروية الثؤلولية هي أورام عابية خلقية حميدة تتكون من الخلايا الكيراتينية. يعرض علم الأنسجة في الغالب فرط التقرن والشواك والورم الحليمي ونادرا ما تكون سمات فرط التقرن الحال للبشرة. نعرض هنا تقرير حالة لصبي يبلغ من العمر 6 سنوات مصاب بوحمة بشروية خطية متناظرة ثنائية تتبع خطوط بلاشكو ويظهر فيها فرط التقرن الحال للبشرة بحسب النسجيات. على حد علمنا، يعتبر هذا التقرير الأول للوحمات البشروية الثؤلولية من باكستان.

الكلمات المفتاحية: وحمة بشروية ثؤلولية؛ فسيسائية؛ فرط التقرن الحال للبشرة؛ ورم عابي؛ تقرير حالة؛ باكستان.

Epidermal nevi are congenital hamartomas of embryonal ectodermal origin. Verrucous epidermal nevi (VEN) are composed of hamartomatous proliferation of keratinocytes.[1] VENs are characterised by skin-coloured to tan verrucous papules and plaques arranged in a blaschkoid pattern [Table 1]. The term systematised is used for linear lesions present on more than one site according to Levers classification of epidermal *nevus*.[2] Bilaterally symmetric VEN is also called ichthyosis hystrix. The characteristic histopathology of epidermal nevi exhibits varying acanthosis degrees, papillomatosis and hyperkeratosis and, infrequently, epidermolytic hyperkeratosis.[3] Epidermolytic epidermal nevi are rare and are thought to exhibit a mosaic form of the congenital ichthyosis, bullous ichthyosiform erythroderma (BIE). We present a case of a 6-year-old boy with bilaterally symmetrical VEN following the Blaschko's lines but sparing the face and palmoplantar skin. Histology showed features of epidermolytic hyperkeratosis. This report intends to highlight the rarity of the clinical presentation and characteristic histology of this case.

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

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Table 1: Lesions following a blaschkoid pattern

Macules and patches	Papules and plaques
Incontinentia pigmenti	Lichen striatus
Hypomelanosis of Ito	Adult blaschkitis
Linear and whorled nevoid hypermelanosis	Darier's disease
Nevus depigmentosis	Linear VEN
Linear fixed drug eruption	Inflammatory linear VEN Linear psoriasis Linear lichen planus

VEN = verrucous epidermal nevi.

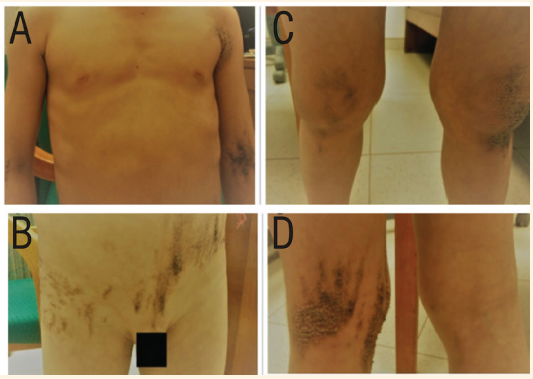

Figure 1: Verrucous hyperpigmented linear plaques in a 6-year-old boy involving (**A**) bilateral cubital fossae, axillae, (**B**) lower abdomen and (**C & D**) flexural and extensor surfaces of knee joints.

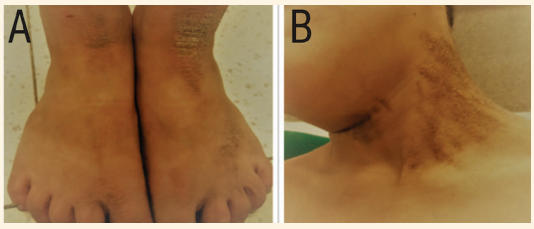

Figure 2: Hyperpigmented papules and plaques on the (**A**) *dorsum* of feet and (**B**) neck following Blaschko's lines.

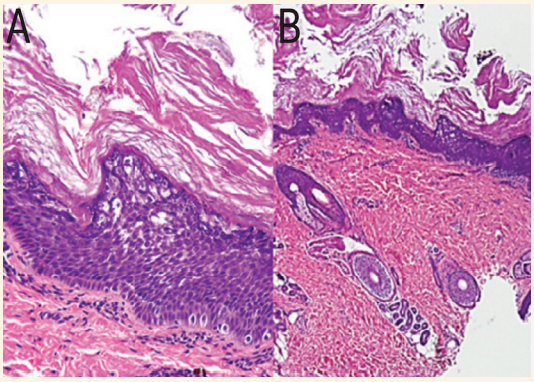

Figure 3: Haemtoxylin and eosin stains showing epidermolytic hyperkeratosis in a 6-year-old boy with (**A**) focal coronoid *lamella* at x100 magnification and (**B**) papillomatosis of the epidermis at x40 magnification.

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*.[4] 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.[5] The term systematised linear epidermal *nevus* is used for linear nevi present on more than one body part.[2]

Recently, keratinocytic epidermal nevi are sub-classified, based on histology, into epidermolytic and non-epidermolytic.[6] 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.[7] 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.[7]

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.[8] 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.[9] 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, while their offspring who had generalised EHK also had this mutation in 50% of all cell types examined.[10] Tsubota *et al*. reported *K1* gene mutation in a Japanese boy with extensive epidermal nevi with EHK.[11] 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.[10–12] 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 alikeness to BIE, patients with epidermolytic VEN do not have blistering at birth, which was also evident in the current case.[12] Patients with this type of epidermal *nevus* may have offspring that have features of classic BIE.[1]

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.[9] 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.[13] Ichthyosis hystrix of Curth and Macklin exhibits extensive spiky hyperkeratosis with palmoplantar keratoderma and the histology shows hyperkeratosis, binucleate keratinocytes and papillomatosis without epidermolysis.[14]

Treatment of systematised epidermal *nevus* is largely symptomatic. Topical therapies with corticosteroids, retinoic acid, 5-fluorouracil, calcipotriol and podophyllin have been reported.[7] 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.[15,16] Surgical excision, carbon dioxide laser and cryotherapy treatment have shown recurrences.[7]

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 icthyosiform 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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