Verrucous Epidermal Nevus – A Brief Review

Yusuf SM, MSc, FWACP;
Dermatology unit, Department of Medicine,
Aminu Kano Teaching Hospital Kano Nigeria.
E-mail: shehumy@yahoo.com

ABSTRACT

Epidermal nevi are hamartomatous lesions arising from embryonic ectoderm. Verrucous epidermal nevus (VEN) is a variant of epidermal nevi. It is exclusively derived from keratinocytes. Verrucous epidermal nevus may be localized to a single small area of involvement or generalized. A few, however, may follow the lines of Blaschko, reflecting the mosaic nature of the condition. No single treatment modality has been shown to be very effective. The aim of this review was to show the various clinical forms of this disorder as it manifests on the dark skinned and review the existing treatment options.

INTRODUCTION

Epidermal nevi (EN) are hamartomas that are characterized by hyperplasia of the epidermis and adnexal structures. Lesions with prominent adnexal components (sebaceous, follicular, and/or apocrine) are sometimes referred to as "organoid", while lesions with primarily epidermal differentiation are known as "non-organoid" or "keratinocytic" nevi[1]. Epidermal nevus occurs in approximately 1 to 3 per 1000 live births.[2] It has no sexual or racial predilection. Most of these nevi occur sporadically, with a few cases in families. Sixty percent of EN occur at birth, while 95% of cases are present by age 7 years. Variants of epidermal nevi include verrucous epidermal nevus (VEN), nevus sebaceous, nevus comedonicus and eccrine nevus.[3,4]

EPIDEMIOLOGY

Verrucous epidermal nevus (VEN) is the commonest variant of epidermal nevus. It arises from embryonic ectoderm as a circumscribed hamartomatous lesions comprised almost exclusively of keratinocytes that tend to become more pigmented and verrucous over the years.[5]

The worldwide incidence is 0.1%-0.5%. Most of these nevi are diagnosed in infancy or early childhood and display growth commensurate with growth of the child. Extension generally ceases by the end of adolescence after which lesions remain stable.[6]

PATHOGENESIS

Epidermal nevi originate from pluripotential germinative cells in the basal layer of the embryonic epidermis. It is believed that a large proportion of epidermal nevi are caused by a mosaicism of activating *FGFR3* mutations in the human epidermis, secondary to a post zygotic mutation in early embryonic development.[7] When such mutation occurred very early in embryonic life, it gives rise to more extensive epidermal nevi and, may potentially affect additional organ systems. Extensive lesions can be unilateral or bilateral, and follow the lines of Blaschko, reflecting the mosaic nature of the condition. Mosaicism arising from somatic mutations early in embryogenesis.[8] Two distinct cell lines result and migrate along developmental lines (Blaschko lines) producing patchy and linear abnormalities. Thus, clinically, presenting as alternating bands of normal and affected skin following blaschko's line. This variant of segmental manifestation has been termed type 1.[9] A second type of segmental manifestation is characterized by a more diffuse clinical presentation of the disease. An explanation of this phenotype is a germ line mutation of the gene which occurs after a post zygotic mutation leading to double inactivation of the gene. Thus resulting in loss of heterozygosity and giving rise, in a segmental area, to a homozygous or hemizygous state of the mutation.[10]

CLINICAL FEATURES

Epidermal nevi most commonly present as a single linear lesion (figures1and 2), but sometimes multiple unilateral or bilateral linear plaques are seen. Most lesions consist of well-circumscribed, hyperpigmented, papillomatous papules or plaques

that are usually asymptomatic. Nevus verrucosus is the most common type, it is characterized by a solitary hyperpigmented, warty plaque measuring 2 to >10cm. The lesions are commonly seen over the trunk, extremities, cervical region and over the face.[11]

Nevus unius lateralis is a variant of linear verrucous epidermal nevus which is confined to one side of the body. The common sites for Nevus unius lateralis are the trunk and limbs. Systematised epidermal naevi are less common and are sometimes known as ichthyosis hystrix.[12] There are multiple lesions that usually arise in a swirled pattern (figure 2 and 3), arising on one (figure 4) or both sides of the body (figure 5), reflecting the mosaic nature of the condition.[3] The lesions in this mosaic form follow segmental and linear skin lines which are V-shaped or a circling pattern on the chest and a linear distribution on the extremities (figure 5).[11] Papillomatous nevi are found in the new born children have flat velvety soft lesions, while in adolescence, they occur as hard keratotic, verruciform lesions. The lesion colour may vary from the coloured type to brown colour.[3,11,12]

Figure1 (a,b,c &d): Solitary hyperpigmented, linear and clustered verrucous papules and plaque of epidermal nevus

Figure 2: Unilateral Verrucous plaques in a swirled distribution following the lines of Blaschko on face.

Figure 3: Verrucous papules and plaques in a swirled distribution on the back of a patient with epidermal nevus

Figure 4 (a&b): Systematized epidermal nevus along the line of Blaschko involving the left side of the body

Figure 5 (a&b): Systematized verrucous epidermal nevus

Figure 6 (a&b): Inflammatory verrucous epidermal nevus

When there are multiple lesions of VEN, there may be associated defects in other tissues, particularly the skeleton and the CNS; the term 'epidermal nevus syndrome' is often applied here. Inflammatory Linear Verrucous Epidermal Nevus (ILVEN) is of rare variety of epidermal verrucous nevus commonly seen in females.[11] Inflammatory Linear Verrucous Epidermal Nevus (ILVEN) is clinically characterized by the appearance of recurrent inflammatory chronic eczematous (figure 6) or psoriasiform conditions which may be commonly unilateral in distribution associated with severe itching.[11,13] Rarely, malignant transformation to basal cell and squamous cell carcinomas may be seen.[14,]

DIAGNOSIS

The diagnosis of an epidermal nevus is generally made clinically. Histologically, these lesions may appear identical to seborrheic keratoses or acanthosis nigricans.[10] Epidermal verrucous nevus can present a great variety of histological patterns; however, hyperkeratosis, acanthosis and papillomatosis are almost always found (figure 7). The rete ridges are elongated, and focal thickening of the granular layer and parakeratotic columns are seen.[3] Frequently, hyperpigmentation in the basal cell layer is evident. Perinuclear vacuolizations can occur in 5 to 19% of epidermal nevi.[15]

TREATMENT

The treatment of epidermal nevi is challenging. Many therapies have been tried with variable outcome. Treatment is most often for cosmetic improvement.[16] Partially improvement may be seen with corticosteroids applied under occlusion or by injection, as well as tretinoin cream applied topically.[3] Oral retinoids may be beneficial in widespread epidermal nevi, but may require life-long therapy.[17] The treatment of choice for small epidermal nevi is surgical excision, dermabrasion, cryosurgery, electrosurgery, and laser surgery.[3,10,18,19,20] However, recurrences can occur months or years after removal. There is also a higher risk of postoperative scarring.[10]

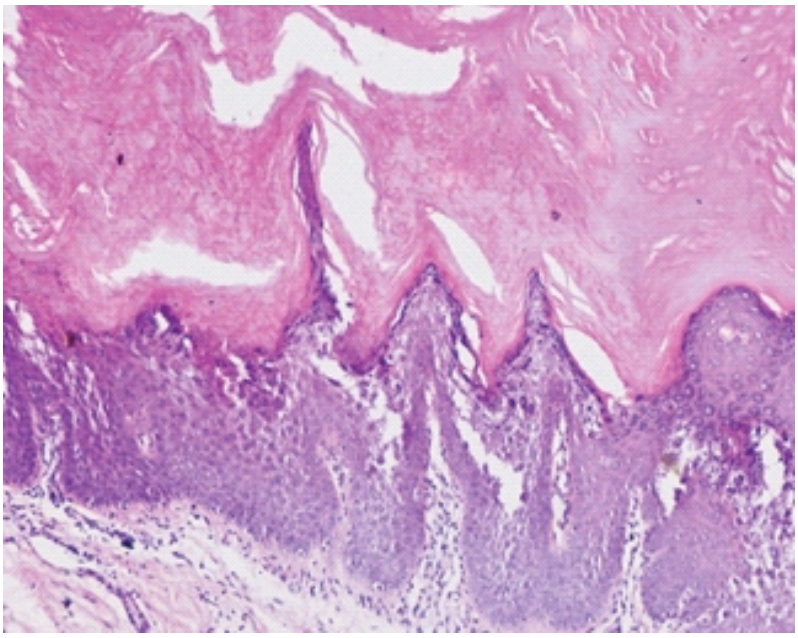

Figure 7: A biopsy specimen showing hyperkeratosis, acanthosis and hyperpigmentation of the basal layer (H&E stain, ×100)

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