

Appearance of Verruca Over Linear Verrucous Epidermal Nevus – An Example of Locus Minoris Resistentiae: A Report of Three Cases

Abstract

Locus minoris resistentiae (LMR) is a site of the body that offers lesser resistance than the rest of the body to the onset of disease. It can be congenital or acquired. Areas of cutaneous mosaicism such as epidermal nevi can act as congenital LMR, leading to the development of inflammatory skin conditions or skin tumors on these. The occurrence of an infectious condition such as warts over nevi is rare. We report three cases of verrucous epidermal nevi (VENs) with the development of verruca overlying the nevus later in life. The three patients had VEN on forehead, preauricular, and presternal area, respectively, since birth, with development of a warty lesion overlying these a few months before presenting to us. Skin biopsy and histopathological examination of the linear verrucous lesion were suggestive of VEN with hyperkeratosis, thickened epidermis, and papillomatosis. There was no evidence of epidermolytic hyperkeratosis or increased sebaceous glands in the dermis. Biopsy of the new warty lesion showed findings of verruca in all the patients. With the above findings, a diagnosis of verruca superimposed on linear VEN was made in all the three cases. The warts were removed by electrofulguration. Several acquired skin disorders, including inflammatory dermatoses, adnexal disorders, and neoplasms, have been shown to occur superimposed on epidermal or sebaceous nevus. Ours is probably the first ever description of a wart occurring on VEN.

Keywords: *Locus minoris resistentiae, verruca, verrucous epidermal nevus*

Introduction

Locus minoris resistentiae (LMR) is a site of the body that offers lesser resistance than the rest of the body to the onset of disease. Trauma, irradiation, healed herpes scars, or chronic lymph stasis commonly act as LMR, thereby leading to localization of numerous inflammatory and neoplastic conditions.^[1] Areas of cutaneous mosaicism can also be sites of LMR. The occurrence of an infectious condition such as warts over areas of cutaneous mosaicism is rare. Here, we report three cases of warts superimposed on linear verrucous epidermal nevi (VENs).

Case Reports

A 25-year-old male patient had hyperpigmented linear papules since birth extending down from the center of forehead adjacent to hairline at a distance of 3 cm. He had developed a single warty lesion on these papules in the last 4 months [Figure 1]. There were no warty lesions elsewhere.

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Another patient, a 35-year-old female had a linear verrucous lesion 6 cm long since birth in the preauricular area extending to the angle of mandible. She developed two filiform warts on the lower portion of the linear lesion in the last 3 months [Figure 2].

Third case, an 18-year-old female had a 5 cm long linear verrucous lesion over the presternal area since birth over which she had a warty lesion in the last 5 months [Figure 3]. Skin biopsy and histopathological examination of the linear verrucous lesion was suggestive of VEN with hyperkeratosis, thickened epidermis, and papillomatosis. There was no evidence of epidermolytic hyperkeratosis. A few sebaceous lobules were seen but no evidence of increased or prominent sebaceous glands was there in the dermis. Biopsy of the new onset warty lesion showed findings of verruca in all the patients [Figure 4a and b]. With the above findings, a diagnosis of verruca superimposed on linear VEN was made in all the three cases. The warts were removed by electrofulguration.

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**P. S. S. Ranugha,
Jayadev B.
Betkerur,
S. Veeranna,
Vijaya Basavaraj¹**

Departments of Dermatology and STD and ¹Pathology, JSS Medical College and Hospital, JSS University, Mysuru, Karnataka, India

Address for correspondence:

*Dr. P. S. S. Ranugha,
Department of Dermatology
and STD, JSS Medical College
and Hospital, JSS University,
Mysore, Karnataka, India.
E-mail: renukaderm@gmail.com*

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Figure 1: A solitary wart over the upper part of nevus close to frontal hairline

Discussion

An immunocompromised district (ICD) is a skin area more vulnerable than the rest of the body either due to genetic or acquired reasons. Its vulnerability mainly consists of a local dysregulation of the immune control, prone to developing opportunistic infections, tumors, or dysimmune reactions (often of granulomatous type) strictly confined to the district itself; however, the opposite may also occur, with systemic immune disorders or malignancies that selectively spare the district (LMR).^[1] An ICD may have either a congenital or a postnatal origin.

The acquired causes responsible for localized immune dysregulation are multifarious, being represented by chronic lymph stasis, herpetic infections, ionizing or UV radiations, burns, all sorts of trauma (especially amputation), tattooing, intradermal vaccinations, and others of disparate nature (e.g., paralytic stroke, poliomyelitis).^[2,3]



Figure 2: Two filiform warts seen over the lowest portion of the nevus at the angle of mandible

There are several examples of skin disorders (infective, inflammatory) occurring in acquired areas of LMR such as lupus vulgaris,^[4] Churg Strauss syndrome over healed scar,^[5] Sweet's syndrome over previously irradiated skin,^[6] *Staphylococcus aureus*-induced bullous dermatosis limited to the sites of glucocorticosteroid-induced striae atrophicae,^[7] granuloma annulare, and dermatophytosis on herpes zoster scar^[8,9] (Wolf's postherpetic isotopic response).

Cutaneous regions with innate anomalies of the skin barrier or with gross anatomic malformations (e.g., primary lymphedema) or with developmental defects that give rise to mutated cell clones (skin mosaicism) are candidates to become congenital ICDs in the lifespan of the individual.^[11-31] Cutaneous mosaicism refers to cutaneous segments or areas (mosaic areas) which house cell populations with antigenic structure and immunologic properties different from those pertaining to the rest of the body. These defects originate in somatic mosaicism, a postzygotic mutational event that causes loss of heterozygosity of some genes, which generates a segment of homozygous or hemizygous tissue where potentially generalized diseases can find an opportunistic location. Well-known examples of congenital cutaneous mosaicism are several types of epidermal nevi, incontinentia pigmenti, and segmental neurofibromatosis.^[10]



Figure 3: Filiform wart on the nevus in the presternal area

VEN are congenital, noninflammatory cutaneous hamartomas composed of keratinocytes. Several acquired skin disorders including inflammatory dermatoses, adnexal disorders, and neoplasms have been shown to occur superimposed on known areas of cutaneous mosaicism (epidermal or sebaceous nevus). Few examples are occurrence of keratoacanthoma on epidermal nevus,^[11] acne on Becker's nevus,^[12] sarcoma on giant congenital melanocytic nevus,^[13] and development of benign and malignant tumors on sebaceous nevus.^[14] The genetic predisposition in these genetically mosaic cells makes them more susceptible to display other pathologies compared with the healthy neighboring cells, the mosaicism lesion acting as an area of LMR.

The occurrence of an infectious lesion over an area of cutaneous mosaicism is rare. In a study of 596 cases of nevus sebaceous (NS), Cribier *et al.* found that benign secondary tumors occurred in 81 cases out of which two cases had developed warts on NS.¹⁴ In a study of 44 cases of NS, 22 had secondary tumors of which three patients had warts.^[15] This is probably the first ever report of warts superimposed over VEN.

Human papillomavirus (HPV) colonization of human skin occurs very early in life and with a great multiplicity of different HPV subtypes. The HPV types of the skin are widespread among humans and give rise to persistent subclinical infections without causing warts or other lesions in the skin of healthy individuals.^[16] HPV DNA was detected in 82% of NS and both the cases of EN^[15] when nested polymerase chain reaction was done on the DNA extracted from nevus skin of 44 cases of NS and 2 cases of VEN.

Whether the commensal HPV infection of the nevus skin got manifest clinically or there was an exogenous acquired HPV infection in the nevus because of localized cutaneous predisposition cannot be explained and needs further studies. However, these three cases further strengthen the concept of areas of cutaneous mosaicism acting as LMR.

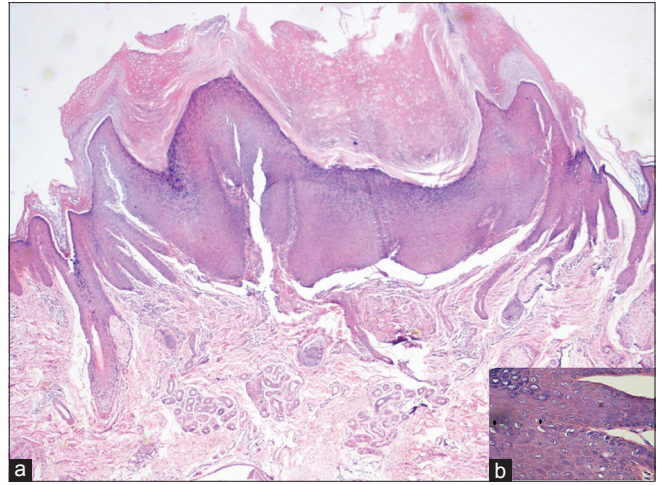


Figure 4: (a) Hematoxylin and eosin (H and E) stain of the warty lesion ($\times 2$) showing hyperkeratosis, acanthosis, and papillomatosis with incurving of rete ridges at the edge of the lesion consistent with verruca; (b) (inset) H and E stain ($\times 20$) showing koilocytes in the epidermis (marked with arrow)

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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