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Nubs and Excrescences-Verrucous Carcinoma

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Editorial

Verrucous carcinoma emerges as a subtype of squamous cell carcinoma involving various cutaneous or mucosal surfaces. Characteristically, the low grade neoplasm is gradually progressive and expounds bland histological features. Cutaneous lesions are associated with superior prognostic outcomes. A verrucous lesion of extensive duration or cyst non responsive to definitive therapy may indicate the occurrence of verrucous carcinoma. Alternatively designated as Ackerman tumour, oral florid papillomatosis or papillomatosis cutis carcinoides, oral verrucous carcinoma may concur with factors as alcohol consumption, cigarette smoking, chewing of areca nut or oral microbiota. Mucosal or genital lesions of verrucous carcinoma may exceptionally concur with human papillomavirus (HPV) DNA wherein viral colonization may be incidental. Additionally, tumefaction may be associated with various inflammatory and neoplastic conditions. Appropriate tumour discernment may be delayed on account of bland histopathological features wherein the lesion may recapitulate certain reactive processes. Cogent tumour categorization upon assessment of superficial or fragmented tissue samples may be challenging.

A male predilection is encountered. Elderly subjects between 50 years to 70 years are implicated. Majority (~75%) of individuals are > 60 years [1,2]. Verrucous carcinoma arises within diverse cutaneous surfaces of sites as the wrist, fingers, nail bed, sole of the foot, ear, nose, eyelid, scalp, gluteal region, anorectal region, penis, vulva, shoulder, axilla, abdominal wall and oral cavity or lip. The feet are preponderantly (~90%) implicated [1,2]. Lesions confined to oral cavity may be designated as Ackerman tumour or oral florid papillomatosis. Neoplasm is associated with somatic mutations within HRAS, PIK3CA and BRAF genes. However, genomic mutations within PTEN, EGFR and GNAS genes appear infrequently within a spectrum of lesions progressing from verrucous carcinoma to differentiated vulvar intraepithelial dysplasia [2,3]. Verrucous carcinoma may be engendered due to carcinogens which intervene with DNA replication and induce single strand breaks within DNA along with genetic mutations which promote tumour growth. Verrucous carcinoma may arise due to chronic inflammation or irritation, repetitive trauma and carcinogens as alcohol, tobacco consumption as smoking and ingestion of areca nut, especially lesions confined to the oral cavity [2,3].

Tumefaction may emerge in concurrence with chronic inflammatory conditions as lichen sclerosus, scarring due to burns, chronic ulcer or infection due to leishmanial spp and low risk variants of human papilloma virus (HPV). Meticulous histological assessment may exceptionally concur with detectable low risk variants of human papilloma virus (HPV) [2,3]. Verrucous carcinoma may arise in concordance with diverse lesions as syringocystadenoma papilliferum (SCAP), congenital venous malformation or cutaneous horn [2,3]. Cutaneous lesions appear as uni-centric, warty neoplasms with significant hyperkeratosis. The gradually progressive neoplasm of extensive duration may or may not exhibit destruction of adjacent or localized soft tissue. Verrucous carcinoma manifests as an exophytic tumour with prominent hyperkeratosis. Specific anatomical sites as the foot or oral cavity may be characteristically implicated [3,4]. Upon gross examination, a fungating, verrucous or polypoid lesion is encountered. Few lesions demonstrate superficial ulceration. Neoplasm may invade subjacent bone with consequent bony destruction [3,4]. Upon microscopy, lesions confined to diverse sites appear morphologically identical. Neoplasm is composed of well differentiated foci of proliferating squamous epithelial cells delineating distinct exophytic and endophytic components. The exophytic component demonstrates focal papillomatosis and significant hyperkeratosis. Frequently, an expansive granular cell layer and focal parakeratosis is observed. The

endophytic component is constituted of blunt projections composed of well differentiated squamous epithelium and deep seated bulbous processes. Neoplastic cellular islands depict a 'pushing' perimeter [3,4]. Tumefaction is composed of enlarged, polygonal squamous epithelial cells pervaded with abundant eosinophilic cytoplasm and enlarged nuclei. Nuclear atypia is minimal and may appear within several layers confined to interface of bulbous tips. Circumscribing stroma appears inflamed and oedematous and is infiltrated by mature lymphocytic cells preponderantly abutting the advancing edge of tumour. Soft tissue intervening the bulbous processes appears significantly decimated and demonstrates decreased vascularity [3,4].

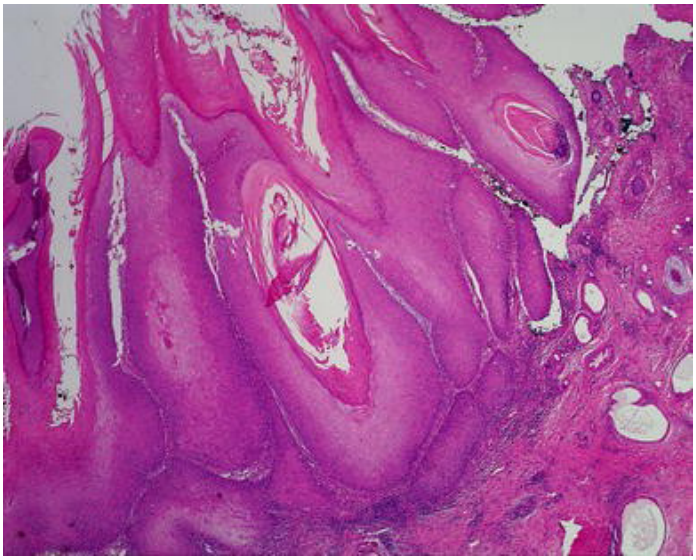

Figure 1: Verrucous carcinoma demonstrating bulbous projections of well differentiated squamous epithelial cells with focal hyperkeratosis and parakeratosis. Tumour cells are enlarged, polygonal and imbued with abundant, eosinophilic cytoplasm and enlarged nuclei delineating minimal nuclear atypia [5].

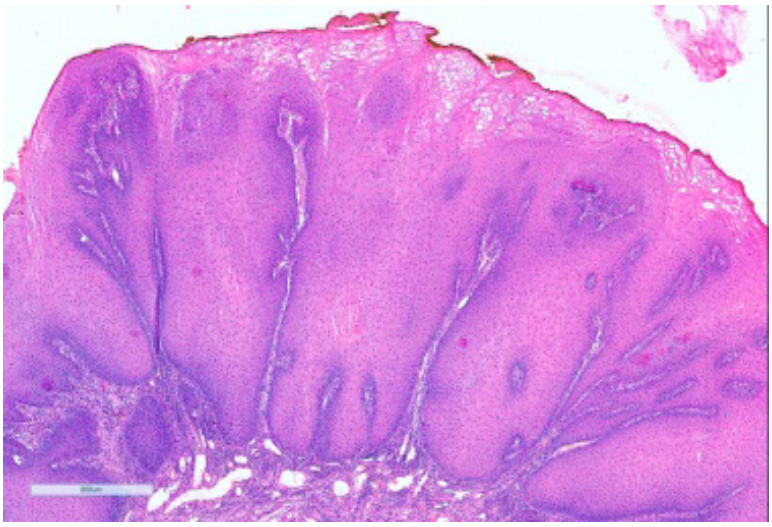

Figure 2: Verrucous carcinoma depicting bulbous projections of well differentiated squamous epithelial cells with focal hyperkeratosis and parakeratosis. Tumour cells appear enlarged, polygonal and impregnated with abundant, eosinophilic cytoplasm with enlarged nuclei expounding minimal nuclear atypia [6].

Staging of Cutaneous Squamous Cell Carcinoma

Tumour staging is contingent to factors as magnitude of lesion, depth of neoplastic invasion, cellular differentiation and accompanying perineural invasion and is categorized as American Joint Committee on Cancer (AJCC) classification (seventh edition) applicable to cutaneous squamous cell carcinoma of the head and neck is comprised of:

- T1: Tumour diameter < 2 centimetres and accompanying < 2 high risk factors.
- T2: Tumour diameter ≥ 2 centimetres or lesion associated with ≥ 2 high risk factors.
- T3: Tumour depicting invasion of orbit, maxillary, mandibular or temporal bone.
- T4: Tumour delineating invasion of axial skeleton or appendicular skeleton or perineural invasion confined to base of skull.

Factors contributing to propensity of tumour emergence appear as tumour thickness > 2 millimetres, lesions with Clark level IV or V, poorly differentiated or undifferentiated tumefaction, lesions associated with perineural invasion or neoplasms confined to ear or lip.

American Joint Committee on Cancer (AJCC) classification (eighth edition) is comprised of:

- T1: Tumour diameter ≤ 2 centimetres.
- T2: Tumour diameter ≥ 2 centimetres and < 4 centimetres.
- T3: Tumour diameter ≥ 4 centimetres or lesions displaying minimally a singular high risk feature.
- T4a: Tumour demonstrating gross invasion of cortical bone or marrow of bones as orbit, maxillary, mandibular or temporal bone.
- T4b: Tumour demonstrating invasion of base of skull or neural foramina confined to skull base.

Features contributing to predilection of tumour emergence appear as perineural invasion, especially within a nerve subjacent to the dermis or nerve ≥ 0.1 millimetre thickness or clinical or radiographic involvement of specific nerves in the absence of invasion or transgression of base of skull, deep seated tumour invasion > 6 millimetre thickness or beyond subcutaneous adipose tissue and minor bony erosion.

Brigham and Women's Hospital (BWH) classification is expounded as:

- T1: Lesions with absence of high risk factors.
- T2a: Lesions associated with singular high risk factor.
- T2b: Lesions associated with two to three high risk factors.
- T3: Lesions demonstrating ≥ 4 high risk factors or bone invasion.

Factors associated with enhanced propensity of tumour emergence appear as tumour diameter ≥ 2 centimetres, poorly differentiated neoplasms, tumours with perineural invasion within nerves ≥ 0.1 millimetre diameter or tumour invasion beyond subjacent adipose tissue [4,7].

Verrucous carcinoma requires segregation from neoplasms as giant condylomata or Buschke-Löwenstein tumour, pseudoepitheliomatous epidermal hyperplasia(PEH),verrucous psoriasis, fungal/ protozoal/ mycobacterial infection associated with extensive pseudoepitheliomatous hyperplasia, keratoacanthoma, conventional or non verrucous subtype of squamous cell carcinoma and carcinoma cuniculatum or epithelioma cuniculatum [7,8]. Upon imaging, an endophytic, deep seated neoplasm is exemplified along with or devoid of bony invasion. Tissue samples obtained with shave or punch biopsy may demonstrate well differentiated squamous epithelial proliferation which requires appropriate clinical correlation and concordance with imaging features. Nevertheless, upon morphological assessment of superficial tissue samples, tumefaction may be misinterpreted as a benign squamous lesion [8,9]. Definitive neoplastic discernment necessitates sampling from deep seated tissue or cogent excision of the tumour. Sampling from deep-seated tissue expounds broad bands of epidermal cellular proliferation along with parakeratosis confined to centric zones. Base of neoplastic proliferation appears enlarged, bulbous and may infiltrate deep seated dermis in a 'pushing' manner [8,9]. Surgical extermination of the lesion is an optimal and recommended mode of therapy. Alternatively, methodologies as cryosurgery, carbon dioxide laser, chemotherapy, intralesional or iontophoretic methods, photodynamic therapy, systemic retinoid therapy or radiotherapy may be suitably adopted as cogent therapeutic manoeuvres [8,9]. Inadequately excised neoplasms are associated with significant proportionate tumour reoccurrence. In contrast to primary neoplasms, repetitive tumours are preponderantly aggressive and accompanied by bony or cartilaginous invasion and significant destruction of circumscribing soft tissue [8,9]. Enlargement of regional lymph nodes is frequently observed and appears indicative of reactive hyperplasia occurring as a consequence of inflammatory reaction to the neoplasm. Distant metastases are exceptionally documented and are preponderantly associated with oral and mucosal lesions. Tumour progression into aggressive squamous cell carcinoma may ensue following radiation therapy or chemotherapy [8,9].

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