

The Variegated Vortex-Squamous Cell Carcinoma

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Squamous cell carcinoma emerges from epidermal keratinocytes demonstrating malignant cytological features and variable cellular differentiation. Tumour grading is contingent to cellular differentiation and focal keratinization.

Additionally designated as cutaneous squamous cell carcinoma, squamous cell carcinoma in situ or Bowen's disease, squamous cell carcinoma frequently emerges within cutaneous zones exposed to sunlight or radiation such as scalp, ear, lip, nose or eyelid. A male predominance is observed [1,2].

Cutaneous squamous cell carcinoma arises due to exposure to ultraviolet radiation which induces genetic mutations within TP53, CDKN2A, NOTCH1 and NOTCH2, EGFR or TERT genes and activates molecular pathways such as RAS, RAF, MEK, ERK and PI3K/AKT/mTOR [1,2].

Besides, chronic immunosuppression, actinic keratosis, albinism, xeroderma pigmentosum, arsenic ingestion, scarring associated with burns, chronic ulceration or chronic inflammation, configuration of sinus tract, infection with human papillomavirus infection and various tars or oils may induce squamous cell carcinoma [1,2].

Typically, squamous cell carcinoma manifests as an erythematous plaque, nodule or ulcer. Attenuated foci of squamous cell carcinoma demonstrate scaly, erythematous, thinned-out papules or plaques. Frequently, an associated precursor lesion such as actinic keratosis, keratinocytic dysplasia or squamous cell carcinoma in situ may be encountered [1,2].

Features on gross examination are characteristic and indicative of disease wherein definitive disease discernment may be achieved by evaluation of shave, punch or excisional tissue specimens [1,2].

Upon gross examination, a hyperkeratotic plaque with superficial scaling is frequently observed. Focal induration, ulceration or haemorrhage may occur [1,2].

Upon microscopy, malignant keratinocytes appear to infiltrate subjacent dermis. Tumefaction may expand inferiorly and appears submerged by superficial epidermal layer [1,2].

Squamous cell carcinoma is subdivided into

- Well differentiated neoplasm which simulates normal squamous epithelium and exhibits abundant keratinization, intercellular bridges, minimal pleomorphism and mitotic activity within basal epithelial layer.
- Moderately differentiated tumefaction depicting focal keratinization, cellular and nuclear pleomorphism and atypia along with cytological features intermediate to well differentiated and poorly differentiated neoplasm.

- Poorly differentiated squamous cell carcinoma exemplifies minimal or absent keratinization, loss of intercellular bridges, significant nuclear atypia and cytological de-differentiation wherein squamous cell origin of tumour cells may be challenging to ascertain [1,2].
- Undifferentiated squamous cell carcinoma demonstrates an absence of keratinization and cytological or nuclear anaplasia. Pertinent immunohistochemistry is required for confirmation of epithelial origin of tumour cells and exclusion of malignant melanoma, lymphoma or undifferentiated sarcoma [1,2].

Commonly, squamous cell carcinoma exhibits diverse histological configurations denominated as

- Low grade, well differentiated neoplasms are comprised of keratoacanthoma, verrucous carcinoma or clear cell squamous cell carcinoma [1,2].
- Advanced grade neoplasms are constituted of acantholytic squamous cell carcinoma, invasive Bowen's disease, spindle cell squamous cell carcinoma, desmoplastic squamous cell carcinoma or adenosquamous carcinoma [1,2].

Infrequently, variants such as lympho-epitheliomatous or pseudo-vascular squamous cell carcinoma, squamous cell carcinoma with sarcomatoid differentiation or squamous cell carcinoma with osteoclast-like cells may be encountered [1,2].

Staging of cutaneous squamous cell carcinoma of head and neck as per eighth edition of American Joint Committee on Cancer is denominated as:

- T1: Tumour magnitude ≤ 2 centimetre.
- T2: Tumour magnitude ≥ 2 centimetre and < 4 centimetre.
- T3: Tumour magnitude ≥ 4 centimetre or association with a high risk feature.
- T4a: Tumefaction exhibiting gross infiltration of cortical bone or bone marrow of maxilla, mandibular orbit or temporal bone, extrinsic muscles of tongue as genioglossus, hyoglossus, palatoglossus or styloglossus, maxillary sinus or facial cutaneous surfaces.
- T4b: Tumefaction exemplifying invasion of base of skull or skull base foramina, masticator space, pterygoid plates or encases internal carotid artery [3,4].

High risk features are designated as perineural invasion of subjacent dermal nerves or nerves ≥ 0.1 millimetre diameter or clinical or radiographic incrimination of specific nerves in the absence of infiltration or transgression of base of skull, deep-seated tumour infiltration beyond subcutaneous adipose tissue or > 6 millimetre depth and minor bone erosion [3,4]:

- NX: Regional lymph nodes cannot be assessed.
- N0: Regional lymph node metastasis absent.
- N1: Metastasis within a singular, ipsilateral lymph node ≤ 3 centimetre magnitude.

- N2a: Metastasis within a singular, ipsilateral lymph node between 3 centimetre to 6 centimetre diameter.
- N2b: Metastasis within multiple, ipsilateral lymph nodes ≤ 6 centimetre diameter.
- N2c: Metastasis within bilateral or contralateral lymph nodes ≤ 6 centimetre diameter.
- N3: Metastasis within a lymph node > 6 centimetre diameter [3,4].
- M0: Distant metastasis absent.
- M1: Distant metastasis present [3,4].

Brigham and Women's Hospital classifies cutaneous squamous cell carcinoma of head and neck as

- T1: Absence of high risk factors.
- T2a: Presence of singular high risk factor.
- T2b: Presence of two to three high risk factors.
- T3: Occurrence of ≥ 4 high risk factors or bony infiltration.

Cogent high risk factors are denominated as tumour dimension ≥ 2 centimetres, poorly differentiated variant of squamous cell carcinoma, perineural invasion ≥ 0.1 millimetre nerve magnitude or tumour infiltration beyond subcutaneous adipose tissue [3,4].

Squamous cell carcinoma is immune reactive to various keratins as AE1/AE3, MNF116, 34 β -E12, CK5, CK5/6, EMA, p63 and p40. Tumefaction is immune non reactive to CAM5.2, CK20, S100 protein, SOX10, MelanA, BerEP4 and α -smooth muscle actin [3,4].

Squamous cell carcinoma requires segregation from conditions as inflammatory dermatoses such as hypertrophic lichen planus, pseudo-epitheliomatous hyperplasia or miscellaneous keratosis as proliferative actinic keratosis, inverted follicular keratosis, clonal seborrheic keratosis or malignant neoplasms as basal cell carcinoma, malignant melanoma, various sarcomas or lymphomas and adnexal tumefaction as eccrine porocarcinoma or microcystic adnexal carcinoma [3,4].

Advanced squamous cell carcinoma can be appropriately treated with Moh's procedure or surgical extermination of lesion with removal of broad perimeter of uninvolved tissue [3,4].

Squamous cell carcinoma can be subjected to curettage, electrodesiccation, cryotherapy or radiation therapy. Inoperable neoplasms can be treated with immunotherapy [3,4].

Surgical extermination of neoplasm is associated with superior outcomes. Enhanced proportionate localized reoccurrence, distant metastasis and tumour-associated mortality may be encountered in certain individuals [3,4].

Tumour magnitude > 2 centimetres enhances possible tumour reoccurrence and distant metastasis. Tumour depth > 2 millimetres is associated with enhanced localized reoccurrence [3,4].

Tumour infiltration beyond subcutaneous adipose tissue is accompanied by enhanced possible distant metastasis. Lymphoid, vascular or perineural invasion with magnitude of incriminated nerves ≥ 0.1 millimetre contributes to emergence of lymph node metastases [3,4].

Poorly differentiated neoplasms exhibit inferior prognostic outcomes [3,4].

Tumefaction occurring within immunosuppressed individuals, emerging within sun-exposed areas as scalp, ear, lip, nose, eyelid, burn scars, ulcers, radiation-induced dermatitis or chronic injuries exemplify enhanced tumour reoccurrence and distant metastasis [3,4].

Reappearance of neoplasms subjected to preceding therapy demonstrate unfavourable prognostic outcomes [3,4].

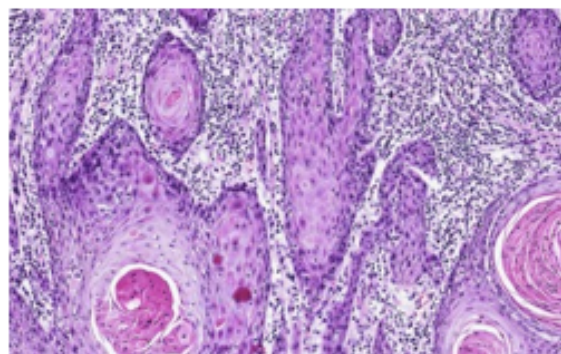


Figure 1: Squamous cell carcinoma depicting keratinized whorls of squamous epithelial cells with nuclear hyperplasia, hyperchromasia and lack of intercellular bridges surrounded by chronically inflamed stroma [5].

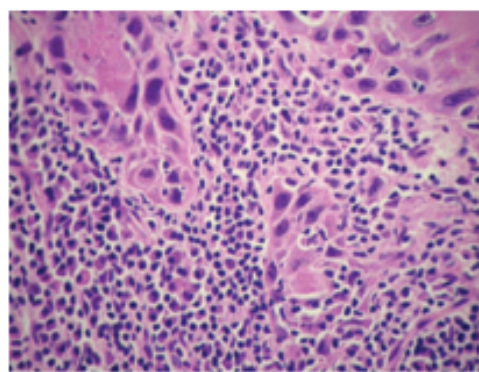


Figure 2: Cutaneous squamous cell carcinoma demonstrating significant cellular anisocytosis, nuclear hyperplasia, anisonucleosis with hyperchromatic nuclei, absent intercellular bridges and circumscribing fibrous tissue infiltrated by lymphocytes and plasma cells [6].

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5. Image 1 Courtesy: Science direct.
6. Image 2 Courtesy: Research gate.

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