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Case Report

Equidistant and Plebeian- Basal Cell Carcinoma

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Basal cell carcinoma is a frequently discerned, malignant, cutaneous neoplasm arising from inter-follicular or follicular epithelium. The locally aggressive neoplasm is associated with minimal mortality wherein distant metastasis to pulmonary parenchyma or bones is exceptional. Tumefaction is comprised of nests and aggregates of basaloid cells with peripheral nuclear palisading circumscribed with fibromyxoid stroma. Additionally designated as basal cell epithelioma, basalioma or fibroepithelioma of Pinkus, ulcerated nodular basal cell carcinoma was initially scripted as 'rodent ulcer'. Moh's micrographic surgical technique is frequently adopted for evaluation of surgical perimeter of tissue samples and is accompanied by superior proportionate 5-year tumour alleviation and decimated reoccurrence [1,2].

Basal cell carcinoma is commonly discerned within Caucasian population demonstrating Fitzpatrick type I and type II cutaneous subtypes [1,2]. Middle aged adults are frequently incriminated wherein proportionate tumour emergence enhances with increasing age. A male predominance is observed with male to female proportion of 1.5:1. Incriminated younger subjects demonstrate a female predisposition. Tumefaction arising within younger individuals is associated with aggressive biological behaviour [1,2].

Basal cell carcinoma commonly emerges upon sun exposed cutaneous surfaces. Nodular variant is preponderant upon head and neck whereas superficial variant incriminates the trunk. Exceptionally, tumefaction is discerned upon ano-genital region, nail unit, palm or sole [1,2]. Basal cell carcinoma initiated from ultraviolet radiation induced carcinogenesis is associated with genomic mutations within TP53, PTCH1, CDKN2A or RAS genes along with activating mutations within SMO gene [1,2]. Multiple neoplasms appear associated with diverse genetic disorders as nevoid basal cell carcinoma syndrome or Gorlin syndrome, xeroderma pigmentosum, Bazex-Dupré-Christol syndrome, oculo-cutaneous albinism, Muir-Torre syndrome, nevus sebaceous or immunosuppression [1,2].

Nodular basal cell carcinoma represents as a pearly-pink or flesh coloured, papule or nodule imbued with arborizing and branching vascular articulations. Characteristically, ulcerated tumefaction exhibits a 'rolled' tumour perimeter [1,2]. Superficial variant represents with scaly macules, patches or plaques superimposed with an erythematous superficial surface [1,2]. Pigmented variant simulates nodular or superficial basal cell carcinoma although the pigmented superficial surface requires segregation from melanoma [1,2]. Untreated tumefaction may engender significant cutaneous, soft tissue and bony destruction with severely disfigured anatomic areas.

Gross appearance of the neoplasm is variable and simulates diverse clinical variants as described [1,2]. Cytological examination exhibits complexes and aggregates of intensely adherent basaloid cells with peripheral palisading. Tumour cells depict enhanced nuclear/cytoplasmic ratio, minimal cellular or nuclear atypia and mitotic activity [1,2]. Basal cell carcinoma exhibits various microscopic subtypes as•nodular or nodulocystic basal cell carcinoma is a circumscribed tumefaction composed of enlarged, solid or cystic, mucin impacted lobules of basaloid cells with peripheral nuclear palisading. Tumour cells depict mild pleomorphism, apoptosis and variable mitotic activity [1,2]. Necrosis can be significant. Cellular lobules may adhere to superimposed epidermis or follicular epithelium. Circumscribing stroma is fibromyxoid wherein a cleft is configured between tumour lobules and encompassing stroma [1,2].

adenoid subtype enunciates a reticulate or pseudo-glandular tumour configuration composed of basaloid cells which may simulate true glandular articulations. Encompassing stroma is mucinous [1,2].

micro-nodular subtype is constituted of miniature nests of basaloid cells with minimal peripheral palisading and absence of retraction artefact. Tumour cell aggregates may diffusely infiltrate subjacent dermis and extend into subcutaneous tissue [1,2]. infiltrative subtype is constituted of miniature, irregular clumps of basaloid cells. Peripheral palisading of tumour cells is restricted. Circumscribing fibromyxoid stroma is loosely configured with significant mucin content. Tumour dissemination is extensive and perineural invasion may occur [1,2]. morpheaform or sclerosing or morphoeic basal cell carcinoma is constituted of attenuated strands or nests of basaloid cells with minimal peripheral palisading. Encompassing stroma is dense and sclerotic. Tumour dissemination is significant and perineural infiltration may ensue [1,2]. keratotic basal cell carcinoma configures horn cysts. Basosquamous or metatypical basal cell carcinoma is a biphasic tumefaction enunciating neoplastic foci of differentiating squamous epithelial cells [1,2]. pigmented basal cell carcinoma is constituted of nodular and superficial variants. Pigmented tumour cell aggregates may colonize with melanocytes and appear admixed with stromal melanophores [1,2]. superficial basal cell carcinoma denominates isolated lobules of basaloid cells which appear to protrude from inferior epidermal perimeter [1,2]. ulcerative basal cell carcinoma delineates focal ulceration and an infiltrative pattern of tumour

evolution. Infrequently, a nodulocystic variant may be associated with ulceration [1,2]. fibroepitheliomas subtype or fibroepithelioma of Pinkus is constituted of anastomosing strands and cords of basaloid cells. Tumour cell clusters appear adherent to superimposed epidermis. Peripheral nuclear palisading along with configuration of follicular, germ-like articulations may occur. Isthmic differentiation is exceptional. Circumscribing stroma is fibrotic and may differentiate towards follicular papillae, especially within zones demonstrating germ-like configurations [1,2] Exceptional variants of basal cell carcinoma manifest as

•pleomorphic or giant cell basal cell carcinoma associated with monster cells expounds significant mitotic activity, apoptosis, cellular pleomorphism and configuration of giant cells. Focal atypia is devoid of prognostic significance [1,2].

•clear cell basal cell carcinoma exhibits focal or comprehensive component of clear cells engendered due to lysosomal degeneration. Tumour cells display clear or finely granular, eosinophilic cytoplasm. Peripheral nuclear palisading is observed [1,2]. signet ring cell subtype is additionally denominated as basal cell carcinoma with myoepithelial differentiation. Tumefaction is comprised of tumour cells with laterally displaced nuclei. Tumour cells are immune reactive to S100 protein, glial fibrillary acidic protein and smooth muscle actin, indicative of myoepithelial differentiation [1,2]. granular basal cell carcinoma is constituted of tumour cells imbued with abundant, granular, eosinophilic cytoplasm [1,2]. basal cell carcinoma with differentiation towards adnexal structures exhibits neoplastic aggregates differentiating towards cutaneous adnexa as sebaceous, follicular, eccrine or apocrine configurations [1,2]. infundibulocystic subtype is additionally termed as basal cell carcinoma with follicular differentiation. Tumefaction displays proliferating basaloid cells configuring anastomosing cords and strands with peripheral nuclear palisading, confined to superficial dermis. Infundibular cysts may be discerned. Characteristically, circumscribing stroma is scanty [1,2]. metaplastic basal cell carcinoma enunciates malignant, metaplastic features confined to circumscribing stroma. Carcinoma-sarcoma is exemplified with foci of chondroid, osteoid and smooth muscle differentiation [1,2]. basal cell carcinoma with matricial differentiation or shadow cell basal cell carcinoma enunciates tumour cells differentiating towards matricial cells of hair follicle with shadow cells and trichohyalin granules. •keloidal basal cell carcinoma demonstrates thick, sclerotic collagen bundles configuring stroma circumscribing tumour cell nests [1,2]. basal cell carcinoma with thickened basement membrane exemplifies tumour cell complexes encompassed with thickened basement membrane [1,2]. base-melanocytic subtype is a tumefaction displaying combined or intermixed basal cell and melanomatous neoplastic components [1,2]. basal cell carcinoma with neuroid category of nuclear palisading delineates centric nuclear palisading simulating nuclear component of schwannoma [1,2].

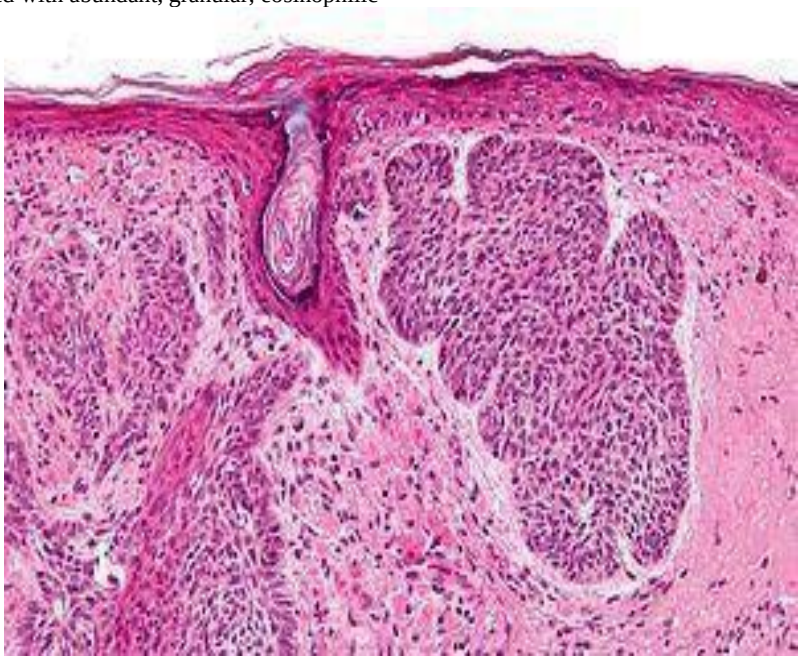

Figure: 1 *Basal cell carcinoma depicting nests of basaloid cells with peripheral nuclear palisading and surrounding fibro myxoid stroma (5).*

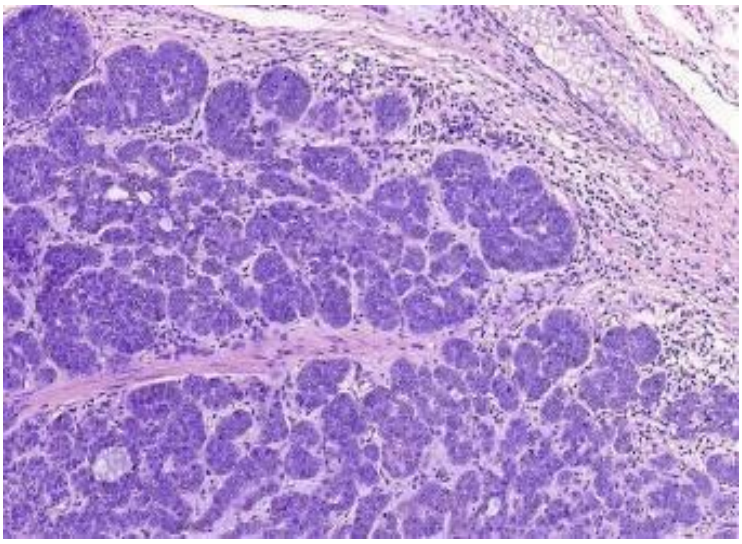

Figure: 2 *Basal cell carcinoma delineating lobules of basaloid cells with centric mucin, peripheral palisading and surrounding fibro myxoid stroma infiltrated with chronic inflammatory cells and cutaneous adnexal structures (6).*

TNM staging of basal cell carcinoma as per American Joint Committee on Cancer eighth edition is designated as [1,2] TX: Primary tumour cannot be assessed Tis: Carcinoma in situ. T1: Tumour ≤ 2cm in greatest dimension T2: Tumour >2cm although ≤4cm in greatest dimension T3: Tumour > 4cm or minor bony erosion or perineural invasion or deep invasion. T4: Tumour with gross cortical bone or marrow invasion or infiltration of skull base or skull base foramina. T4a: Tumour with gross cortical bone or bone marrow invasion T4b: Tumour with skull base invasion or incriminated skull base foramina

•NX: Regional lymph nodes cannot be assessed N0: Regional lymph node metastasis absent •N1: Metastasis in single ipsilateral node≤3cm with absent ENE N2: Metastasis in single ipsilateral node ≤3cm with ENE, >3cm and ≤6cm with absent ENE, metastasis in multiple ipsilateral nodes <6cm with absent ENE or bilateral or contralateral nodes <6cm with absent ENE. N2a: Metastasis in single ipsilateral node ≤3cm with ENE, single ipsilateral node >3cm and ≤6cm with absent ENE
~N2b: Metastasis in multiple ipsilateral nodes <6cm with absent ENE
~N2c: Metastasis in bilateral or contralateral nodes <6cm with absent ENE. N3: Metastasis in lymph node >6cm with absent ENE or single, ipsilateral node >3cm with ENE or multiple, ipsilateral, contralateral or bilateral nodes with ENE or a single, contralateral node with ENE N3a: Metastasis in lymph node >6cm with absent ENE. N3b: Metastasis in single, ipsilateral node >3cm with ENE or multiple, ipsilateral, contralateral or bilateral nodes with ENE or a single, contralateral node with ENE

•M0: Distant metastasis absent M1: Distant metastasis present

Tumour depth (millimetres) is measured from normal granular epidermal layer to deepest point of tumefaction. Deep invasion is defined as tumour depth or thickness> 6millimetres or infiltration beyond subcutaneous adipose tissue. Perineural invasion denominates infiltration of large calibre nerve >0.1millimetre or nerve present beyond the dermis.

Basal cell carcinoma is immune reactive to CK AE1/AE3, BerEP4, p63, p53, CAM5.2, androgen receptor, 34 β-E12, bcl2 or CD10(3,4). Basal cell carcinoma is immune non-reactive to CK20, CK7, CEA, EMA, adipophilin, SOX10, S100 protein, MelanA/MART1, HMB45, CD34 or CD44 [3,4]. Basal cell carcinoma exhibits genomic gains upon chromosome 6p, 6q, 9p, 7 and X chromosome [3,4]. Besides, regional loss within chromosome 9q with inclusion of genomic region 9q22.3 may be discerned, a focus where Patched gene can be mapped [3,4]. Basal cell carcinoma requires segregation from neoplasms such as follicular induction or follicular basal cell hyperplasia, trichoepithelioma, trichoblastoma, desmoplastic trichoepithelioma, basaloid follicular hamartoma, tumours of follicular infundibulum, syringoma, squamous cell carcinoma variants as basaloid, clear cell or sarcomatoid, microcystic adnexal carcinoma, sebaceous carcinoma, Merkel cell carcinoma, adenoid cystic carcinoma, clear cell melanoma, clear cell eccrine porocarcinoma, clear cell hidradenocarcinoma, trichilemmal carcinoma, pilomatrix carcinoma, cylindroma, fibroepithelioma of Pinkus, nevi malignant melanoma malignancies with cutaneous metastasis and cutaneous T cell lymphoma as mycoses fungoides or Bowen's disease. Additionally, inflammatory conditions such as pigmented reticulated seborrheic keratosis, dermatitis, ringworm, intradermal nevus, lichenoid benign keratosis, eczema, actinic keratosis, sebaceous hyperplasia or keratoacanthoma necessitate a demarcation [3,4]. Basal cell carcinoma can be appropriately discerned with cogent evaluation of clinical, dermoscopic and histological features [3,4]. Basal cell carcinoma can be suitably treated with surgical intervention or Moh's micrographic surgical technique. Curettage or electro-desiccation can be adopted for tumours with minimal possible tumour reoccurrence [3,4]. Alternatively, radiation therapy, topical therapy with 5-fluorouracil or imiquimod, photodynamic therapy with aminolevulinic acid, porfimer sodium or nicotinamide and systemic therapy with sonic hedgehog pathway inhibitors as sonidegib or vismodegib can be employed [3,4]. Factors which contribute to prognostic outcomes are tumour magnitude, neoplastic localization, circumscription of tumour perimeter, perineural and lympho-vascular invasion, status of surgical margins, history of non-melanoma cutaneous carcinoma, institution of radiotherapy or PUVA therapy and immunosuppression [3,4].

Cogent histological subtypes of basal cell carcinoma are associated with localized tumour reoccurrence [3,4].Basosquamous, sclerosing or morpheaform, keloidal, infiltrating, basal cell carcinoma with sarcomatoid differentiation and micro-nodular variants enunciate enhanced possible tumour reoccurrence. Nodular, superficial, pigmented, infundibulocystic and fibro-epithelial subtypes are accompanied with minimal tumour reoccurrence [3,4].

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5. Image 1 Courtesy: Libre Pathology
6. Image 2 Courtesy: Pathology Outlines