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Commentary

Big C and Seepage-Acinic Cell Carcinoma

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Acinic cell carcinoma is a low to intermediate grade, malignant epithelial neoplasm of salivary glands characteristically demonstrating serous acinar cell differentiation. A proportion of neoplastic cells depict cytoplasmic zymogen granules.

Acinic cell carcinoma exhibits favourable prognostic outcomes with minimal localized tumour reoccurrence, distant metastasis or metamorphosis into high grade neoplasms.

Acinic cell carcinoma preponderantly incriminates Caucasian population. Median age of disease occurrence is 52 years although no age of tumour emergence is exempt and children or elderly adults are commonly implicated. A mild female predominance is observed with female to male proportion of 1.6:1 [1,2].

Acinic cell carcinoma frequently occurs within parotid gland (80%). Submandibular, sublingual or minor salivary glands are exceptionally involved. Tumefaction may arise within oral cavity, especially upon sites such as buccal mucosa or upper lip [1,2].

Acinic cell carcinoma may be engendered due to preceding exposure to radiation. Alternatively, a familial predisposition is observed [1,2].

Clinically, acinic cell carcinoma represents as a characteristic, gradually progressive tumefaction. Symptoms such as pain, fixation to circumscribing soft tissue or dysfunction of VIIth cranial nerve are infrequently discerned. Regional lymph node metastasis into cervical lymph nodes is uncommon (~10%) [1,2].

Grossly, a well circumscribed, soft, rubbery, tan yellow to pink tumefaction is observed. Majority (85%) of neoplasms are < 3 centimetre diameter although tumour magnitude varies from < 1 centimetre to 13 centimetres. Cut surface is homogenous and may demonstrate foci of haemorrhage or cystic change. Neoplasm is devoid of specific histologic grading system [1,2].

Upon cytological examination, the cellular aspirate demonstrates acinar-like cells which configure miniature groups, loosely cohesive cellular clusters and singular cells. Cells appear enlarged and morphologically simulate normal acinar cells with abundant, finely vacuolated to granular cytoplasm, spherical nuclei and miniature nucleoli. Besides, stripped or bare nuclei simulating lymphocytes appear admixed with the cellular component. Chronic inflammatory infiltrate composed of lymphocytes may be prominent. Foci of laminated calcific concretions or psammoma body-like calcification may be delineated [1,2].

Upon microscopy, neoplasm manifests diverse morphologic patterns as solid, micro-cystic, papillary cystic or follicular. Tumefaction is configured of multiple cellular subtypes such as serous acinar, intercalated ductal, vacuolated, nonspecific glandular and clear cells [1,2].

Enlarged, polyhedral acinar cells are imbued with basophilic, finely vacuolated to granular cytoplasm and eccentric, spherical nuclei with conspicuous nucleoli. Periodic acid Schiff's stain with diastase resistance exhibits focal cytoplasmic reaction [1,2].

Tumour cell aggregates are circumscribed by prominent infiltrate of lymphocytic cells wherein lymphoid proliferation may be randomly disseminated, patchy or diffuse and dense with configuration of well formed lymphoid follicles with germinal centres within the expanse of neoplastic cells [1,2].

Mitotic activity, focal necrosis and significant cellular or nuclear pleomorphism is usually absent [1,2].

Lymph node resection necessitated for appropriately categorizing malignant neoplasms of salivary glands may be described as

- Level I sub classified into sublevel IA composed of submental group of lymph nodes and sublevel IB comprised of submandibular group of lymph nodes
- Level II composed of lymph nodes abutting upper third of internal jugular vein or upper jugular group of lymph nodes, sub classified into sublevels IIA or IIB or ascertained upon dissection of surgical specimen of neck
- Level III constituted of middle jugular group or nodes abutting middle third of internal jugular vein or nodes discernible upon dissection of neck specimen
- Level IV constituted of lower jugular group or nodes abutting lower third of internal jugular vein or nodes detected upon dissection of neck specimen, situated anterior to sternocleidomastoid muscle
- Level V demonstrating lymph nodes confined to posterior triangle, sub classified into sublevel VA and VB
- Level VI exhibiting lymph nodes confined to anterior central compartment designated as pre tracheal and paratracheal nodes along with precricoid or perithyroidal lymph nodes
- Level VII composed of superior mediastinal lymph nodes [2,3].

Extra-nodal extension (ENE) is defined as tumour confined to lymph node with extension into lymph node capsule, circumscribing connective tissue along with or devoid of accompanying stromal reaction.

Extra-nodal extension is categorized into:

- Extra-nodal extension macroscopic (ENEma) with tumour deposits exceeding > 2 millimetre diameter
- Extra-nodal extension microscopic (ENEmi) with tumour deposits ≤ 2 millimetre diameter [2,3].

Residual tumour or tumefaction which remains following curative therapy as surgical extermination of neoplasm is categorized as:

- RX: Residual tumour cannot be assessed
- R0: Residual tumour absent
- R1: Residual tumour assessed with microscopic examination
- R2: Residual tumour assessed upon macroscopic examination [2,3].

Acinic cell carcinoma is immune reactive to pancytokeratin, NR4A3, epithelial membrane antigen (EMA), carcinoembryonic antigen (CEA), DOG1 and SOX10. Tumour cells can be stained with Periodic acid Schiff's stain with diastase resistance [3,4].

Acinic cell carcinoma is immune non reactive to calponin, p63, actin, mammaglobin or S100 protein [3,4].

Acinic cell carcinoma demonstrates repetitive genetic rearrangements of t(4;9)(q13;q31) with consequent chromosomal translocation of active enhancer regions emerging from secretory Ca binding phosphoprotein (SCPP) genetic cluster into region upstream of nuclear receptor subfamily 4 group A member 3 (NR4A3) with consequent overexpression of NR4A3 upon immunohistochemistry [3,4].

Acinic cell carcinoma requires segregation from neoplasms such as secretory carcinoma, normal acinar elements, mucoepidermoid carcinoma, epithelial myoepithelial carcinoma, myoepithelioma, oncocytoma, metastatic clear cell renal cell carcinoma or thyroid follicular neoplasms [3,4].

Acinic cell carcinoma can be suitably discerned upon ultrasonography, computerized tomography (CT) or magnetic resonance imaging (MRI) which is optimal in delineating presence and extent of tumefaction. In contrast to CT, MRI is advantageous in evaluating tumour infiltration of adjacent anatomic structures [3,4].

Fine needle aspiration cytology (FNAC) or core needle tissue sampling is minimally sensitive when adopted for detecting diseases of parotid gland. Appropriate neoplastic discernment can be challenging due to morphologic concurrence with normal acini or tumour cells devoid of secretory granules [3,4].

Neoplasms depicting transformation into high grade lesions may be aptly discerned with aforesaid investigative modalities.

Upon ultrasonography, a well demarcated, lobular, hypoechoic, heterogeneous, inadequately vascularized neoplasm is observed. Computerized tomography (CT) enunciates non specific features which may concur with benign neoplasms. Preponderantly, a solid to cystic tumefaction may demonstrate focal areas of minimal attenuation concordant to cystic degeneration or haemorrhage within the tumefaction [3,4].

Postoperative positron emission tomography (PET) is beneficially adopted to categorize metamorphosis into high grade neoplasms.

Surgical manoeuvers as resection of parotid gland appear optimal for tumour detection [3,4].

Acinic cell carcinoma is appropriately treated with comprehensive surgical extermination of the neoplasm. Radiotherapy is indicated for incompletely eradicated or metastatic neoplasms [3,4].

Systemic therapy is applicable for high grade tumefaction, tumour occurrence within surgical perimeter, advanced disease stage or neoplasms depicting distant metastasis [3,4].

Acinic cell carcinoma exhibits 5 year survival at ~ 97% with localized reoccurrence at ~33% and distant metastasis within ~16% tumefaction. Tumour reoccurrence is delayed and neoplasm may reappear within several years or decades following initial tumour detection [3,4].

Factors contributing to adverse prognostic outcomes are designated as tumour encountered within males beyond > 45 years, tumour magnitude at initial representation > 3 centimetres, tumour necrosis, nuclear pleomorphism and mitotic activity > 2 per 10 high power fields, decimated lymphocytes within tumour stroma, Ki67 proliferative index > 5%, neoplasms with vascular or perineural invasion, extracapsular tumour extension, tumour emergence within surgical perimeter, tumefaction depicting metamorphosis into high grade lesions, infiltration of base of skull or distant metastasis [3,4].

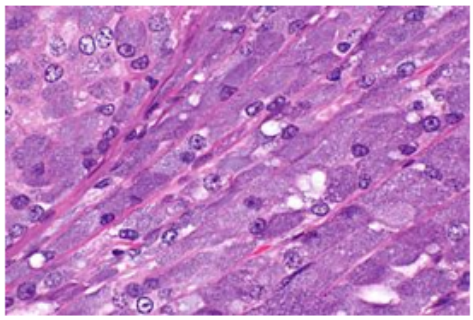

Figure 1: *Acinic cell carcinoma depicting enlarged acinar cells imbued with secretory granules, enlarged spherical nuclei and conspicuous nucleoli [5].*

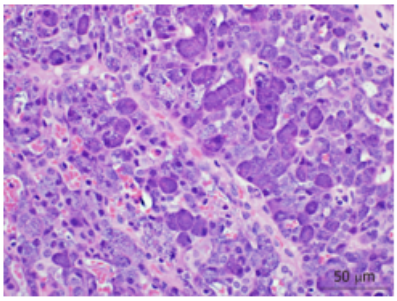

Figure 2: *Acinic cell carcinoma depicting an acinar pattern configured of secretory cells imbued with granular, basophilic cytoplasm, spherical nuclei and conspicuous nucleoli traversed by fibrous tissue septa [6].*

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5. Image 1 Courtesy: Libre Pathology.

6. Image 2 Courtesy: Baishideng Publishing Group.

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