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Commentary

Canker and Conglomeration-Epithelial Myoepithelial Carcinoma

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Epithelial myoepithelial carcinoma is an uncommonly discerned, primary, malignant, biphasic salivary gland neoplasm constituted of intrinsic luminal ductal epithelial cells surrounded by extraneous myoepithelial cells. The adjuvant terminology of adenomyoepithelioma appears debatable and is not recommended.

Epithelial myoepithelial carcinoma manifests up to 2% of salivary gland tumours.

The infrequent, biphasic, primary salivary gland neoplasm comprised of an amalgamation of epithelial cells and myoepithelial elements depicts superior prognostic outcomes.

Inferior prognostic outcomes are associated with factors such as tumour arising within minor salivary glands, enlarged tumefaction > 4 centimetre diameter, elevated proliferation index, tumour cells entrapped within resected surgical margins or high grade neoplastic transformation.

Mean age of disease emergence is 64 years although no age of disease occurrence is exempt. A mild female preponderance is observed with male to female proportion of 1:1.6 [1,2].

Epithelial myoepithelial carcinoma preponderantly incriminates major salivary glands as the parotid (70%) or submandibular gland. Besides, minor salivary glands confined to palate or upper aero-digestive tract may be implicated [1,2].

Epithelial myoepithelial carcinoma is posited to arise from intercalated ducts. Nearly 85% of neoplasms depict HRAS genetic mutation.

Epithelial myoepithelial carcinoma demonstrates HRAS genetic mutation confined to codon 61. Besides, chromosomal mutations within PLAG1 or HMGA2 may be observed. Exceptionally, SMARCB1 genomic deletion and genetic mutations within FBXW7 or TP53 may occur.

Epithelial myoepithelial carcinoma of salivary gland may arise de novo or in concurrence with pre-existing pleomorphic adenoma [1,2].

Generally, tumefaction manifests as a unilateral, painless, gradually progressive neoplasm. Exceptionally, symptoms such as facial nerve palsy or lymphadenopathy may ensue, indicative of high grade neoplastic transformation [2,3].

Cytological assessment is unsatisfactory and proportionate false negative diagnoses are significant. Tumefaction may be misinterpreted as pleomorphic adenoma on account of concordant cytological features.

Smears depict bland cytological features and are composed of biphasic clusters of ductal epithelial cells admixed with enlarged, clear myoepithelial cells. Cellular aggregates are intermingled with naked myoepithelial cell nuclei and scanty fragments of stroma. Occasionally, globules of hyalinised, basal luminal substance may be encountered [2,3].

Frozen section is not recommended as appropriate tumour discernment may be challenging [3,4].

Grossly, the lobulated tumefaction may emerge as a partially encapsulated, firm, grey to tan, rubbery tumefaction. An estimated 30% neoplasms depict foci of cystic change [3,4].

Upon microscopy, tumour cells are bi-layered and composed of miniature luminal cells permeated with eosinophilic cytoplasm and extraneous myoepithelial cells pervaded with clear, glycogen rich cytoplasm. Intracytoplasmic glycogen can be highlighted by periodic acid Schiff's stain (PAS+) with diastase sensitivity.

Generally, epithelial cell component is comprised of sheets and solid nests of significantly atypical tumour cells. Elevated mitotic activity and focal tumour necrosis may be discerned [3,4].

Myoepithelial cell component is frequently comprised of spindle shaped cells or clear cells. Tumefaction exhibits foci of basement membrane-like hyalinised, intercellular matrix.

An estimated 20% of neoplasms depict foci of high grade transformation, indicative of inferior prognostic outcomes [3,4].

Contingent to proportionate epithelial cell and myoepithelial cell component, cogent morphologic subtypes appear as

- Classic subtype.
- Epithelial dominant subtype.
- Myoepithelial dominant subtype.
- Tubular, glandular or solid growth pattern.

Besides, papillary zones or cystic areas may be represented [3,4].

Additional morphological variants manifest as

- Oncocytic variant incriminating elderly subjects. Tumefaction represents with papillary configuration and focal calcification. Luminal cells are pervaded with dense, granular cytoplasm.
- Apocrine variant is constituted of ductal cells permeated with bright, eosinophilic cytoplasm, apical snouts and intra-luminal secretions. Neoplasm displays cribriform to solid pattern of tumour evolution. Tumour cells appear immune reactive to androgen receptor (AR) or gross cystic disease fluid protein 15 (GCDFP-15). Exceptionally, foci of squamous differentiation, sebaceous differentiation or ancient cells with Verocay-like bodies may be delineated [3,4].

Generally, ultrastructural examination appears superfluous for cogent neoplastic discernment. Ductal epithelial cells appear to adhere with junctional complexes or desmosomes and demonstrate microvilli situated upon the luminal surface. Myoepithelial cells are permeated with abundant glycogen, appear electron lucent and are pervaded with cytokeratin filaments. Besides, subplasmalemmal plaques or foci of multi-layered basal lumina may be exemplified [3,4].

Benign Epithelial Tumours	Malignant Epithelial Tumours
Pleomorphic adenoma	Mucoepidermoid carcinoma
Basal cell adenoma	Adenoid cystic carcinoma
Warthin tumour	Acinic cell carcinoma
Oncocytoma	Secretory carcinoma
Salivary gland myoepithelioma	Micro-secretory adenocarcinoma
Canalicular adenoma	Polymorphous adenocarcinoma
Cystadenoma of salivary gland	Hyalinising clear cell carcinoma
Ductal papilloma	Basal cell adenocarcinoma
Sialadenoma papilliferum	Intra-ductal carcinoma
Lymphadenoma	Salivary duct carcinoma
Sebaceous adenoma	Myoepithelial carcinoma
Intercalated duct adenoma and hyperplasia	Epithelial-myoepithelial carcinoma
Striated duct adenoma	Mucinous adenocarcinoma
Sclerosing polycystic adenoma	Sclerosing micro-cystic adenocarcinoma
Keratocystoma	Carcinoma ex pleomorphic adenoma
Sialolipoma (mesenchymal tumour of salivary gland)	Carcinosarcoma of salivary glands
	Sebaceous adenocarcinoma
	Lympho-epithelial carcinoma
	Squamous cell carcinoma
	Sialoblastoma
	Salivary carcinoma (NOS) and emerging entities

Table: *WHO classification of salivary gland tumors (5th edition) [3].*

Ductal epithelial cells appear immune reactive to cytokeratin AE1/AE3, epithelial membrane antigen (EMA) or DOG1. Myoepithelial cells appear immune reactive to p63, smooth muscle actin (SMA), calponin, DOG1, CK5/6, p40 or smooth muscle myosin heavy chain (SMMHC). Epithelial cells and myoepithelial cells appear immune reactive to S100 protein or SOX10.

Epithelial myoepithelial carcinoma is immune non reactive to PAX8, HER2, GATA3, KIT or androgen receptor (AR) [5,6].

Epithelial myoepithelial carcinoma of salivary gland requires segregation from neoplasms such as pleomorphic adenoma, adenoid cystic carcinoma, basal cell adenoma or clear cell variant of mucoepidermoid carcinoma [5,6].

Epithelial myoepithelial carcinoma can be appropriately discerned with cogent clinical examination. Additionally, radiographic investigations as magnetic resonance imaging (MRI) or minimally invasive manoeuvers as fine needle aspiration cytology (FNAC) appear as unsatisfactory measures for obtaining a definitive, preoperative neoplastic categorization [5,6].

Epithelial myoepithelial carcinoma can be appropriately treated with comprehensive surgical eradication of the neoplasm.

Adjuvant radiotherapy may be beneficially adopted in order to decimate localized or regional tumour reoccurrence although proportionate survival appears unaltered.

Epithelial myoepithelial carcinoma of salivary gland is associated with a mean survival of up to 165 months. Majority (~81%) subjects appear disease free at 15 years following initial tumour detection [5,6].

Factors predictive of decimated disease free survival are comprised of

- Status of surgical margins.
- Neoplasms delineating lymphatic and vascular invasion.
- Occurrence of tumour necrosis.
- Myoepithelial anaplasia demonstrated as > irregular nuclear membranes, coarse nuclear chromatin, presence of macro-nucleoli and three times variation or magnification of nuclear magnitude.

Also, factors contributing to decimated disease free survival are composed of age exceeding > 80 years upon initial tumour discernment, incrimination of African American population or adoption of nonsurgical therapeutic modalities [5,6].

Adverse prognostic outcomes are associated with tumours arising within minor salivary glands, enlarged tumefaction > 4 centimetre diameter, elevated proliferation index, status of excised surgical perimeter with entrapped tumour cells or malignant metamorphosis into high grade neoplasm [5,6].

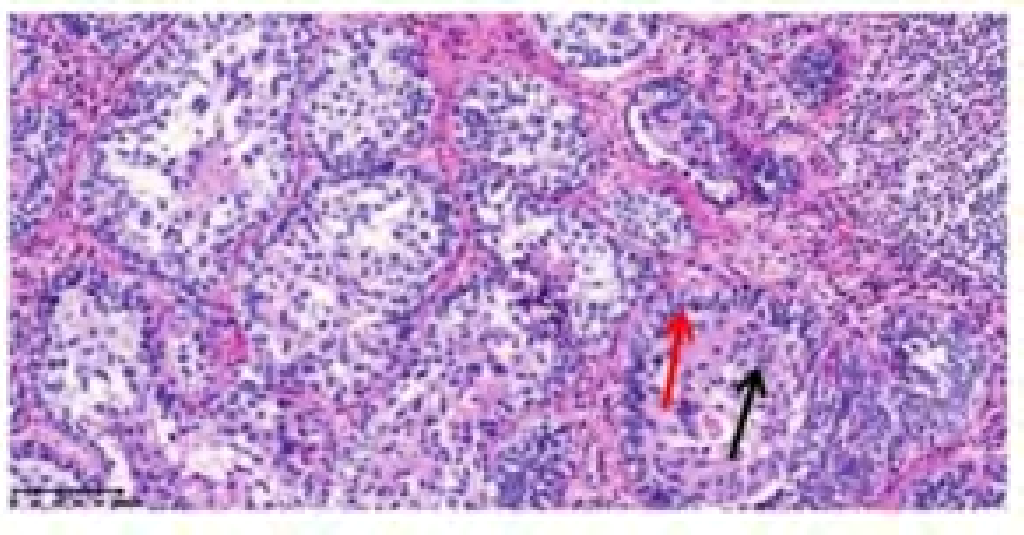

Figure 1: *Epithelial myoepithelial carcinoma demonstrating nests and aggregates of intrinsic epithelial cells incorporated with eosinophilic cytoplasm and an extrinsic layer of myoepithelial cells permeated with glycogen rich cytoplasm encompassed by abundant, fibrotic stroma [7].*

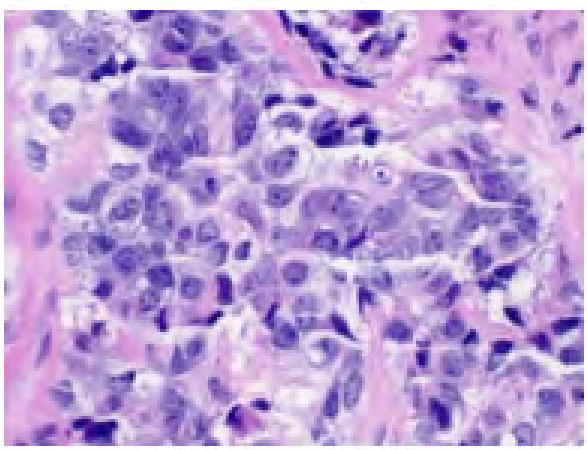

Figure 2: *Epithelial myoepithelial carcinoma delineating aggregates and clusters of innate epithelial cells imbued with eosinophilic cytoplasm and nuclear atypia and an extraneous layer of myoepithelial cells with clear, glycogen rich cytoplasm surrounded by abundant, fibrotic stroma [8].*

Bibliography

1. Sun J., *et al*. "Epithelial-Myoepithelial Carcinoma of the Submandibular Gland: Case Report". *Journal of Nippon Medical School* 88.3 (2021): 238-241.

2. Wockner RS., *et al*. "Epithelial-myoepithelial carcinoma of the maxillofacial and sinonasal region: a systematic review of presenting characteristics, treatment modalities, and associated outcomes". *International Journal of Oral and Maxillofacial Surgery* 52.1 (2023): 1-12.

3. Nishida H., *et al*. "Histopathological Aspects of the Prognostic Factors for Salivary Gland Cancers". *Cancers (Basel)* 15.4 (2023): 1236.

4. Okuyama K., *et al*. "Epithelial-Myoepithelial Carcinoma of the Minor Salivary Glands: Case Series with Comprehensive Review". *Diagnostics (Basel)* 11.11 (2021): 2124.

5. Wang F., *et al*. "Clinical and pathological analysis of 10 cases of salivary gland epithelial-myoepithelial carcinoma". *Medicine (Baltimore)* 99.41 (2020): e22671.

6. Lee YS., *et al*. "Epithelial-myoepithelial carcinoma originating from a minor salivary gland in the nasal septum: A case report and literature review". *Medicine (Baltimore)* 99.5 (2020): e19072.

7. Image 1 Courtesy: Frontiers.com.

8. Image 2 Courtesy: Webpathology.com.

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