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Commentary

The Transitioned Slabber-Myoepithelial Carcinoma-Salivary Gland

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Received: June 13, 2023; **Published:** June 22, 2023

Myoepithelial carcinoma of salivary gland emerges as a carcinoma constituted of myoepithelial cells in entirety or demonstrating an almost comprehensive population of myoepithelial cells. Myoepithelial carcinoma of salivary gland exhibits an infiltrative pattern of tumour growth.

Tumefaction may arise *de novo* or as myoepithelial carcinoma ex pleomorphic adenoma. Generally, myoepithelial carcinoma appears as an under-reported entity. Additionally, the terminology of malignant myoepithelioma appears debatable and non advocated.

Comprehensively composed of myoepithelial cells, myoepithelial carcinoma of salivary gland is devoid of a contemporary, well defined grading system.

Salivary gland myoepithelial carcinoma is subcategorized as myoepithelial carcinoma *de novo* or myoepithelial carcinoma ex pleomorphic adenoma. An estimated > 50% neoplasms exhibit PLAG1 genetic fusion.

Myoepithelial carcinoma of salivary gland may incriminate paediatric subjects, adolescents or elderly population and is discerned between 14 years to 90 years with median age of disease representation at 59 years. A specific gender predilection is absent. Myoepithelial carcinoma constitutes ~ 4% of salivary gland neoplasms [1,2].

Genetic fusion partners emerge as FGFR1, TGFBR3, ND4 or diverse genes. Additionally, clear cell myoepithelial carcinoma may exhibit EWSR1 genomic fusion. Few neoplasms depict HMGA2 genetic fusion. Myoepithelial carcinoma of salivary gland commonly emerges within parotid gland which displays up to three fourths (73%) of lesions.

Minor salivary glands, especially palatal glands and submandibular gland may be implicated in decreasing order of frequency, subsequent to incrimination of parotid gland.

Clinical symptoms are generally non specific. Commonly, a painless tumefaction may be represented [1,2].

Cytological examination depicts a hyper cellular tumefaction constituted of myoepithelial cells in entirety. Constituent myoepithelial cells demonstrate an admixture of plasmacytoid cells, epithelioid cells or spindle shaped cells exemplifying nuclear pleomorphism. Mitotic figures may be delineated. Singular neoplastic cells or miniature cell groups may be intermingled within scanty, metachromatic stroma [1,2].

Grossly, myoepithelial carcinoma of salivary gland exhibits a nonspecific countenance. Frequently, tumefaction represents as an expansible, lobulated to multinodular, grey/white or beige mass. Tumour perimeter may be inadequately defined. An infiltrative tumour margin is encountered [2,3].

Upon microscopy, myoepithelial carcinoma exhibits distinct tumour invasion which typically exemplifies an expansible, infiltrative, multinodular pattern of tumour growth. Besides, infiltration of singular cells or miniature cellular clusters may ensue. Desmoplastic stromal reaction is exceptionally observed [2,3].

Tumour nodules frequently display a hypo-cellular centric zone confined within circumscribing hyalinised stroma. Foci of bland tumour necrosis may be encompassed by a hyper-cellular, peripheral zone.

Hyper-cellular centric zone of a neoplastic nodule is permeated with aggregates of tumour necrosis. Occurrence of tumour necrosis appears indicative of high grade myoepithelial carcinoma [2,3].

Myoepithelial carcinoma is constituted almost entirely of myoepithelial cells with varying cytological features as clear cells, epithelioid cells, plasmacytoid cells or spindle shaped cells. Intervening stroma appears as hyalinised, myxoid or myxochondroid, as commonly encountered within myoepithelial carcinoma *de novo* and myoepithelial carcinoma ex pleomorphic adenoma [2,3].

Generally, neoplasm displays distinct architectural patterns as solid, trabecular, cords or nests with dissemination of singular cells. A component of pre-existing or residual pleomorphic adenoma component may be enunciated within myoepithelial carcinoma ex pleomorphic adenoma [3,4].

TNM staging of malignant salivary gland tumours is designated as [3,4]:

Primary tumour

- TX: Primary tumour cannot be assessed.
- T0: No evidence of primary tumour.
- Tis: Carcinoma *in situ*.
- T1: Tumour is miniature, non invasive and ≤ 2 centimetre in greatest dimension.
- T2: Tumour is enlarged, non invasive and between 2 centimetres to 4 centimetres in greatest dimension.
- T3: Tumour is > 4 centimetres and < 6 centimetres in greatest dimension, enlarged and invades adjacent anatomical structures with sparing of 7^{th} cranial nerve or facial nerve.
- T4a: Tumour of any magnitude which infiltrates adjoining cutaneous surface, maxilla or mandible, external auditory canal or facial nerve.
- T4b: Tumour infiltrates base of skull, adjacent bones and encases carotid artery or neighbouring arteries.

Regional lymph nodes

- NX: Regional lymph nodes cannot be assessed.
- N0: Regional lymph node metastasis absent.
- N1: Regional lymph node metastasis present into singular ipsilateral lymph node as the primary tumour wherein magnitude of incriminated lymph node is ≤3 centimetres.

- N2: is comprised of
  - N2a: Regional lymph node metastasis into singular ipsilateral lymph node as the primary tumour wherein magnitude of incriminated lymph node is ≤3 centimetres and tumour extends beyond the lymph node.
  - N2b: Regional lymph node metastasis into > singular ipsilateral lymph node as the primary tumour wherein magnitude of incriminated lymph node is ≤ 6 centimetres and tumour invasion beyond the lymph node is absent.
  - N2c: Regional lymph node metastasis into > singular ipsilateral or contralateral lymph node with magnitude of incriminated lymph node ≤ 6 centimetres and tumour invasion beyond lymph node is absent.
- N3 is categorized as
  - N3a: Regional lymph node metastasis > 6 centimetre in greatest dimension with absent tumour invasion beyond lymph node.
  - N3b: Regional lymph node metastasis into singular, ipsilateral lymph node > 3 centimetre in greatest dimension with tumour invasion beyond the lymph node OR regional lymph node metastasis into> singular, ipsilateral, contralateral or bilateral lymph node as the primary tumour ≤ 3 centimetre in greatest dimension with tumour invasion beyond the lymph node OR regional lymph node metastasis into singular, contralateral lymph node ≤3 centimetre magnitude with tumour extension beyond the lymph node.

Distant metastasis

- MX: Distant metastasis cannot be assessed.
- M0: Distant metastasis absent.
- M1: Distant metastasis present into sites as pulmonary parenchyma.

Staging of malignant salivary gland tumours is designated as

- Stage 0: Tis, N0, M0
- Stage I: T1, N0, M0
- Stage II: T2, N0, M0
- Stage III: T3, N0, M0 OR T0, T1, T2, T3, N1, M0
- Stage IVA: T0, T1, T2, T3 or T4a, N2, M0 OR T4a, N0 or N1, M0
- Stage IVB: Any T, N3, M0 OR T4b, any N, M0
- Stage IVC: Any T, any N, M1.

Myoepithelial carcinoma of salivary gland is immune reactive to cytokeratin as AE1/AE3, CAM5.2 and myoepithelial immune markers as S100 protein, calponin, smooth muscle actin (SMA), glial fibrillary acidic protein (GFAP), p63, p40, SOX10 or PLAG1.

Neoplastic cells appear immune non reactive to melanocytic markers as human melanoma black 45 (HMB45) antigen or melan A.

Genetic fusion of PLAG1 is commonly discerned and is encountered in ~50% of myoepithelial carcinoma *de novo* or myoepithelial carcinoma ex pleomorphic adenoma [4,5].

Fluorescent *in situ* hybridization (FISH) can appropriately discern EWSR1 genomic rearrangements. Nevertheless, ascertainment of corresponding genomic fusion transcripts may be challenging and debatable.

Myoepithelial carcinoma of salivary gland requires segregation from neoplasms such as myoepithelioma, pleomorphic adenoma, polymorphous adenocarcinoma or myoepithelial tumour of soft tissue [4,5].

Cogent diagnosis may be obtained upon precise surgical tissue sampling with ascertainment of tumour invasion and concurrence of pure, singular myoepithelial cell population within the neoplasm.

Upon computerized tomography (CT), a solitary, lobulated or multinodular tumour mass with partially, poorly defined perimeter and heterogeneous image enhancement is encountered [4,5].

Myoepithelial carcinoma of salivary gland can be appropriately subjected to surgical extermination of the neoplasm. Obtaining a tumour free surgical perimeter is optimal, recommended and advisable.

Myoepithelial carcinoma of salivary gland exemplifies an aggressive clinical course. Localized tumour reoccurrence appears in around one third instances whereas distant metastasis may ensue in up to 27% neoplasms. In contrast to regional metastasis, distant metastasis are frequently observed [4,5].

Factors contributing to adverse prognostic outcomes appear as occurrence of myoepithelial carcinoma ex pleomorphic adenoma, tumour necrosis, elevated mitotic index > 4 per 10 high power fields and tumour cells confined to surgical perimeter [4,5].

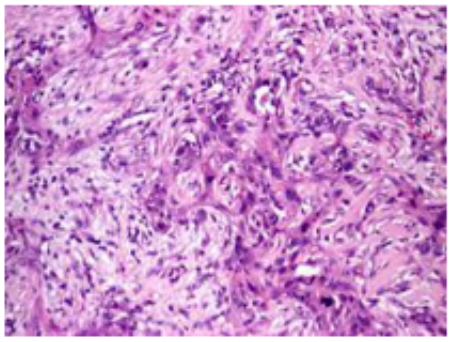

Figure 1: *Myoepithelial carcinoma demonstrating trabeculae and cords composed of myoepithelial cells admixed with spindle shaped cells. Surrounding stroma is myxoid and fibroblastic with a hypo-cellular centric zone [6].*

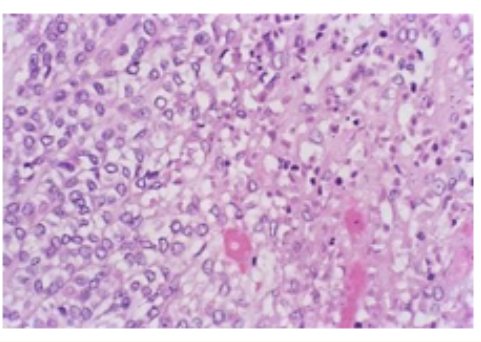

Figure 2: *Myoepithelial carcinoma exhibiting cords and aggregates of myoepithelial cells and spindle shaped cells intermingled with hyalinised and fibrotic stroma [7].*

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6. Image 1 Courtesy: Research gate.

7. Image 2 Courtesy: Medscape.

Volume 22 Issue 7 July 2023