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Editorial

Plenary and Malevolent-Myoepithelial Carcinoma Salivary Gland

Anubha Bajaj*

Consultant, Histopathologist, A.B., Diagnostics, India

***Corresponding Author:** Anubha Bajaj, Consultant, Histopathologist, A.B., Diagnostics, India.

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Myoepithelial carcinoma of salivary gland emerges as a malignant neoplasm singularly constituted of myoepithelial cells which demonstrates an infiltrative pattern of tumour evolution. Myoepithelial carcinoma of salivary gland may arise de novo or as myoepithelial carcinoma ex pleomorphic adenoma. PLAG1 genetic fusion is encountered in >50% neoplasms. The alterative terminology of malignant myoepithelioma is not recommended. Currently, an acceptable, well defined tumour grading system is absent. Myoepithelial carcinoma configures around 4% of salivary gland neoplasms. Nevertheless, tumour frequency may be underrated as myoepithelial carcinoma can be underdiagnosed. Myoepithelial carcinoma may incriminate paediatric subjects. Median age of disease representation is 59 years although the neoplasm may emerge between 14 years to 90 years. A specific gender predilection is absent [1,2].

Myoepithelial carcinoma frequently implicates the parotid gland followed in frequency by minor salivary glands, especially palatal glands or submandibular gland. Parotid gland is commonly incriminated in up to three fourths (~73%) of neoplasms [1,2]. Myoepithelial carcinoma de novo or ex pleomorphic adenoma frequently depicts PLAG1 genetic fusion, as encountered in an estimated 50% of neoplasms. Besides, various genetic fusion partners as FGFR1, TGFBR3 or ND4 may be enunciated. Additionally, clear cell myoepithelial carcinoma may delineate EWSR1 genetic fusion. Fluorescent in situ hybridization (FISH) can be optimally employed to discern EWSR1 genetic rearrangements. Nevertheless, corresponding fusion transcripts remain unidentified and demonstrate an obscure significance. Few neoplasms depict HMGA2 genetic fusion [1,2]. Clinical symptoms are nonspecific. Commonly, tumefaction represents as a painless nodule [2,3].

Cytological examination depicts a hyper-cellular specimen comprehensively comprised of myoepithelial cells. Neoplastic myoepithelial cells represent as an admixture of plasmacytoid, epithelioid or spindle shaped cells and configure miniature cellular groups and aggregates or appear as disseminated singular cells. Intervening stroma is scanty and can be highlighted with metachromatic stains as azure B or methyl violet. Mitotic figures and pleomorphic nuclei may be exemplified [2,3]. Upon gross examination, tumefaction exhibits a nonspecific countenance. Neoplasm commonly represents as an expansible, lobulated or multinodular mass with grey/white to beige hues. Tumour perimeter may be poorly defined or infiltrative [3,4]. Upon microscopy, a characteristic, invasive, expansible, multinodular neoplastic growth is observed. Infrequently, myoepithelial carcinoma may demonstrate infiltration of singular cells or miniature clusters of tumour cells. Desmoplastic reaction within encompassing stroma is exceptionally discerned. Tumour nodules display a hypo-cellular centric zone circumscribed by hyper-cellular peripheral zone. Encompassing stroma is hyalinised. Foci of bland tumour necrosis appear confined within hyper-cellular centric zone of tumour nodules. Generally, tumour necrosis is contemplated as a feature of high-grade transformation of myoepithelial carcinoma. Tumefaction is composed of myoepithelial cells in entirety. Neoplastic cells depict variable cytological features as clear cell, epithelioid cell, plasmacytoid cell or spindle shaped cells. Myoepithelial carcinoma de novo or myoepithelial carcinoma ex pleomorphic adenoma may variably delineate hyalinised, myxoid or myxochondroid stroma [3,4]. Myoepithelial carcinoma commonly demonstrates architectural patterns as solid, trabeculae, cords and cellular nests or disseminated singular cells. Occurrence of pre-existing or residual component of pleomorphic adenoma may be discerned within myoepithelial carcinoma ex pleomorphic adenoma [3,4].

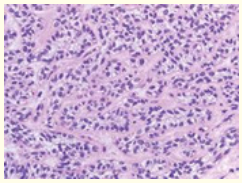

Figure 1: Myoepithelial carcinoma demonstrating tubules, cords and trabeculae of neoplastic myoepithelial cells surrounded by desmoplastic stroma. Tumour necrosis is absent. Mitotic figures are minimal [7].

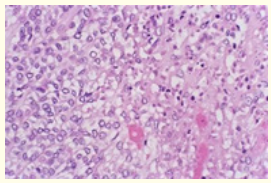

Figure 2: Myoepithelial carcinoma delineating cords and nests of malignant appearing myoepithelial cells enmeshed within a desmoplastic stroma. Tumour necrosis is absent. Mitotic figures are minimal [8].

Tumour subtype	Chromosome	Gene/Mechanism
Pleomorphic adenoma	8q12,12q13-15	PLAG1 or HMGA2 fusion/amplification
Basal cell adenoma	3p22.1,16q12.1,16p13.3, 5q22.2	CTNNB1, CYLD, AXIN1, APC mutation
Myoepithelioma-oncocytic	8q12	PLAG1 fusion
Sialadenoma papilliferum	7q34	BRAFV600E mutation
Sclerosing polycystic adenoma	3q26.32	PIK3CA mutation high
Mucoepidermoid carcinoma	t (11;19) (q21; p13), t (11;15) (q21; q26),9p21.3	CRTC1-MAML2 CRTC3-MAML2 CDKN2A deletion
Adenoid cystic carcinoma	6q22.23, 8q13,9q34.3	MYB or MYBL1 fusion/activation/ amplification, NOTCH mutation
Acinic cell carcinoma	9q31, 19q31.1	NR4A3 fusion/activation, MSANTD3 fusion/ amplification
Secretory carcinoma	t (12; 15) (p13; q25), t (12; 10) (p13; q11), t (12;7) (p13; q31), t (12;4) (p13; q31), t (10;10) (p13; q11)	ETV6-NTRK3 or ETV6-RET or ETV6-MET or ETV6-MAML3 or VIM-RET fusion
Micro-secretory adenocarcinoma	t (5q14.3) (18q11.2)	MEF2C-SS18 fusion
Polymorphous adenocarcinoma		
Classic subtype	14q12	PRKD1 mutation
Cribriform subtype	14q12, 19q13.2, 2p22.2	PRKD1, PRKD2 or PRKD3 fusion
Hyalinising clear cell carcinoma	t (12; 22), q (21; 12)	EWSR1-ATF1 or EWSR1-CREM fusion
Basal cell adenocarcinoma	16q12.1	CYLD mutation
Intra-ductal carcinoma		
Intercalated duct subtype	10q11.21	RET fusion
Apocrine subtype	3q26.32, 11p15.5	PIK3CA, HRAS mutation
Salivary duct carcinoma	17q21.1, 8p11.23, 17p13.1, 3q26.32, 11p15.5, Xq12, 10q23.31, 9p21.3	HER2, FGFR1 amplification, TP53, PIK3CA, HRAS mutation, AR copy gain, PTEN, CDKN2A loss
Myoepithelial carcinoma	8q12, t (12; 22) (q21; q12)	PLAG1 fusion, EWSR1 rearrangement
Epithelial-myoepithelial carcinoma	11p15.5	HRAS mutation
Mucinous adenocarcinoma	14q32.33, 17p13.1	AKT1 E17K or TP53 mutation
Sclerosing microcystic adenocarcinoma	1p36.33	CDK11B mutation
Carcinoma ex pleomorphic adenoma	8q12,12q13-15, 17p13.1	PLAG1 or HMGA2 fusion/amplification, TP53 mutation
Sebaceous adenocarcinoma	2p21	MSH2 loss

Table 1: Genetic alterations in salivary gland tumours [3].

Myoepithelial carcinoma appears immune reactive to cytokeratin, AE1/AE3 or CAM 5.2. Immune reactivity to myoepithelial markers as S100 protein, calponin, smooth muscle actin (SMA) or glial fibrillary acidic protein (GFAP) may be observed. Besides, immune reactivity to p63, p40, SOX10 or PLAG1 may be discerned. Tumour cells are immune non-reactive to melanocytic markers as human melanoma black 45 (HMB45) or melan A [5,6]. Myoepithelial carcinoma of salivary gland requires segregation from neoplasms such as myoepithelioma, pleomorphic adenoma, polymorphous adenocarcinoma or myoepithelial tumour of soft tissues [5,6].

Radiological concurrence is paramount in order to determine site of tumour emergence. Definitive diagnosis of myoepithelial carcinoma may be achieved with cogent examination of surgical resection specimen which may indicate tumour infiltration or tumefaction entirely comprised of 'pure' myoepithelial cell component. Computerized tomography (CT) exemplifies a solitary, lobulated or multinodular tumour mass with heterogeneous image enhancement and a partial, poorly defined neoplastic perimeter. Myoepithelial carcinoma of salivary gland may be optimally managed with surgical eradication of the neoplasm with achievement of tumour free surgical margins [5,6]. Myoepithelial carcinoma of salivary gland is a clinically aggressive neoplasm. Localized reoccurrence occurs in >33% tumefaction and up to 27% neoplasms develop distant metastasis. Nevertheless, in contrast to regional metastasis, distant metastasis is commonly encountered [5,6]. Factors contributing to adverse prognostic outcomes are designated as ~occurrence of tumour necrosis ~mitotic index >4 per 10 high power fields ~tumour cells confined to surgical perimeter ~emergence of myoepithelial carcinoma ex pleomorphic adenoma [5,6].

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7. Image 1 Courtesy: Springer link.

8. Image 2 Courtesy: Medscape reference.