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Canker and Slobber-Salivary Gland Adenocarcinoma-NOS

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Salivary gland adenocarcinoma not otherwise specified (NOS) represents as an invasive tumefaction demonstrating glandular or ductal differentiation. Generally, tumefaction is devoid of morphological features characteristic of diverse subtypes of malignant salivary gland neoplasms. With a frequently aggressive biological course, salivary gland adenocarcinoma (NOS) comprehensively configures up to 10% of malignant salivary gland tumours. Salivary gland adenocarcinoma (NOS) is essentially a diagnosis of exclusion.

Salivary gland adenocarcinoma (NOS) may metastasize into cervical lymph node (~23%) whereas distant metastases occur within 37% tumours. 5 year disease specific survival emerges at ~57%.

Salivary gland adenocarcinoma (NOS) is frequently discerned within a broad age range of 10 years to ~90 years with mean age of disease occurrence at 58 years and median age of neoplastic emergence at 67 years. A mild male predilection or equivalent gender predominance is encountered [1,2].

Salivary gland adenocarcinoma (NOS) commonly incriminates parotid gland, submandibular gland and minor salivary glands confined to palate or buccal mucosa. Tumefaction preponderantly represents ~17% of malignant neoplasms of parotid gland and ~15% of malignant tumours of minor salivary glands [1,2].

Salivary gland adenocarcinoma (NOS) exhibits genetic amplification of EGFR with elevated copy number of EGFR gene. Besides, amplification of HER2 with enhanced copy number of HER2 gene may be encountered. Exceptionally, KRAS genetic mutation may be discerned [1,2].

Generally asymptomatic, salivary gland adenocarcinoma (NOS) manifests as a tumefaction which is frequently adherent to superimposed cutaneous surface or deep seated soft tissue. Lesions confined to palate commonly appear ulcerated and may infiltrate subjacent bone [2,3].

Grossly, an inadequately circumscribed neoplasm with an infiltrative tumour perimeter is observed. Cut surface is solid, tan and exhibits focal haemorrhage and necrosis [2,3].

Upon microscopy, an invasive tumefaction demonstrating glandular or ductal differentiation is encountered. However, characteristic features of morphological subtypes of diverse malignant salivary gland neoplasms are lacking [3,4].

Tumefaction exhibits distinct architectural patterns as glandular spaces with configuration of cysts or papillae, solid sheets, hyalinised 'shadow' nodules or foci of comedonecrosis [3,4].

Cuboidal, spherical or elliptical tumour cells configure miniature clusters wherein neoplastic cells are incorporated with abundant cytoplasm and display a distinct cellular perimeter. Neoplasm may be configured of clear cells or oncocytic cells [4,5].

Contingent to cytological and morphological features, salivary gland adenocarcinoma (NOS) may be categorized into low grade, intermediate grade or high grade neoplasm. Generally, tumefaction exhibits a prominent *in situ* component, constituted of ~68% of tumour parenchyma [4,5].

TNM staging of major salivary gland neoplasms [4,5]

Primary tumour

- TX: Primary tumour cannot be assessed.
- T0: No evidence of primary tumour.
- Tis: Carcinoma *in situ*.
- T1: Tumour ≤ 2 centimetre in greatest dimension in the absence of extra-parenchymal extension.
- T2: Tumour > 2 centimetre and ≤ 4 centimetre in greatest dimension with absence of extra-parenchymal extension.
- T3: Tumour > 4 centimetre in greatest dimension OR tumour with extra-parenchymal extension.
- T4: Is comprised of
    - T4a: Moderately advanced, localized disease wherein tumour invades cutaneous surface, mandible, external auditory canal and/or facial nerve.
    - T4b: Very advanced, localized disease wherein tumour invades base of skull, pterygoid plates or encases carotid artery.

Extra-parenchymal extension indicates clinical or macroscopic, pathological evidence of soft tissue tumour invasion in concurrence with microscopic evidence of disease dissemination.

Regional lymph nodes (clinical staging)

- NX: Regional lymph nodes cannot be assessed.
- N0: Regional lymph node metastasis absent.
- N1: Regional lymph node metastasis confined within singular, ipsilateral lymph node ≤3 centimetre magnitude with absent extra-nodal extension (ENE-).
- N2: Is categorized as
    - N2a: Regional lymph node metastasis confined to singular, ipsilateral lymph node > 3 centimetre and ≤ 6 centimetre magnitude with absent extra-nodal extension (ENE-).
    - N2b: Regional lymph node metastasis confined to multiple, ipsilateral lymph nodes ≤ 6 centimetre magnitude with absent extra-nodal extension (ENE-).
    - N2c: Regional lymph node metastasis confined to bilateral or contralateral lymph nodes ≤ 6 centimetre magnitude with absent extra-nodal extension (ENE-).

- N3: Is categorized into
  - N3a: Regional lymph node metastasis into a node > 6 centimetre magnitude with absent extra-nodal extension (ENE-).
  - N3b: Regional lymph node metastasis into a node demonstrating clinically overt extra-nodal extension (ENE+ or ENEc) OR 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 nodes 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.

Regional lymph nodes (pathological staging)

- NX: Regional lymph nodes cannot be assessed.
- N0: Regional lymph node metastasis absent.
- N1: Regional lymph node metastasis confined within singular, ipsilateral lymph node ≤ 3 centimetre magnitude with absent extra-nodal extension (ENE-).
- N2: Is categorized into
  - N2a: Regional lymph node metastasis confined within singular, ipsilateral lymph node > 3 centimetre and ≤ 6 centimetre magnitude with absent extra-nodal extension (ENE-) OR regional lymph node metastasis confined to singular, ipsilateral lymph node ≤ 3 centimetre magnitude with extra-nodal extension (ENE+).
  - N2b: Regional lymph node metastasis confined to multiple, ipsilateral lymph nodes ≤6 centimetre magnitude and absent extra-nodal extension (ENE-).
  - N2c: Regional lymph node metastasis confined to bilateral or contralateral lymph nodes ≤6 centimetre magnitude and absent extra-nodal extension (ENE-).
- N3: Is categorized as
  - N3a: Regional lymph node metastasis confined to lymph node >6 centimetre magnitude with absent extra-nodal extension (ENE-).
  - N3b: Regional lymph node metastasis confined to singular, ipsilateral lymph node > 3 centimetre magnitude with extra-nodal extension (ENE+) OR multiple, ipsilateral, contralateral or bilateral lymph nodes with extra-nodal extension (ENE+) within singular or multiple sites OR singular, contralateral lymph node of variable magnitude and extra-nodal extension (ENE+).

Distant metastasis

- M0: Distant metastases absent.
- M1: Distant metastasis present into sites as pulmonary parenchyma.
- pM1: Distant metastasis present, confirmed with microscopic examination.

Salivary gland adenocarcinoma (NOS) demonstrates an immuno-phenotype of CK7+/CK20-. Tumour cells are immune reactive to epidermal growth factor receptor (EGFR), survivin, phospho-STAT3, CK18 or HER2 [5,6].

Additionally, uniform periductal immunostaining of reactive myofibroblastic cells may be obtained with immune markers as calponin, smooth muscle actin (SMA) or heavy chain of smooth muscle myosin [5,6].

Salivary gland adenocarcinoma (NOS) appears immune non reactive to MYB [6,7].

Salivary gland adenocarcinoma (NOS) requires segregation from neoplasms such as hybrid carcinoma, membranous adenoma, metastatic adenocarcinoma, polymorphous low grade adenocarcinoma or undifferentiated carcinoma [6,7].

Salivary gland adenocarcinoma (NOS) can be appropriately treated with comprehensive surgical extermination of the neoplasm [6,7].

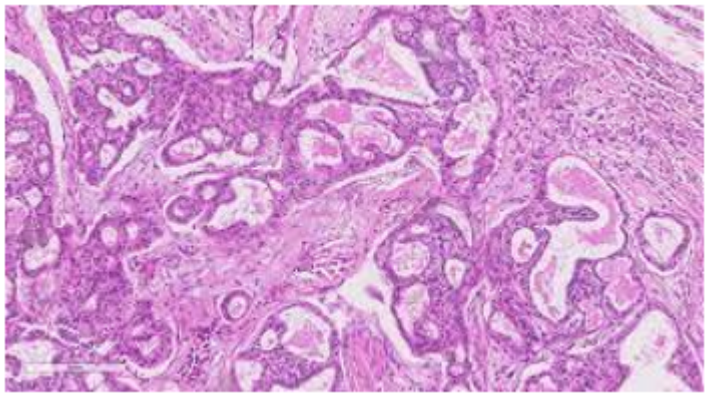

Figure 1: *Salivary gland adenocarcinoma (NOS) demonstrating glandular architecture with atypical glands lined by cuboidal epithelial cells imbued with abundant eosinophilic cytoplasm and distinct cellular outline. Neoplastic cells configure miniature clusters [8].*

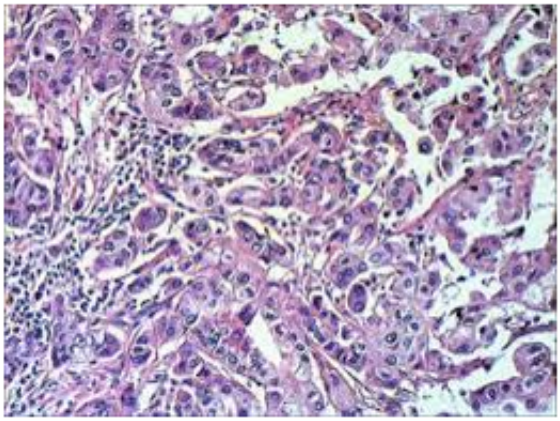

Figure 2: *Salivary gland adenocarcinoma (NOS) delineating glandular articulations lined by cuboidal cells incorporated with abundant eosinophilic cytoplasm and well defined cellular outline. Tumour cells configure miniature clusters. Surrounding stroma is desmoplastic [9].*

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8. Image 1 Courtesy: Research gate.

9. Image 2 Courtesy: Springer link.

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