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Secretory Carcinoma of the Salivary Glands

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A 29-year-old woman presented with a 3-month history of an enlarging right infra-auricular mass. A fine needle aspiration biopsy revealed a cellular aspirate consistent with a salivary gland neoplasm of uncertain malignant potential (The Milan System for Reporting Salivary Gland Cytopathology Category IV-B). She subsequently underwent superficial parotidectomy, revealing a poorly circumscribed tumor measuring 1.8 x 1.2 x 1.0 cm in the superficial lobe of the parotid gland.

On microscopic examination, the tumor was composed of microcystic, follicular, and tubular structures lined by mildly atypical, hobnailed cells with abundant granular to foamy, pale, eosinophilic cytoplasm, and round to oval, vesicular nuclei containing finely granular chromatin and prominent, centrally located nucleoli. *(Figure 1)* Intraluminal secretions were present within the microcysts and tubules, staining positive for Periodic Acid Schiff (PAS) that was resistant to diastase digestion. *(Figure 2)* Immunohistochemistry studies for S100, SOX10, and Mammaglobin showed strong, diffuse positivity in the tumor cells, in contrast to the absence of staining observed for DOG1. *(Figure 3)* Given the described morphological and immunological findings, a diagnosis of secretory carcinoma was rendered. No foci of high-grade transformation, i.e., areas with a solid growth pattern, nuclear anaplasia, increased mitoses, or necrosis, were noted.

Secretory Carcinoma or Mammary Analogue Secretory Carcinoma (MASC) is a recently described low grade salivary gland malignancy that bears a morphologic resemblance to mammary secretory carcinoma, harboring a similar chromosomal translocation, t(12;15)(p13;q25), that most commonly produces a fusion of the ETV6 and NTRK3 genes.[1-5] Occurring in adults (mean patient age of 46.5 years) without a predilection for either sex, these tumors most commonly arise in the parotid gland.[1,2]

Historically, secretory carcinomas have been diagnosed as either acinic cell carcinoma – due to the close morphological similarity of having a microcystic or follicular growth pattern

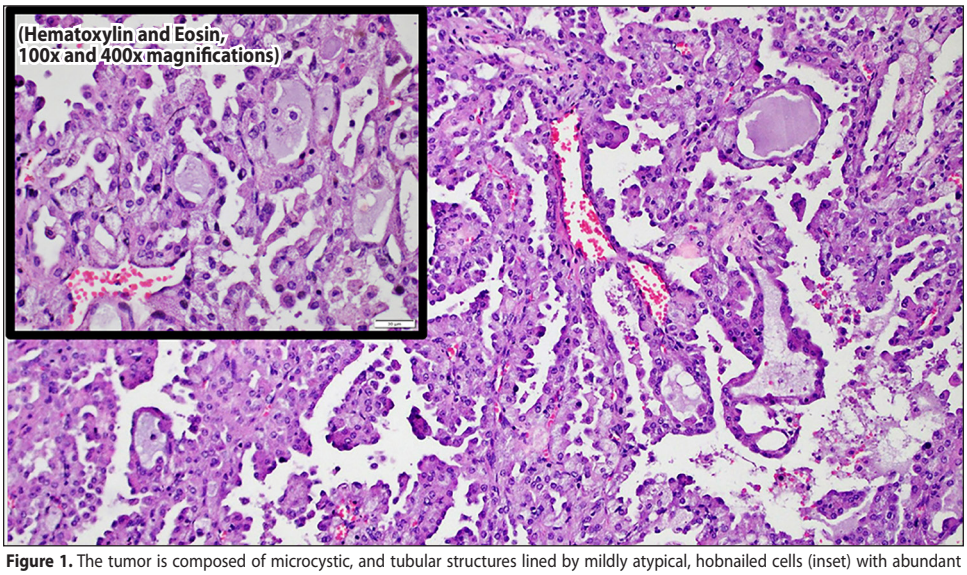

Figure 1. The tumor is composed of microcystic, and tubular structures lined by mildly atypical, hobnailed cells (inset) with abundant granular to foamy, pale, eosinophilic cytoplasm and round to oval, vesicular nuclei containing finely granular chromatin and prominent, centrally located nucleoli (Hematoxylin and Eosin, 100x and 400x magnifications).

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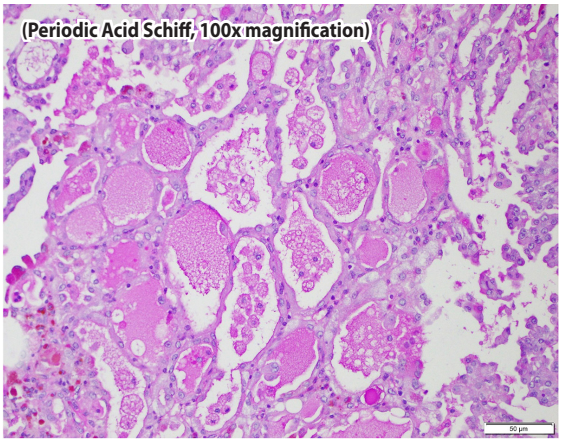

Figure 2. Intraluminal secretions stain positive for Periodic Acid Schiff (PAS) (Periodic Acid Schiff, 100x magnification).

- or adenocarcinoma that is not otherwise specified. Aside from the characteristic ETV6-NTRK3 gene fusion, secretory carcinomas may be differentiated from acinic cell carcinoma by having no basophilic zymogen cytoplasmic granules in the tumor cells in contrast to the latter, and the diffuse expression of S100 and Mammaglobin as well as the absence of DOG1 expression in secretory carcinoma on immunohistochemistry. [1,2] Low grade mucoepidermoid carcinoma may also present as a possible morphological differential diagnosis. Immunohistochemistry studies for p63 (expressed in epidermoid cells of mucoepidermoid carcinoma), as well as S100 and Mammaglobin (no expression expected in mucoepidermoid carcinoma) may be sufficient to differentiate between the two entities. On a cytogenetic level, most low grade mucoepidermoid carcinomas harbor a chromosomal translocation, t(11:19), that results in a characteristic CRTC1-MAML2 gene fusion in contrast to the ETV6-NTRK3 fusion seen in secretory carcinoma.[1-3] The light microscopic features of this particular case however are sufficiently distinct from a mucoepidermoid carcinoma that we felt that this entity could be excluded based on routine H&E morphology. It is granted however, that molecular testing, e.g., in-situ hybridization to demonstrate characteristic chromosomal aberrations, may prove valuable in morphologically ambiguous cases. Its unavailability in the local setting is thus a limitation.

Secretory carcinomas are mostly reported to be indolent though are associated with lymph node metastasis in up to 25% of cases. Like other low grade salivary gland carcinomas, locoregional recurrence and distant metastasis have been documented in rare cases. However, high clinical grade and high-grade morphological transformation have been reported and are associated with adverse outcomes.[1,2,4,5] The patient tolerated the surgical procedure well, and had no evidence of disease eight months after the operation. Reporting this fairly uncommon entity is encouraged to further expand our understanding of its biology and natural history.

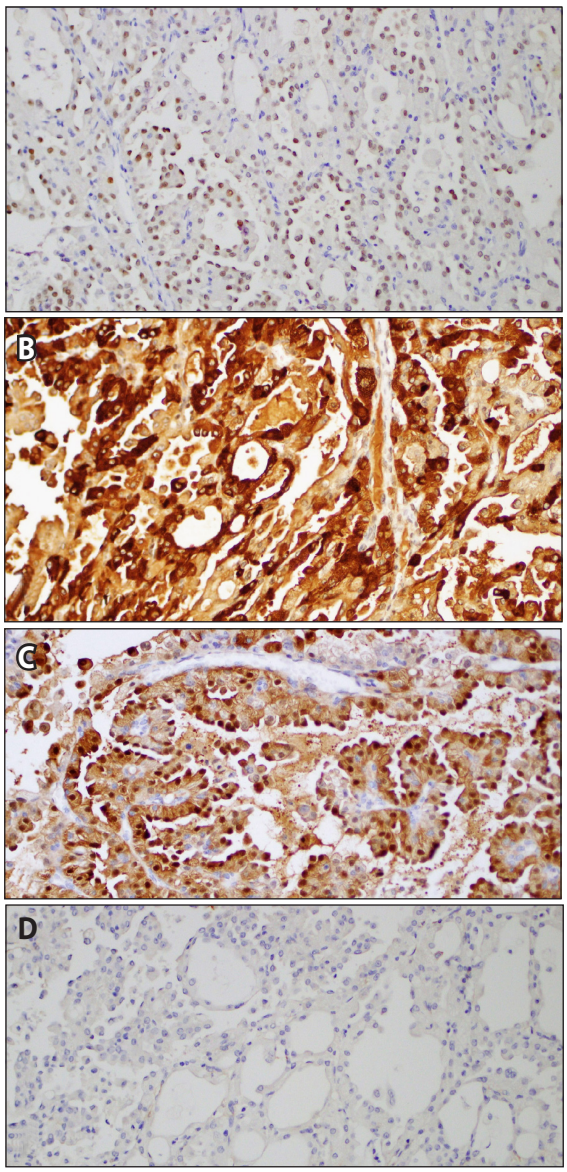

Figure 3. Strong nuclear staining for SOX10 **A**, cytoplasmic staining for Mammaglobin **B**, and nuclear and cytoplasmic staining for S100 **C,** are observed in the tumor cells. DOG1 was negative **D**. (Horse Radish Peroxidase Method, 400x magnification).

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