

## Secretory carcinoma of the parotid with adenoid cystic carcinoma cytological pattern: A cytological-pathological correlation with literature review

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### A B S T R A C T

Secretory carcinoma (SC) is a rare low-grade malignant tumor, defined by ETV6-NTRK3 fusion, identifiable by FISH. We describe a case in a 58-year-old male with a painless slowly growing 16 mm palpable mass within left superficial parotid. FNA of the mass showed highly cellular specimen with moderate to large pleomorphic cells with round to ovoid nuclei with vesicular chromatin and distinct nucleoli. Cells had moderate to large amounts of vacuolated cytoplasm. Abundant globular metachromatic material, resembling that of adenoid cystic carcinoma, was noted. This material was seen extracellularly and intracytoplasmic, and stained magenta on Diff-Quik and blue-green on Papanicolaou-stained slides. The tumor cells on a cell block preparation were positive for Mammaglobin and S-100. PAS stain highlighted extracellular and intracytoplasmic secretions. FNA diagnosis was “Positive for Malignancy. Morphologic features most compatible with Mammary Analogue Secretory Carcinoma”. ETV6 FISH studies as well as histologic examination of excised tumor confirmed the diagnosis. Finding the globular metachromatic material in SC, that is generally seen in adenoid cystic carcinoma, broadens a cytological differential diagnosis of both entities. Cytological differential diagnosis, clinical, histological, immunohistochemical, and molecular features of secretory carcinomas are discussed in this study.

### 1. Introduction

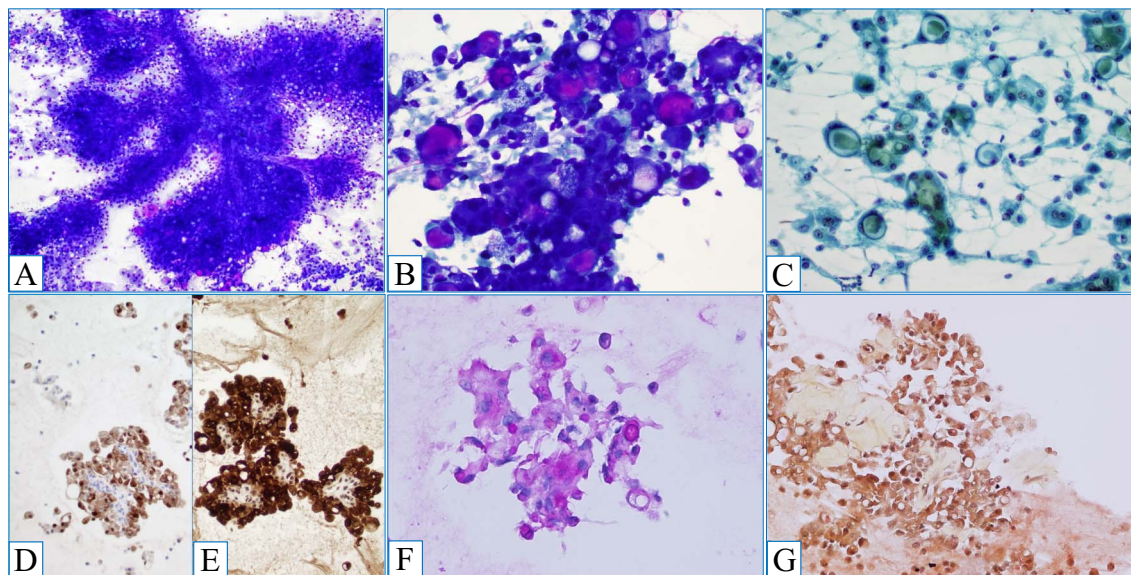
Secretory carcinoma (SC) is a low-grade malignant tumor histologically similar to secretory carcinoma of the breast, defined by t(12;15) (p13;q25) translocation, resulting in ETV6-NTRK3 fusion. Most patients with SC present with a slowly growing painless tumor. SC has wide age range (5–77 years) with slight male predilection and occurs most commonly in a parotid gland. SC has moderate risk of local recurrences and lymph node metastases and low risk of distant metastases [1–3]. ETV6-NTRK3 fusion gene encodes a chimeric tyrosine kinase. The same molecular abnormality is present in a subset of acute leukemias and there is a targeted therapy with tyrosine kinase inhibitors, that can be used also for SC treatment [4,5]. We describe a case of a secretory carcinoma with cytomorphological features resembling adenoid cystic carcinoma. To our knowledge, this cytological pattern of MASC has not been previously reported.

### 2. Materials and methods

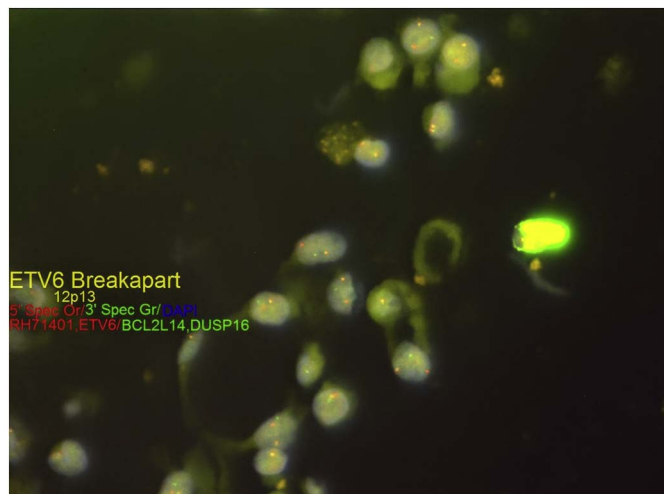
Fine-needle aspiration was performed with on-site evaluation of air-dried Diff-Quik (DQ) stained slides and preliminary evaluation of the sample. Three DQ-stained and 3 alcohol-fixed Papanicolaou (Pap) stained direct smears, and cell block preparation with one hematoxylin and eosin (H&E) stained slide were evaluated. Immunohistochemical stains with monoclonal antibodies to S-100 and Mammaglobin were performed on a cell block using an automated immunostainer with appropriate control staining. Clone 4C4.9 S-100 antibodies in 1:750 dilution from Cell Marque were used for S-100 immunohistochemical stain, and clone 304-1A5 Mammaglobin antibodies in 1:150 dilution from Dako were used for Mammaglobin immunohistochemical stain. PAS with and without diastase and Mucicarmine stains were performed using standard laboratory protocol on cell block preparation with appropriate control staining. One-hundred interphase cells from tumor were analyzed using break apart DNA probes from Vysis for the ETV6

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**Fig. 1.** Composite cytology image. A. Low power magnification showing highly cellular specimen with tumor cells arranged in solid and papillary-like structures (DQ, 10 ×). B. High power view demonstrating moderate to large pleomorphic tumor cells with vacuolated cytoplasm filled with magenta-colored globular material (DQ, 40 ×). C. High power view demonstrating moderate to large pleomorphic tumor cells with vacuolated cytoplasm filled with blue-green globular material (PAP, 40 ×). D. S-100 stain show strong nuclear positivity (IHC, 20 ×). E. Mammaglobin stain show strong nuclear and cytoplasmic positivity (IHC, 20 ×). F. Periodic acid-Schiff–diastase (PAS-D) stain show positivity in the cytoplasmic secretions (40 ×). G. Mucicarmine show negative staining of the tumor cells (20 ×). (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)



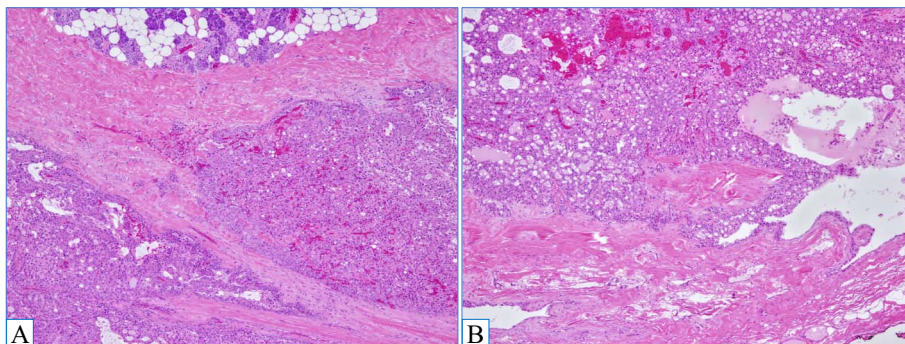
**Fig. 2.** ETV6 break apart FISH. Red signals (ETV6 gene) and green signals (DUSP16 gene, normally located close to ETV6 gene) are separate, confirming ETV6 rearrangement. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

locus by fluorescence in situ hybridization (FISH) in paraffin-embedded tissue. The entire tumor in the parotid resection specimen was submitted for histologic examination. Histological sections were processed in a standard routine processing algorithm. Tissue was embedded in paraffin, cut on a microtome and stained with H&E.

**3. Case report**

A 58-year-old male with a history of squamous cell carcinoma of the larynx presented with a palpable 16 mm mass within the posterior superficial lobe of the left parotid gland with cutaneous and subcutaneous involvement based on the CT scan. This lesion has been increasing in size but remained otherwise asymptomatic. Fine needle aspiration (FNA) of the mass was performed.

Cytology slides showed highly cellular specimen with moderate to large pleomorphic cells with round to ovoid nuclei with vesicular chromatin and distinct nucleoli. Cells had moderate to large amounts of vacuolated cytoplasm. Abundant globular metachromatic material, resembling that of adenoid cystic carcinoma, was noted. This material was seen extracellularly and intracytoplasmic, and stained magenta on DQ and blue-green on Pap-stained slides (Fig. 1A, B and C). Immunostains and FISH were performed on cell block preparations. The tumor cells were positive for S-100 and Mammaglobin (Fig. 1D and E). PAS stains with and without diastase highlighted extracellular and



**Fig. 3.** Composite low power image. Poorly-circumscribed lobulated mass. The tumor has solid (A), tubular and cystic architectural patterns (B). Homogenous eosinophilic secretions are seen within cystic spaces (H&E, 4 ×).

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