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# Secretory Carcinoma: A Silent Mass Increasing in the Parotid Gland

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## Abstract

**BACKGROUND:** Secretory carcinoma (SC) of the salivary gland, also known as mammary analog secretory carcinoma, is a rare tumor in the parotid gland. This kind of tumor is characterized by generally indolent clinical behavior and expression of a break in the ETV6 gene.

**CASE REPORT:** We present a unique case of secretory carcinoma and show its favorable prognoses.

**CONCLUSION:** Secretory carcinoma of the salivary gland is a low-grade carcinoma with a favorable prognosis. It has low regional lymph node and distant metastasis potential. Due to the possibility of misdiagnosis, immunohistochemical studies and FISH are suggested. The most effective treatment is complete surgical excision with negative surgical margins.

## Introduction

Secretory carcinoma (SC), formerly known as mammary analog secretory carcinoma (MASC), was renamed by WHO in the Classification of Head and Neck Tumors in 2017 [1]. In the beginning, this kind of tumor was first noticed in the breast and was called juvenile breast carcinoma and secretory carcinoma of the breast [2]. In 2010, Skálová found it occurring in the salivary gland and then named it MASC in salivary glands [3]. Secretory carcinoma is a low-grade malignant tumor and usually occurs in salivary glands, especially in the parotid gland (68%) [4].

It can be confused with acinic cell carcinoma (AciCC) and distinguished by immunohistochemical studies and fluorescence in situ hybridization (FISH). Complete surgical excision of secretory carcinoma is the treatment of choice, while gene fusion data can give us a better understanding of target therapy treatment.

We report a case of secretory carcinoma of the left parotid gland diagnosed and treated in our department. Left superficial parotidectomy was performed and the FISH study revealed a break-apart of *ETV6* gene. No local recurrence was observed on physical examination and ultrasound on follow-up for 2 years.

## Case Report

A 37-year-old man presented with a history of a left parotid mass that was gradually increasing in size for 6 months since October, 2017. No tenderness or facial numbness was noticed. On examination, he presented a firm, fixed, and non-tender mass on the left parotid region of about 6 × 5 $cm^2$. Ultrasound showed a cystic mass and the result of fine-needle aspiration cytology report presented atypical cellular change. Contrast-enhanced computed tomography (CT) was performed for pre-surgical operation planning. One 4.1 cm cystic mass with irregular wall thickening at the left parotid gland was noticed (Figure 1).

On the basis of radiological and cytological findings, the left side superficial parotidectomy was

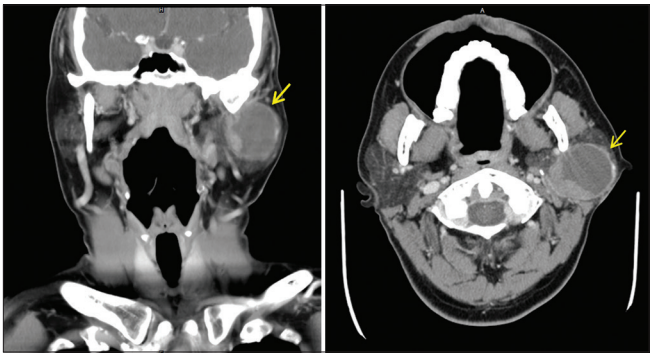

*Figure 1: Computed tomography scan of head and neck showing a 4.1 cm cystic mass (arrow) with irregular wall thickening at the left parotid gland*

performed under facial nerve monitoring (Figure 2). Histopathology revealed secretory carcinoma composed of cuboid or columnar epithelial cells (Figure 3). Immunohistochemical studies were positive for S-100 and CK7 and negative for p63, CK5/6, and DOG-1. FISH study revealed a break-apart of *ETV6* gene (Figure 4).

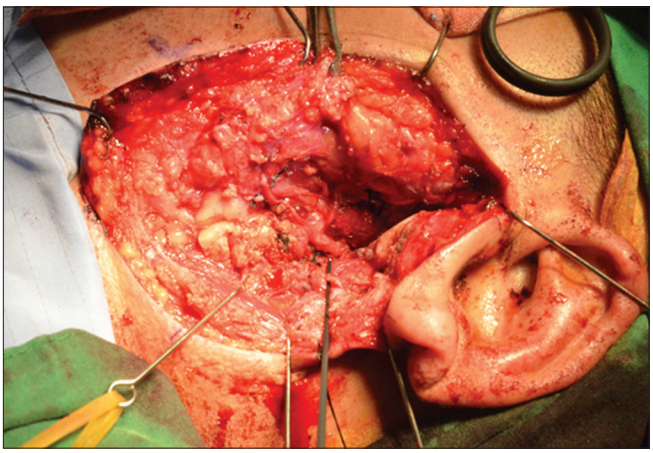

*Figure 2: Photo of the surgery demonstrating left superficial parotidectomy with preservation of facial nerve*

No local recurrence was observed on physical examination and ultrasound on follow-up for 2 years.

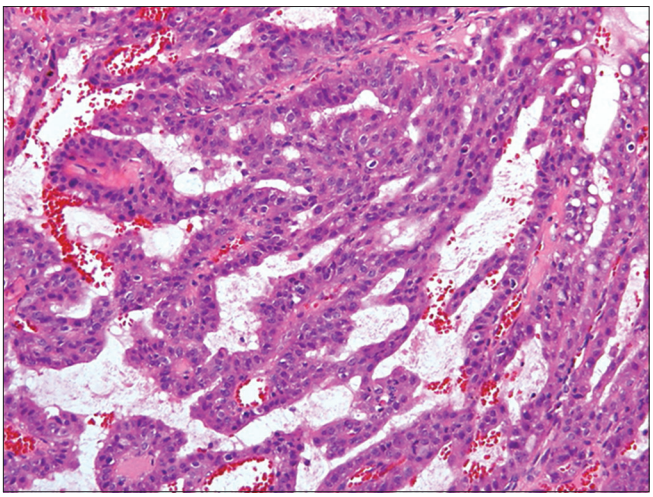

*Figure 3: Histopathology revealed secretory carcinoma composed of cuboid or columnar epithelial cells*

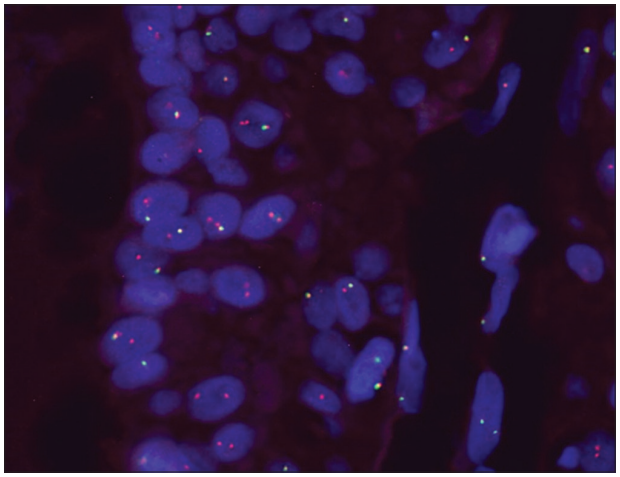

*Figure 4: Fluorescence in situ hybridization study showed positive for ETV6 gene rearrangement with loss of 3' signals (green)*

## Discussion

Secretory carcinoma of the salivary gland is a rare type of tumor with generally indolent clinical behavior [4]. Its incidence is <0.5% in parotid malignant neoplasms [5] and usually presents as an asymptomatic mass in the parotid gland with slight male predilection (1.5:1) and the age span for SC is wide (5–77 years) [4]. It has also been reported in the nasal cavity, vulva, lacrimal gland [6], eyelid [7], skin [8], thyroid [9], and lung [10]. Most patients with SC present with a slowly growing painless tumor.

The diagnostic plan for SC includes ultrasound and image study (head and neck CT/magnetic resonance imaging). Although fine-needle aspiration may be performed during ultrasound evaluation, the cytology diagnosis for SC is poor. According to Kai *et al*., only 2 of 109 cytologists identified SC [11]. Immunohistochemistry and FISH studies using pathologic specimen can yield a definite diagnosis. In immunohistochemistry, SC is positive for S100, mammaglobin, and CK7 and negative for p63, CK5/6, and DOG-1 stains in the literature (Table 1) [12]. By FISH, SC shows *ETV6* gene rearrangements. The most well-known fusion partner gene is NTRK3 (more than 90%) [13]. When fusions happen, the *ETV6* gene enrolls – transcriptional regulator gene and the other genes (ex: NTRK3, MET, and RET) enroll a membrane receptor kinase. The above finding can lead to well-designed-target therapy in the literature [14]: We may choose Trk inhibitors (e.g., entrectinib and larotrectinib) for patients with a NTRK3 fusion gene and c-Met inhibitors (e.g., cabozantinib) for patients with a MET fusion gene if systemic therapy is needed [15] (Table 2).

The treatment of choice for SC is complete surgical excision. Due to the low incidence of lymph node involvement, elective neck dissection is not suggested for every case. Neither radiotherapy nor

chemotherapy is needed after the operation due to its favorable prognosis [4].

**Table 1: Comparison of findings between SC and AciCC**

| | Cytology | Immunostain | | | | FISH |
|---|---|---|---|---|---|---|
| | | Mammaglobin | S100 | Vimentin | DOG-1 | ETV6 split |
| SC | Papillary fragment, mucoid background | + | ++ | ++ | - | + |
| AciCC | Cell groups and single cells, granular with nuclei background | - | + | + | + | - |

SC= secretory carcinoma, AciCC = acinic cell carcinoma

In our case, the immunohistochemical studies were positive for S-100 and CK7 and negative for p63, CK5/6, and DOG-1. FISH study with a break-apart of *ETV6* gene was noticed. The diagnosis of MASC was confirmed.

**Table 2: The gene rearrangements of SC and the suggestive target therapy**

| Transcriptional regulator gene | Membrane receptor kinase-type | Treatment |
|---|---|---|
| *ETV6* | NTRK3(>90%) | Entrectinib and larotrectinib |
| | MET | RXDX105, LOXO292 |
| | RET(2-5%) | Cabozantinib |

Although MASC is considered a low-grade malignant tumor in most cases, recurrence and disease dissemination still happen sometimes. Long-term follow-up is suggested.

## Conclusion

Secretory carcinoma of the salivary gland is a low-grade carcinoma with a favorable prognosis. It has low regional lymph node and distant metastasis potential. Due to the possibility of misdiagnosis, immunohistochemical studies and FISH are suggested. The most effective treatment is complete surgical excision with negative surgical margins. FISH is recommended for SC patients, not only to provide definite result but also to obtain information for further target therapy if needed.

## Ethical Statement

The paper had complied with the guidelines for human studies and animal welfare regulations. The authors state that subjects have given their informed consent and that the study protocol has been approved by the Institute's Committee on Human Research (TMU-JIRB number: N201812013). The authors also state that animal experiments conform to institutional standards.

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