

## A Case of A Mammary Analogue Secretory Carcinoma of the Submandibular Gland Mimicking a Second Branchial Cleft Cyst

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### – ABSTRACT –

A mammary analogue secretory carcinoma (MASC) of the submandibular gland is a rare occurrence. In this case report, we describe an 18-year-old girl with a MASC of the submandibular gland, who presented with symptoms of painful swelling of the level II cervical area. Computed tomography (CT) was performed, and fine needle aspiration cytology was suggested to aid in the diagnosis. An initial diagnosis of a second branchial cleft cyst was made, for which antibiotic therapy and excision of the cyst were performed. Further investigation was done after endoscopic excision via the retroauricular approach for cosmesis. Preoperative computed tomography suggested an infected second branchial cleft cyst; however, the pathology report revealed a MASC of the submandibular gland, which is a rare finding. Although the clinical presentation of the mass was similar to a second branchial cleft cyst, characteristic MASC findings were observed on immunohistochemical examination; a successful endoscopic mass excision was performed. (*J Clinical Otolaryngol* 2016;27:370-374)

**KEY WORDS** : Mammary analogue secretory carcinoma · Submandibular gland · Branchial region · Endoscopic surgical procedure.

### Introduction

A mammary analogue secretory carcinoma (MASC) is a rare salivary gland tumor that histologically and genetically resembles a rare malignancy of the breast, i.e., secretory carcinoma (SC).<sup>1)</sup> Ninety-two cases of MASC have been reported, and the majority (71%) of these tumors were located in the parotid gland. The occurrence of MASC in the submandibular gland is very rare (7%), and the most common clinical pre-

sentation is a slowly enlarging and painless nodule palpable on physical examination.<sup>2)</sup> We report a rare case of MASC in the submandibular gland that presented as a painful swollen mass, and mimicked a second branchial cleft cyst.

### Case Report

An 18-year-old girl presented with a 2-week history of a painful swelling on the right-side of the level II cervical lymph node region that had slowly increased in size over the past 3 months. Computed tomography (CT) showed a 3-cm well-circumscribed cyst partially attached to the right submandibular gland (Fig. 1). We recommended fine needle aspiration cytology (FNAC), but the patient refused to undergo this procedure because of the severe tenderness in the cyst. Considering the young age of the patient and the area of

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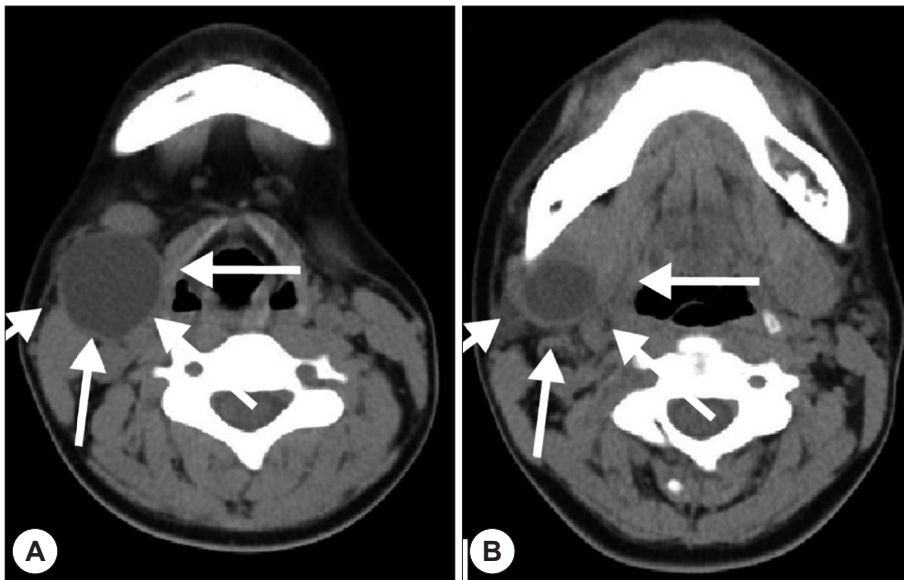
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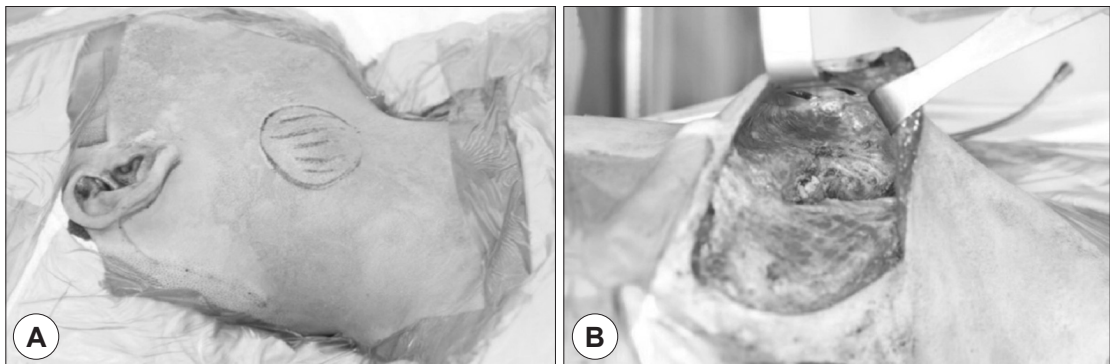
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the inflammation, the mass was clinically diagnosed as an infected second branchial cleft cyst. After 2 weeks of antibiotic medication, complete excision via the endoscopic retroauricular approach was performed in order to ensure cosmesis. We performed en bloc resection including the posterior aspect of the submandibular gland after partial rupture because of its adhesion to the gland. Intraoperative findings were similar to that of a typical branchial cleft cyst, and the visually resected margin was clear (Fig. 2).

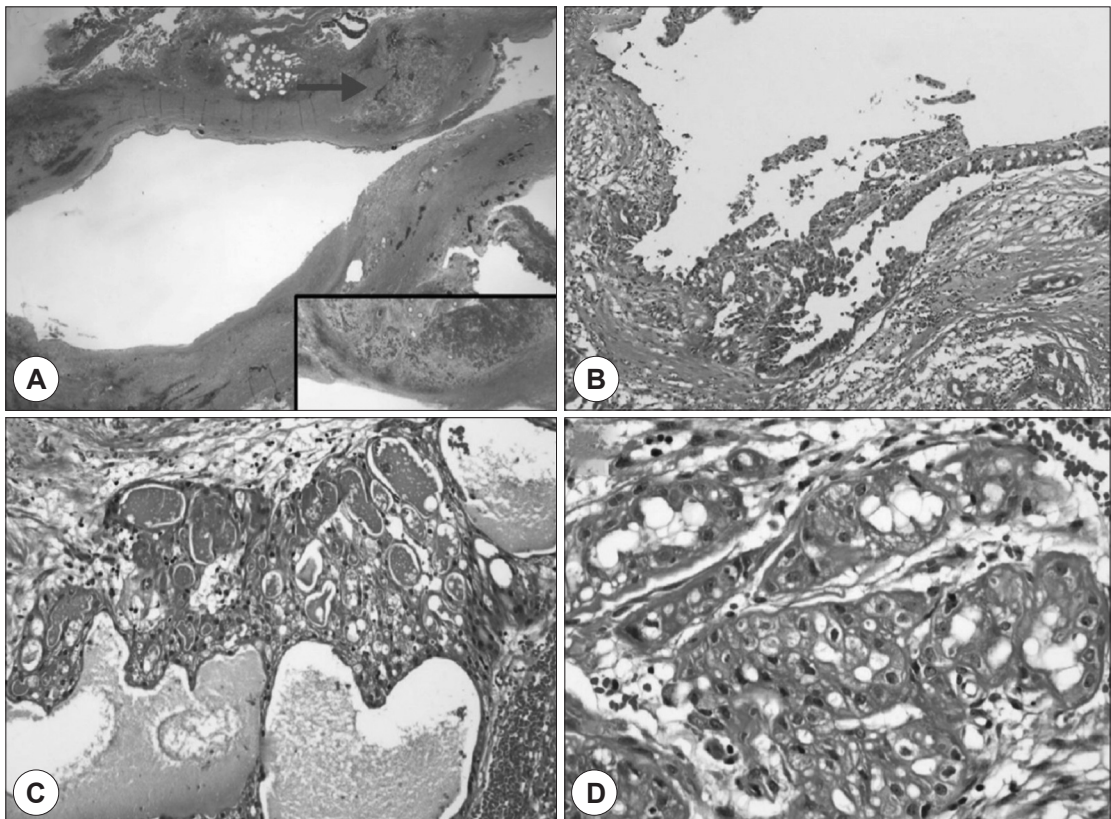
On gross examination, the resected specimen was described as a macrocystic mass (dimensions : 3.0 × 3.0 × 2.8 cm). On microscopic examination, the macrocyst was found to be covered by a fibrous wall containing focal epithelial proliferation islands, and the underlying submandibular gland displayed atrophy and chronic inflammation (Fig. 3). The cyst was lined by largely denuded epithelium and displayed a focal solid proliferation of cuboidal-to-polygonal tumor cells. The tumor patterns included microcystic,



**Fig. 1.** A : The preoperative neck computed tomography scan showing a cystic mass, 3 cm in diameter, in the right level II cervical area. B : The cystic mass exists in the posterior aspect of the submandibular gland.



**Fig. 2.** A : The preoperative photograph showing swelling in the right submandibular gland. B : The postoperative photographs of the endoscopic resection via the retroauricular approach with preservation of the great auricular nerve.

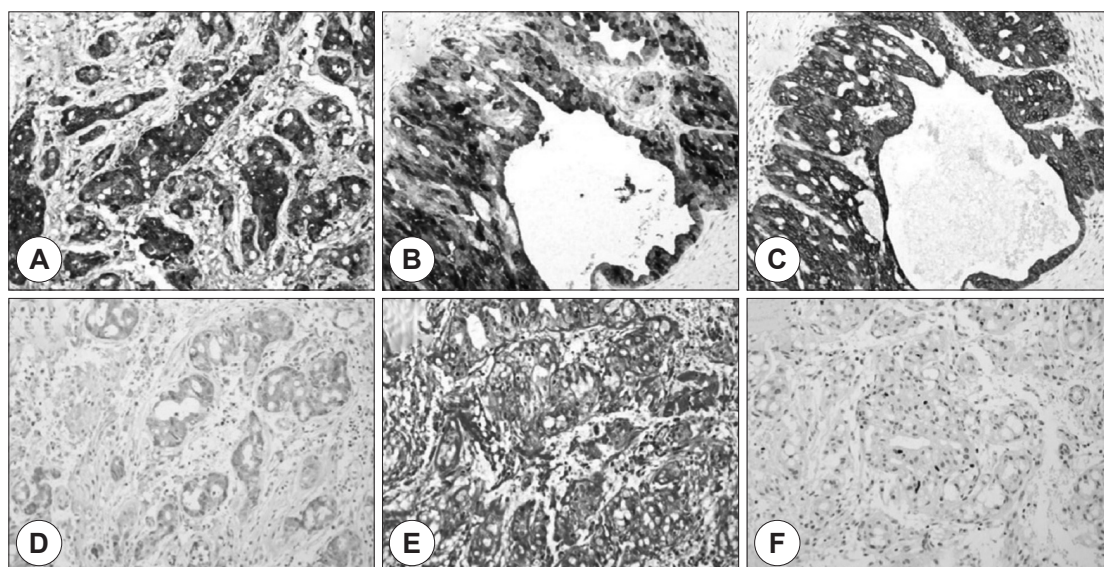


**Fig. 3.** Pathologic analysis of the mammary analogue secretory carcinoma stained with hematoxylin and eosin. A : A low-power microscopic image showing a unilocular cyst with the fibrotic wall containing focal epithelial proliferation islands (arrow), the adjacent submandibular gland with atrophy, and chronic inflammation (inset,  $\times 12.5$ ). B : The cyst is lined by focal solid proliferation of cuboidal-to-polygonal tumor cells ( $\times 100$ ). C : Cystic/glandular patterns of the tumor tissue with intraluminal/intracytoplasmic secretory materials are observed ( $\times 200$ ). D : The high-magnification microscopic image of the tumor cells shows low-grade ovoid/wrinkled vesicular nuclei with inconspicuous nucleoli, and abundant granular/bubbly eosinophilic cytoplasm ( $\times 400$ ).

papillary-cystic, glandular, and solid growth, and the cyst contained pinkish-colored amorphous fluid that stained positive on periodic acid-Schiff (PAS) staining. The tumor cells exhibited low-grade ovoid and wrinkled vesicular nuclei, abundant pale-pink granular or vacuolated “bubbly” cytoplasm, and intraluminal or intracellular secretions. Extraparenchymal extension of the tumor was also evident. However, there was no mitotic activity, angiolymphatic invasion, or necrosis of the tumor cells. On immunohistochemical examination, the tumor cells showed strong but diffuse positive staining for cytokeratin (CK), S-100 protein, gross cystic disease fluid protein 15 (GCD-

FP-15), and CK7. Mammaglobin immunoreactivity was weakly positive (Fig. 4). These findings are all consistent with the finding of MASC in the submandibular gland.

The submandibular gland tumor was classified as pathologic T3N0M0 MASC, without subsequent fluorescence in-situ hybridization analysis. We decided against performing complete submandibular gland excision because of a clear resection margin without any adverse features, which is a characteristic known to represent low to intermediate risk. Adjuvant radiation therapy (4,000 cGy) was administered owing to the presence of extraparenchymal cellular extension.



**Fig. 4.** The immunohistochemical findings of the right submandibular gland mass. A : The tumor cells exhibit strong and diffuse positive staining for S-100 protein. B : Gross cystic disease fluid protein 15 (GCDFP-15). C : CK7. D : Mammaglobin staining is weakly positive. E : Diastase periodic-acid Schiff (D-PAS) staining is positive in the secretory material. F : The Ki-67 proliferative activity is 2%.

At the 1-year follow-up, the patient remained disease-free and she was satisfied with the cosmesis associated with the use of the retroauricular approach.

## Discussion

MASC is a rare malignant salivary gland tumor that was first described in 2010.<sup>1)</sup> It has similar histologic, immunohistochemical, and cytogenetic characteristics as SC of the breast. Skalova et al. reported 16 salivary gland tumor cases showing the absence of zymogen granules, strong staining for mammaglobin as well as the presence of abundant extracellular colloid-like material, and reported that these features were similar to those of SC of the breast. The authors also found the ETV6-NTRK3 gene translocation in 15 of the 16 cases.<sup>1)</sup> The present case was not confirmed cytogenetically, but immunohistochemical staining patterns were typical of MASC.

The most common clinical presentation of MASC is a slowly enlarging non-tender mass palpable on physical examination. The majority (71%) of these

tumors are located in the parotid gland, but they are also found at other sites, including the submandibular gland (7%), soft palate, buccal mucosa, base of the tongue, and lips.<sup>2)</sup> On CT, a well-circumscribed and mildly enhanced lesion is a common finding; however, our case showed an atypical cystic mass.

Cystic nodal metastases may occur in patients, at a mean age of 50 years, and 44% of cervical cyst patients over 40 years of age report malignant origins. In contrast, cystic cervical masses in younger patients are more frequently benign.<sup>3)</sup> FNAC is essential for a differential diagnosis, and a preoperative FNAC should be recommended at the second visit. However, Levin et al. reported a low diagnostic rate, where the initial diagnosis of MASC was confirmed in only 1 of 12 fine needle aspirate cases.<sup>4)</sup>

Histopathologically, the central features of MASC are cystic, tubular, solid and/or papillary architecture, eosinophilic vacuolated cytoplasm, and intraluminal and/or intracellular colloid-like secretions that stain positive for PAS, and these tumors are diastase-resistant, with low-grade, bland, and pale nuclei as well as



positive staining for S-100 mammaglobin and a uteroglobin protein identified in breast tissue, endometrial cancer, and sweat gland carcinomas.<sup>1,4-5)</sup>

The most important differential diagnostic considerations for MASC are acinic cell carcinoma (AciCC), low-grade mucoepidermoid carcinoma, low-grade cribriform cystadenocarcinoma, and adenocarcinoma not otherwise specified. A significant factor for differentiating MASC from AciCC is the low presence of blue-purple cytoplasmic zymogen granules.<sup>6)</sup>

The clinical behavior of MASC is not well documented, but the disease is regarded as a low-grade malignancy. Chiosea et al. followed 14 MASC patients, and the mean disease-free survival, using death or recurrence as the endpoint, was 92 months.<sup>6)</sup>

The treatment for MASC is similar to the standard treatment for a low-grade malignant salivary gland tumor, although no conclusive efficacy has been proven to support this treatment.<sup>7)</sup> This standard treatment entails radical surgical resection and optional postoperative radiation therapy, similar to what was performed in the present case. For the treatment of a submandibular gland tumor, gland excision is adequate only for patients whose tumors are small and confined to the parenchyma. Additional lymphadenectomy and tumor bed resection should be considered in cases with extraparenchymal extension.<sup>8,10)</sup>

In cases of cystic masses at level II, a MASC of the submandibular gland can be suspected and endoscopic excision can be considered for cosmesis.

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