A Rare Case of Mammary Analogue Secretory Carcinoma Localized in the Submandibular Gland

Zülküf Küçüktağ[1], Samet Özlügedik[1], Halit Üner[2]

[1]University of Health Sciences Türkiye, Ankara Etlik City Hospital, Clinic of Otorhinolaryngology-Head and Neck Surgery, Ankara, Türkiye
[2]University of Health Sciences Türkiye, Ankara Etlik City Hospital, , Clinic of Pathology, Ankara, Türkiye

Case Report

Abstract

Mammary analogue secretory carcinoma (MASC) is a recently described rare salivary gland malignant tumor. A limited number of cases localized in the submandibular gland have been reported. A 56-year-old male patient presented with a slow growing mass in the left neck region. On physical examination, there was a mobile mass measuring approximately 5x4 cm in the left submandibular area. Radiologic imaging revealed a septated cystic mass with peripheral contrast enhancement, containing both solid and fluid components. Fine needle aspiration biopsy (FNAB) result was reported as atypia of uncertain significance. Submandibular gland excision was performed in the first stage. Since the pathology result was MASC and the tumor stage was T3, ipsilateral neck dissection was performed. On histopathological examination, neoplastic cells were seen to be rich in eosinophilic cytoplasm and vacuolization. Immunohistochemical examination revealed cytokeratin 7, mammaglobin and gross cystic disease fluid protein-15 positivity. By presenting this case report, we aimed to add a new case to the already limited number of submandibular gland localized MASC cases in the literature and contribute to the pool of knowledge on this subject. MASC should be considered especially in cases with submandibular gland localization in which the FNAB result is reported as atypia of uncertain significance.

Keywords: Mammary analogue secretory carcinoma, salivary gland neoplasms, submandibular gland, case report

ORCID IDs of the authors:
Z.K. 0000-0001-6846-3771
S.Ö. 0000-0001-7909-9100
H.Ü. 0000-0002-5388-4183

Cite this article as: *Küçüktağ Z, Özlügedik S, Üner H. A Rare case of mammary analogue secretory carcinoma localized in the submandibular gland. Turk Arch Otorhinolaryngol. [Epub Ahead of Print]*

Corresponding Author:
Zülküf Küçüktağ, MD;
zkucuk79@yahoo.com

Received Date: 05.02.2025
Accepted Date: 14.04.2025
Epub: 05.05.2025

DOI: 10.4274/tao.2025.2025-1-18

Introduction

Mammary analogue secretory carcinoma (MASC) was first described as a different type of salivary gland carcinoma by Skálová et al. (1) in 2010. Before this date, it was classified as a zymogen-poor variant of acinic cell carcinoma (AciCC). It mostly originates from the parotid gland. Its localization in the submandibular gland and minor salivary glands is very rare (2,3). Patients usually present with a painless mass that gradually grows for months or even years (1,2). It is a low-grade malignant tumor with good clinical prognosis and good response to surgical treatment (4).

In this report, we aimed to contribute to the pool of knowledge on this subject by presenting a case of MASC localized in the submandibular gland.

Case Presentation

Written informed consent was obtained from the patient for publication of this case report. A 56-year-old male patient

presented with a mass on the left side of the neck that had been present for 10 years and was gradually growing. There was no history of malignant disease in the patient or his family. There was no history of smoking and alcohol use. The patient was receiving treatment for hypertension and benign prostatic hypertrophy. Physical examination revealed a mobile, painless mass approximately 5x4 cm in size in the left submandibular region. No palpable lymphadenopathy was detected in the neck. Examination of all cranial nerves, especially the facial nerve, was normal.

Neck ultrasonography revealed a smoothly circumscribed and septated cystic mass with solid components and calcifications in the left submandibular region. Computed tomography (CT) and magnetic resonance imaging (MRI) revealed a septated cystic mass in the submandibular region, with indistinct borders from the gland, demonstrating peripheral contrast enhancement, containing both dense solid and fluid components, and including calcification foci. On radiologic imaging, the mass was located posterior to the submandibular gland, appeared adherent to it, and its borders could not be clearly distinguished from the gland. There was no lymph nodes of pathological size or characteristics (Figures 1, 2).

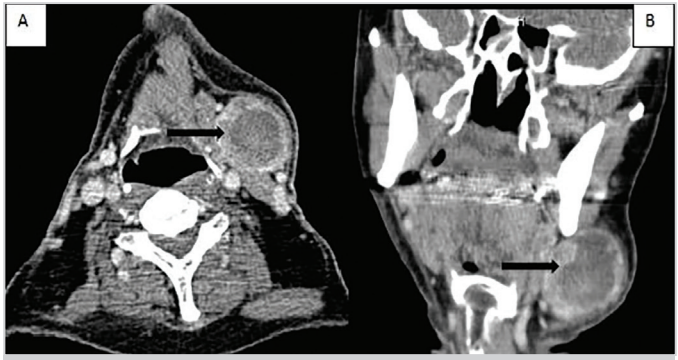

Figure 1. Contrast-enhanced CT images of the mass in the left submandibular area (A: axial, B: coronal)
CT: Computed tomography

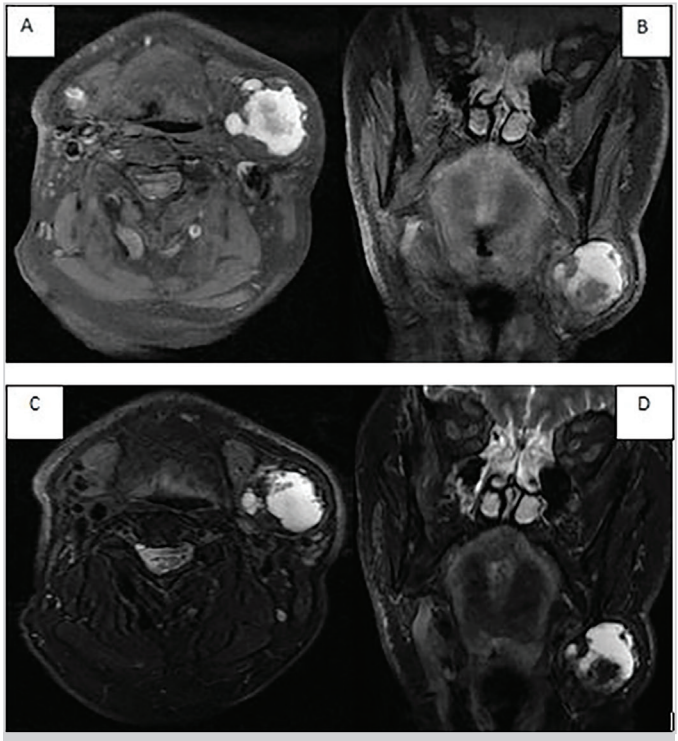

Figure 2. Contrast-enhanced MRI images of the mass in the left submandibular area (A: T1 axial, B: T1 coronal; C: T2 axial, D: T2 coronal)
MRI: Magnetic resonance imaging

Histopathologic examination revealed that the neoplastic cells had a tubular architecture and were rich in eosinophilic cytoplasm with prominent vacuolization (Figure 3). Immunohistochemical analysis demonstrated positive staining for cytokeratin 7 (CK7), mammaglobin, and gross cystic disease fluid protein-15 (GCDFP-15) (Figure 4). There was no evidence of lymphovascular or perineural invasion, and the surgical margins were free of tumor. The tumor was classified as low grade based on its histological features.

Given the diagnosis of MASC originating from the submandibular gland and staged as T3, the patient underwent ipsilateral neck dissection involving levels 1A, 1B, 2, and 3 during a second surgical session. No metastatic lymph nodes

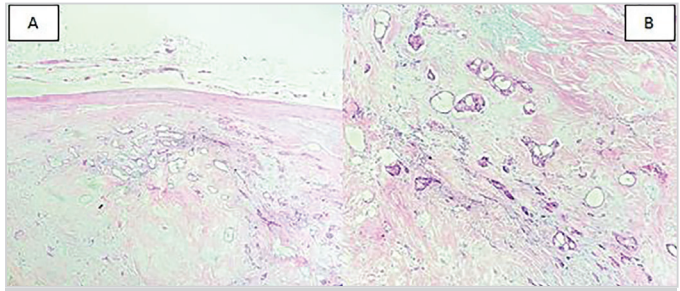

Figure 3. Histopathological appearance of the case (A: well-circumscribed tumor with prominent fibrosclerotic stroma and glandular structures with microcystic, follicular and tubular morphology, B: tumor cells have low grade atypia, characterized by cytoplasmic vesicular features, finely granular nuclear)

Figure 4. Immunohistochemical staining characteristics of the case (A: Tumor cells exhibit diffuse Mammaglobin positivity, B: GCDFP-15 immunohistochemistry is diffusely positive)
GCDFP-15: Gross cystic disease fluid protein-15

were identified. Consequently, no adjuvant therapy such as chemotherapy or radiotherapy was deemed necessary.

At the 20-month postoperative follow-up, which included physical examination, neck CT and MRI, no signs of recurrence were observed. Positron emission tomography-CT was not performed, as the tumor was low grade, surgical margins were negative, and there was no lymph node metastasis.

Discussion

Skálová et al. (1) re-evaluated the pathological features of 16 cases which were previously classified as AciCC or adenocarcinoma not otherwise classified. They classified cases with histopathologic features such as absence of zymogen granules, mammaglobin positive staining and presence of intracellular colloid-like material as MASC.

A limited number of cases of MASC localized in the submandibular gland have been reported in the literature. In a multicenter study, a total of 40 cases of MASC were presented and only two (5%) of them were reported to be localized in the submandibular gland (4). Chiosea et al. (2) reported that only three of 36 cases (8.3%) were localized in the submandibular gland. We believe that our case is also valuable in terms of its rare localization in the submandibular gland.

It is usually impossible to diagnose MASC with FNAB. In almost all cases, definitive diagnosis is made by histopathological examination of the postoperative specimen. In the cases of MASC presented by Wiles et al. (4), 50% of the FNAB results were reported as malignant (19/38). Of the FNAB results, 26% (10/38) were reported as suspicious for malignancy, 18% (7/38) as salivary gland neoplasm with uncertain malignancy potential, and 6% (2/38) as atypia of undetermined significance. In our case, the FNAB result was reported as atypia of undetermined significance and the definitive diagnosis was made by histopathological examination of the postoperative specimen.

Cystic, tubular and/or papillary appearance, presence of eosinophilic vacuolated cytoplasm and intraluminal and/or intracellular colloid-like secretions are histopathologic features of MASC (1,2). In AciCC, which is often confused with MASC, the presence of cytologically zymogen granules, lymphocyte infiltration rather than eosinophilia or absence of intracellular colloidal material is important in differential diagnosis (1).

Mammaglobin, S-100, and vimentin positive staining are typical and allow differentiation from other salivary gland tumors (1). CK7, CK8, GCDFP, MUC-1, MUC-4, BRST-2 and STAT5a positivity have also been shown (1). Our case had a cystic and tubular structure with eosinophilic vacuolated cytoplasm and intracellular colloidal appearance, and only mammaglobin, CK7 and GCDFP15 positivity was present.

Kurokawa et al. (5) defined the characteristic radiological features of MASC cases as a mass lesion with cystic and/or papillary, but not solid, appearance characterized by the presence of high-density cystic content in MRI images. In our case, the mass was radiologically cystic, as described by Kurokawa et al. (5), with peripheral contrast enhancement and containing both dense solid and fluid components, defined as a well-circumscribed cystic mass.

Although MASC has a good prognosis, the risk of lymph node metastasis is higher than AciCC. Chiosea et al. (2) found cervical lymph node metastases in four (22%) of 18 MASC patients who underwent neck dissection, compared to only three (7.9%) of 38 AciCC patients. Wiles et al. (4) reported that 22.5% of their patients had cervical lymph node metastasis and two of them also had brain and lung metastases. In our case, there was no cervical lymph node or distant organ metastasis.

Neck dissection is typically guided by the presence or risk of lymph node metastasis (2). The likelihood of nodal involvement is influenced by the tumor's T stage, histopathological type, and anatomical localization-being particularly higher in MASC cases arising from the submandibular gland (6,7). Postoperative radiotherapy is generally recommended in the presence of cervical lymph node metastasis, close (<5 mm) or positive surgical margins, perineural invasion, and in tumors classified as T3 or T4. In the present case, ipsilateral neck dissection was performed due to the tumor's submandibular origin and T3 staging. Radiotherapy was not required, as no metastatic lymph nodes were detected and surgical margins were negative.

Conclusion

Reported cases of MASC localized in the submandibular gland remain extremely rare. This diagnosis should be considered in salivary gland tumors, particularly when FNAB results indicate atypia of uncertain significance. A definitive diagnosis is established through histopathological and immunohistochemical evaluation of the postoperative specimen.

Ethics

Informed Consent: Written informed consent was obtained from the patient for publication of this case report.

Footnotes

Authorship Contributions

Surgical and Medical Practices: Z.K., S.Ö., Concept: Z.K., S.Ö., Design: Z.K., S.Ö., H.Ü., Data Collection and/or Processing: Z.K., S.Ö., H.Ü., Analysis and/or Interpretation: H.Ü., Literature Search: Z.K., S.Ö., Writing: Z.K., S.Ö.

Conflict of Interest: There is no conflict of interest to disclose.

Financial Disclosure: The authors declared that this study has received no financial support.

Main Points

- Mammary analogue secretory carcinoma (MASC) should be considered in submandibular gland masses when suspected malignancy is reported by fine needle aspiration biopsy.
- The presence of eosinophilic vacuolated cytoplasm and intraluminal and/or intracellular colloid-like secretions on histopathology and the presence of markers such as mammaglobin, vimentin, S-100 in immunohistochemical staining is important in differentiating MASC from other salivary gland tumors, especially AciCC.
- A neck dissection should be performed in addition to gland excision in cases of MASC localized to the submandibular gland or minor salivary glands and/or at an advanced stage (T3-T4).

References

1. Skálová A, Vanecek T, Sima R, Laco J, Weinreb I, Perez-Ordonez B, et al. Mammary analogue secretory carcinoma of salivary glands, containing the ETV6-NTRK3 fusion gene: a hitherto undescribed salivary gland tumor entity. Am J Surg Pathol. 2010; 34: 599-608. [Crossref]
2. Chiosea SI, Griffith C, Assaad A, Seethala RR. Clinicopathological characterization of mammary analogue secretory carcinoma of salivary glands. Histopathology. 2012; 61: 387-94. [Crossref]
3. Khalele BA. Systematic review of mammary analog secretory carcinoma of salivary glands at 7 years after description. Head Neck. 2017; 39: 1243-8. [Crossref]
4. Wiles AB, Gabrielson M, Baloch ZW, Faquin WC, Jo VY, Callegari F, et al. Secretory carcinoma of the salivary gland, a rare entity: An international multi-institutional study. Cancer Cytopathol. 2022; 130: 684-94. [Crossref]
5. Kurokawa R, Kurokawa M, Baba A, Ota Y, Moritani T, Srinivasan A. Radiological features of head and neck mammary analogue secretory carcinoma: 11 new cases with a systematic review of 29 cases reported in 28 publications. Neuroradiology. 2021; 63: 1901-11. [Crossref]
6. Terhaard CH, Lubsen H, Rasch CR, Levendag PC, Kaanders HH, Tjho-Heslinga RE, et al. The role of radiotherapy in the treatment of malignant salivary gland tumors. Int J Radiat Oncol Biol Phys. 2005; 61: 103-11. [Crossref]
7. Al-Mamgani A, van Rooij P, Verduijn GM, Meeuwis CA, Levendag PC. Long-term outcomes and quality of life of 186 patients with primary parotid carcinoma treated with surgery and radiotherapy at the Daniel den Hoed Cancer Center. Int J Radiat Oncol Biol Phys. 2012; 84: 189-95. [Crossref]