Clinical Case Report

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Salivary duct carcinoma of the supraglottis with a distinct presentation

A case report and literature review

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Abstract

Rationale: Salivary duct carcinoma (SDC) is a rare and aggressive subtype of salivary gland carcinoma that histologically resembles in situ and invasive ductal carcinoma of the breast. We present the first case of advanced SDC of the minor salivary gland arising from the supraglottis and review the literature on the clinicopathologic characteristics and prognosis of SDC.

Patient concerns: A 59-year-old male patient with progressive difficulty in swallowing and a muffled voice for 2 months.

Diagnoses: The patient was diagnosed with SDC arising from the supraglottis with extensive tumor invasion into the subsites of the larynx and pharynx.

Interventions: Due to impending airway obstruction, the patient underwent CO_2 laser debulking surgery. In addition to local disease, lymph node and distant metastases were also noted at diagnosis and concurrent chemoradiation therapy was arranged.

Outcomes: Laryngeal function was preserved and tracheostomy was avoided. The patient has survived for >1 year after the initial diagnosis.

Lessons: SDC is a rare and aggressive subtype of salivary gland carcinoma that histologically resembles in situ and invasive ductal carcinoma of the breast. Here we presented the first case of advanced SDC of the minor salivary gland arising from the supraglottis that was treated with CO_2 laser debulking surgery followed by concurrent chemoradiation therapy. Due to their rarity, further studies are required to establish the most effective treatment protocol for advanced SDC.

Abbreviations: AR = androgen receptor, CK7 = cytokeratin 7, GATA-3 = GATA binding protein 3, IHC = immunohistochemical, LVI = lymphovascular invasion, MRI = magnetic resonance imaging, SDC = salivary duct carcinoma.

Keywords: CO_2 laser debulking, minor salivary gland, salivary duct carcinoma, salivary gland carcinoma, supraglottis

1. Introduction

Salivary duct carcinoma (SDC) is an extremely rare malignancy arising from the ductal epithelial cells of the salivary glands. It was first described by Kleinsasser et al in 1968 for its distinct histologic similarity to ductal carcinoma of the breast.[1] The histopathology of this rare carcinoma was described in the World Health Organization's classification of salivary gland tumors in 1991.[2] SDC is estimated to account for approximately 1% to 3% of all salivary gland malignancies.[3–5] It is highly aggressive and has a poor prognosis which is characterized by rapid tumor growth, early regional metastasis, distant metastasis, and a high risk of recurrence. SDC arises predominately in the parotid gland, although it occasionally occurs in the minor salivary gland. As the incidence of SDC of the minor salivary gland is extremely low, only a few cases have been reported in the literature, and the palate was the most frequently reported anatomical site affected by minor salivary gland malignancies.

To the best of our knowledge, there have been only 2 previously published cases of laryngeal SDC arising from a minor salivary gland. The first was reported in 1981 by Ferlito et al[6] and the second in 2003 by Goel et al.[7] In both cases, laryngeal SDC presented as a single fungating mass from the larynx and a total laryngectomy was performed. Here we describe a rare primary SDC arising from the supraglottis with extensive tumor invasion into the subsites of the larynx and pharynx.

2. Case report

A 59-year-old man with hypertension presented with choking easily, muffled voice, and foreign body sensation of the throat for 2 months. He had a history of stroke attack twice in 2010 and 2013. Aspirin was used for the prevention of recurrent ischemic strokes and he abstained from alcohol and cigarettes. The patient visited our institution for professional assistance. Flexible nasopharyngoscopy showed multiple exophytic tumors in the

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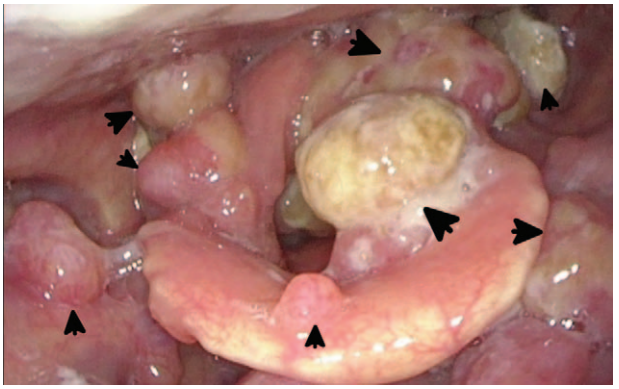

Figure 1. Flexible nasopharyngoscopy showed multifocal tumors (black arrow heads) disseminating on the supraglottis, glottis, pyriform sinus, vallecula, and oropharynx.

larynx and pharynx, especially involving the supraglottis. The tumors' growth pattern presented as a multifocal mass disseminating on the aryepiglottic folds, glottis, pyriform sinus, vallecula, and oropharynx. The tumor nearly obstructed the airway and the glottis was not visible (Fig. 1). Postgadolinium T1-weighted magnetic resonance imaging (MRI) revealed multifocal heterogenous enhancing tumors primarily involving the supraglottis with invasion through the thyroid cartilage. The left tonsil, bilateral aryepiglottic folds, bilateral pyriform sinus, and glottis were also involved further leading to airway narrowing. MRI of the neck confirmed several enlarged bilateral level II lymph nodes with central necrosis suggesting cervical metastasis (Fig. 2). Computed tomography of the chest revealed multiple nodules, up to 1.4 cm in size, in both lungs, which is compatible with lung metastasis.

Since the airway was obstructed by the tumor, CO_2 laser debulking was performed to remove the laryngeal and hypopharyngeal tumors to establish a secured airway.[8] Pathology revealed that the tumor was mainly located in the submucosal layer with invasion of the squamous mucosa. It was composed of nests of moderately differentiated cuboidal to low columnar epithelial cells in solid, cribriform, and tubular arrangements (Fig. 3 A and B). The tumor cells had a pale eosinophilic to cloudy cytoplasm and enlarged nuclei with frequent mitoses and a high nuclear proliferative index ratio (20%). An infiltrative growth pattern of the tumor cells with lymphovascular invasion (LVI) and tumor necrosis was also found. Immunohistochemically, the tumor cells were diffusely positive for cytokeratin 7 (CK7) and androgen receptor (AR) stains, and some tumor cells were also positive for GATA binding protein 3 (GATA-3) stain (Fig. 3C–E). After CO_2 laser debulking, the respiratory and swallowing functions improved significantly and tracheostomy was avoided. Furthermore, the patient was treated with cisplatin-based chemotherapy that was administered concurrently with radiotherapy for the treatment of the primary lesion and the enlarged bilateral neck lymph nodes. The patient has survived for >1 year after the initial diagnosis.

Written informed consent for publication of clinical details and accompanying images were obtained from the patient. Because it was a case report without any research involving human beings or experimental subjects, the ethical approval was not required in our institute.

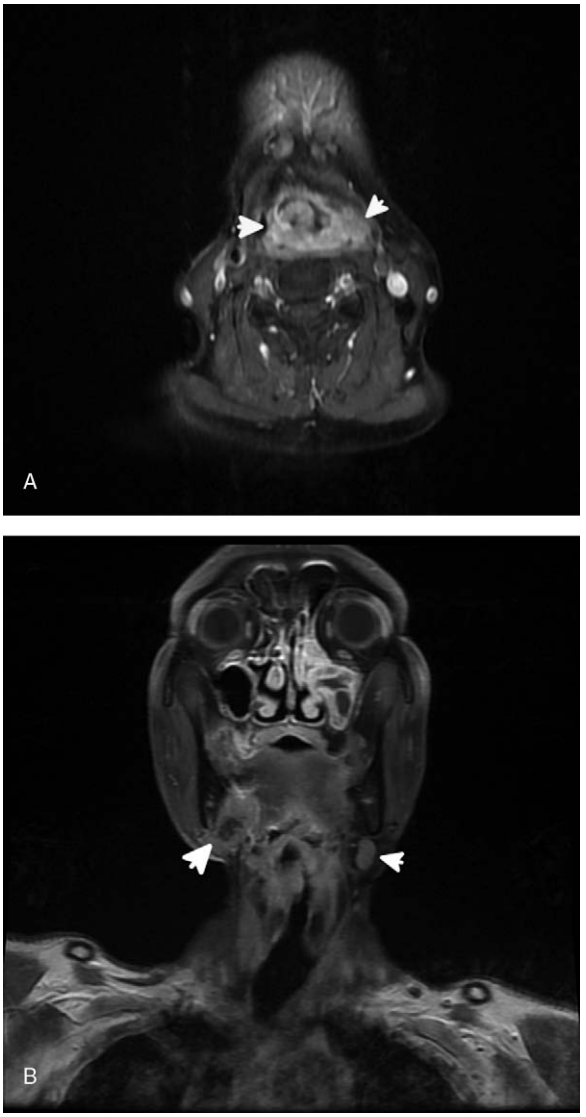

Figure 2. (A) Axial view of contrast-enhanced T1-weighted image revealed an ill-defined, infiltrative, and enhancing lesion (yellow arrow heads) primarily involving the supraglottic region leading to airway narrowing. (B) Coronal view of contrast-enhanced T1-weighted image of the neck demonstrated several enlarged bilateral level II lymph nodes (white arrow heads) with central necrosis, compatible with regional metastasis.

3. Discussion

Less than 1% of laryngeal tumors are nonsquamous cell malignancies.[7] To the best of our knowledge, this is the first reported case of SDC arising from the supraglottis with a distinct growth pattern recorded by flexible nasopharyngoscopy. SDC is a clinically aggressive tumor with a poor prognosis that is characterized by rapidly developing disease with early regional and distant metastases. Jaehne et al[4] reported 50 cases of newly diagnosed SDCs: 33 of 50 patients (66%) presented with advanced T3/T4 stage disease and 28 of 50 patients (56%) had cervical nodal metastasis. The recurrence rate of SDC is high, despite radical surgery and adjuvant chemoradiation therapy.[9,10] SDC occurs 4 times more frequently in men aged over 50 years. The most common site is the parotid gland (78–83%), although a few cases have been described in the submandibular gland (12%) and minor salivary glands

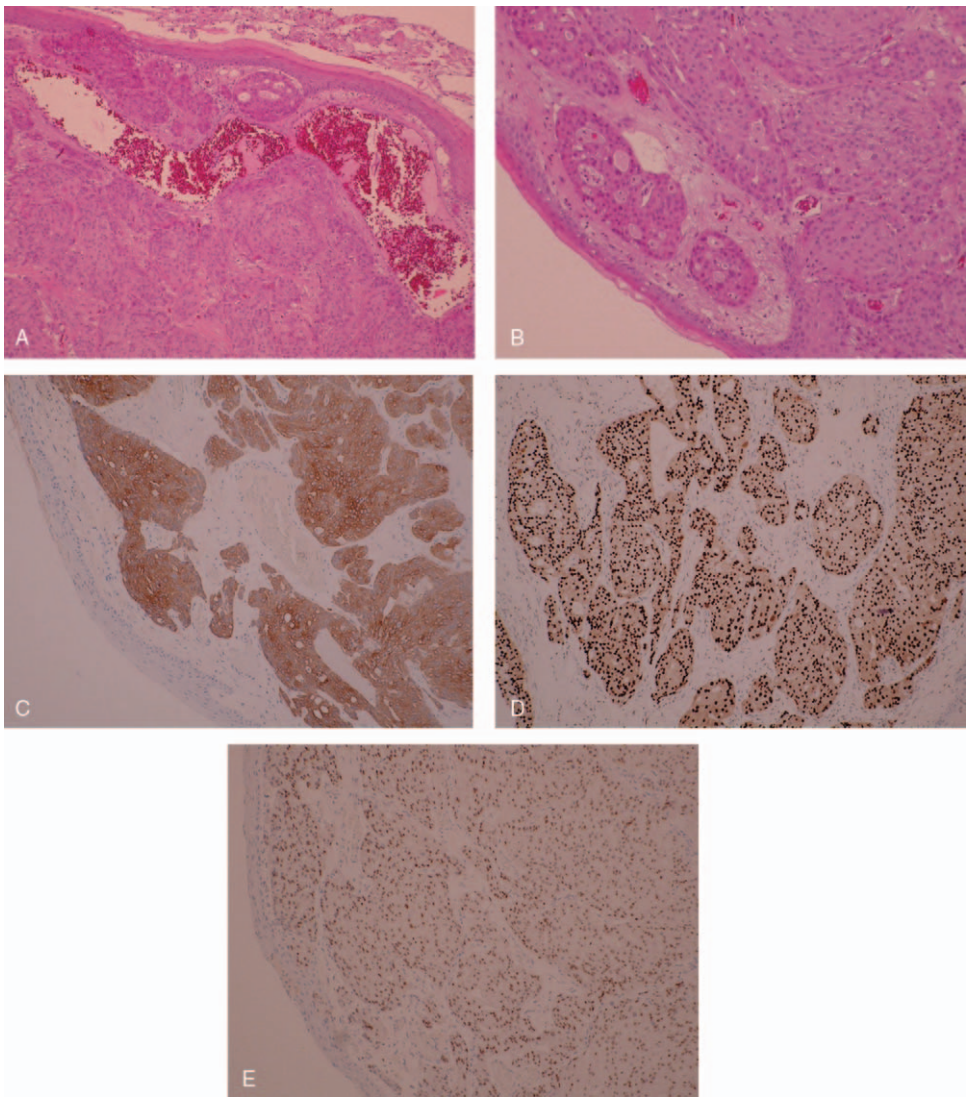

Figure 3. (A) and (B) Microscopically, the tumor cells were arranged in Roman bridge-like ductal and solid nest patterns, morphologically resembling ductal carcinoma of the breast when stained with hematoxylin and eosin. (C) IHC staining revealed the tumor cells were diffusely positive for CK7 staining. (D) IHC staining demonstrated the tumor cells were diffusely positive for AR staining. (E) Some tumor cells were positive for GATA-3 staining.

(<10%).[4,10] Macroscopically, SDC is usually present as an ill-defined firm mass with infiltrative margins and frequent tumor necrosis. Histologically, SDC strongly resembles ductal carcinoma of the breast. The classic morphologic architecture of SDC comprises expanded ductal and cribriform structures lined with epithelial cells with marked cytologic atypia. A Roman bridge-like appearance and comedo-necrosis are typically observed in SDC as well as in ductal carcinoma of the breast.[9,10] Both perineural invasion and LVI are frequently present in approximately 57% to 69% and 61% to 70% of patients, respectively. Furthermore, extranodal extension of the lymph node was identified in 58% of patients. These histopathologic findings are suggestive of a poor prognosis.[3,9,10] In addition to the classical morphology of SDC, some variant morphological features have also been reported, including papillary, micropapillary, mucin-rich, sarcomatoid, and oncocytic types.[9,10]

The histopathologic diagnosis of SDC was based on hematoxylin and eosin stains and confirmed by immunohistochemical (IHC) staining. IHC staining usually reveals positivity for broad spectrum and low molecular weight cytokeratins and epithelial membrane antigen.[9] Tumor cells stained diffusely positive with CK7 and GATA3. Furthermore, SDC also stained positively with the relatively common CK20 stain, in contrast with other salivary gland malignancies, which can aid in distinguishing SDC from morphologically similar carcinomas of breast or lung origin.[11] Nevertheless, SDC and breast carcinoma still share numerous IHC features. The prevalence of AR expression in SDC (67–90%) and breast carcinoma (47–88%) is similar.[9,10] Positive AR expression is often recognized as a marker to confirm the diagnosis of SDC. HER2/neu is also an important biomarker in SDC and is prevalent in 15% to 40% of patients with SDC.[3,9] Gross cystic disease fluid protein-15 is a diagnostic marker for mammary differentiation in breast cancer and has been reported in >80% of SDCs.[9,10] According to the IHC data, SDCs are classified into three categories: AR-positive, HER2/neu overexpression, and basal phenotype.[9]

Due to the limited number of cases of SDC of the minor salivary gland that have been reported to date, there is no consensus on a therapeutic strategy. Complete surgical excision with a wide margin combined with ipsilateral neck dissection is indicated for resectable tumors since more than half of patients have regional metastasis at the time of diagnosis. Contralateral neck dissection should also be considered because of the possible occurrence of bilateral lymphatic drainage. Adjuvant chemoradiation therapy was previously suggested for better locoregional control, especially for advanced SDC.[4,10]

Regardless of multimodal and aggressive treatments, the 5-year disease-specific survival and disease-free survival rates were 43% and 36%, respectively.[10] According to the case series reported by Jaehne et al, local recurrence occurred in 48% of patients at 17.4 months after initial treatment. Moreover, 48% of the patients developed distant metastasis after 29 months. The overall mean survival of these patients was reported to be approximately 36 to 56 months.[3,4] The 5-year survival rates for stage I disease was 42%, stage II was 40%, stage III was 30.8%, and stage IV was 23.2%. SDC of the parotid gland had a better prognosis than of the submandibular and minor salivary glands.[4]

Due to the extremely low incidence of SDC of the minor salivary gland, the prognostic factors remain limited. Based on the study of SDC of the major salivary gland, tumor size >3 cm, age >50 years old, lymph node involvement, higher tumor grading, the presence of perineural invasion, positive surgical margin, and regional and distant metastases have been proposed to be related to poor prognosis.[4,5,12,13] Overexpression of HER2/neu and tumor protein p53 are also regarded as poor prognostic factors, including early regional recurrences, distant metastasis, and lower survival rates.[13,14] Williams et al[13] found that both AR- and estrogen receptor β-negative SDCs correlated significantly with a decreased survival. Considering the features of HER2/neu overexpression in advanced SDCs, targeted therapy with anti-HER2 monoclonal antibodies (trastuzumab) has been suggested for patients with HER2/neu-positive SDC.[15] For AR-positive SDCs, androgen deprivation therapy has also been evaluated as a treatment option.[9,10]

4. Conclusion

Here we presented the first case of advanced SDC of the minor salivary gland arising from the supraglottis that was treated with CO_2 laser debulking surgery followed by concurrent chemoradiation therapy. Laryngeal function was preserved and tracheostomy was avoided. We also reviewed the histopathologic features, prognostic factors, and treatment modalities of SDC. Due to their rarity, further studies are required to establish the most effective treatment protocol for advanced SDC.

Author contributions

Conceptualization: C.C. Hsu, P.-Y. Chu.
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Formal analysis: C.C. Hsu.
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Investigation: P.-Y. Chu, W.-Y. Li.
Supervision: P.-Y. Chu.
Validation: P.-Y. Chu, W.-Y. Li.
Writing – review & editing: P.-Y. Chu.

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