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*Case Report*

# Salivary duct carcinoma originating in the right mandibular gingiva: a case report and literature review

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**Abstract:** Salivary duct carcinoma (SDC) is a rare and aggressive malignant tumor that frequently arises in the major salivary glands, predominantly in parotid glands. This case presents a primary gingival SDC, originating from the gingival ectopic salivary glands in a 66-year-old man. The patient exhibited no symptoms apart from a reddish nodular mass on the right anterior mandible gingiva with recurrent episodes of hemorrhage. The literature was reviewed on gingiva involved SDC and the therapeutic strategies. This case presentation emphasizes that early diagnosis and appropriate systemic therapy might be crucial in reducing adverse events and improving the survival rate in patients with SDC.

**Keywords:** Salivary duct carcinoma, oral cavity, gingiva

## Introduction

Salivary duct carcinoma (SDC) is an uncommon tumor, accounting for 1~3% of all malignant salivary gland neoplasms, which was first described by Kleinsasser et al. in 1968 [1]. It is highly aggressive and has a poor prognosis, nearly 70% of patients die from the distant metastatic disease within three years after diagnosis [2]. SDC arises predominantly in the parotid gland (over 70%) [3], very occasionally in the palatine minor salivary gland. Herein, this is the first report of an extremely rare and aggressive SDC, originating from the gingival ectopic salivary glands and relevant literature is discussed.

## Case report

A 66-year-old man presented with a painless nodular mass on the right mandibular gingiva and recurrent episodes of hemorrhage for past 3 months. The patient initially noticed a soybean-sized nodular mass on the right anterior mandible gingiva, which progressively extended to the opposite lingual gingiva in the oral cavity. The patient expressed the history of hypertension and cataract. However, family history was noncontributory. Upon intraoral examination, a palpable reddish nodular lesion, 4.0 cm × 2.5 cm in size, non-tender, firm in consistency, bleeding on touch was noted. The nodule was located in the attached gingiva between the lateral right mandibular incisor, canine, and premolar. Its surface at the bottom was granular (**Figure 1A**, **1B**). A non-tender, firm, fixed enlarged submental lymph node measuring approximately 2.0 cm in diameter was detected. Cone beam computed tomography (CBCT) revealed a well-circumscribed mass and with no bone involvement (**Figure 2A-C**). The CT scan of the maxillofacial region and neck with contrast medium was suggestive of multiple bilateral enlarged lymph nodes in levels I-V. However, no lesions were detected in bilateral major salivary glands.

After a thorough preoperative evaluation and discussion, surgery and adjuvant radiation combined with systemic therapy (targeting therapy and immunotherapy) were recommended. Tumor resection and bilateral radical neck dissection were performed. Postoperative histopathological examination of the surgical specimen confirmed the diagnosis of SDC (**Figure 3A-C**). The right-side neck dissection speci-

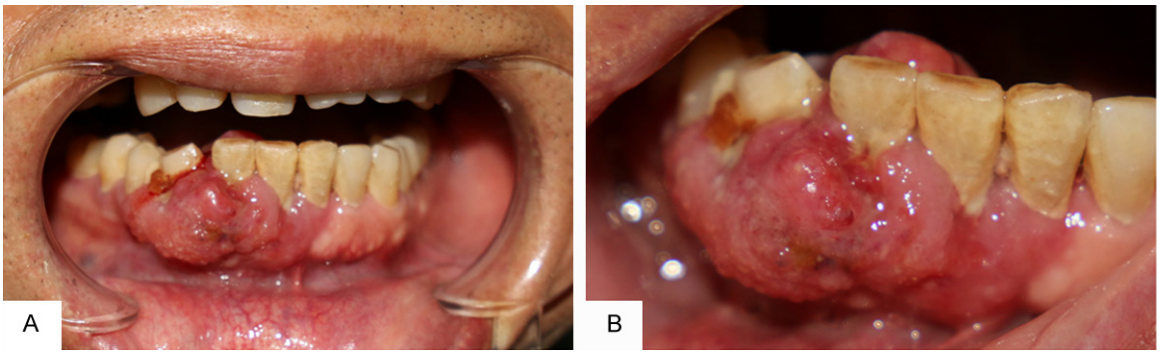


**Figure 1.** Clinical photographs. A, B. Intraoral examination manifested a reddish vulnerable nodular mass on the attached gingiva between the lateral right mandibular incisor, canine, and premolar.

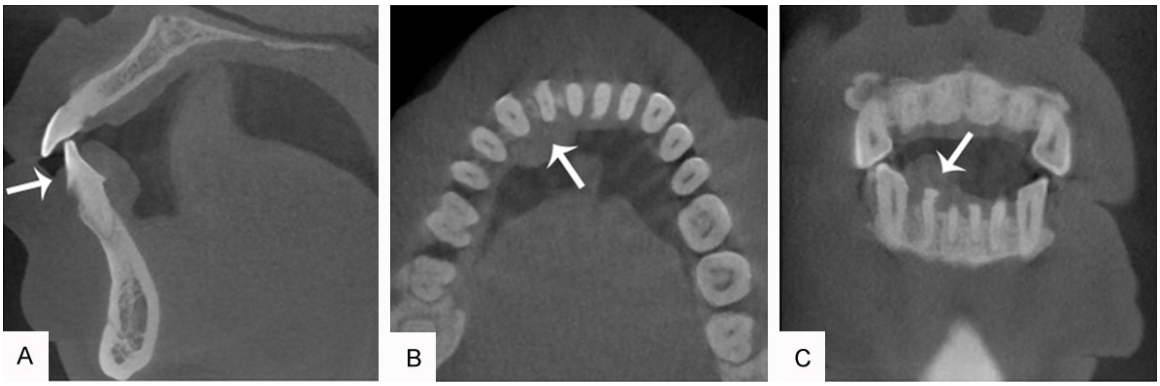


**Figure 2.** Radiographic results. CBCT showed a round nodule (Arrow) that is well-circumscribed and did not show associated bone involvement, as seen on the sagittal (A), axial (B) and coronal planes (C).

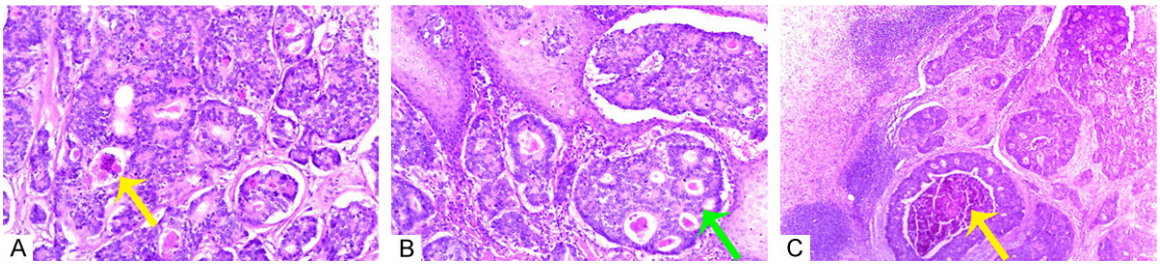


**Figure 3.** Histopathological findings of surgical specimen. A, B. The tumor was comprised of a neoplastic component characterized by atypical ductal epithelial cells, a cribriform growth pattern (Green Arrow), and comedo-like central necrosis (Yellow Arrow) (H&E magnification ×200). C. Metastatic tumor was found in dissected neck lymph nodes (H&E magnification ×100).

mens included 6 lymph node metastases (6/16), and the left included 16 lymph node metastases (16/18). Immunohistochemical staining examination (IHC) revealed neoplastic cells positive for androgen receptor (AR), HER2/neu and gross cystic disease fluid protein 15 (GCDFP15) (**Figure 4A-C**). Unfortunately, four months after the diagnosis of primary gingival SDC, the patient died of complications of pulmonary infection and hepatic failure.

## Discussion

Salivary duct carcinoma predominantly occurs in the major salivary gland. For SDC arising in the minor salivary gland, the hard palate is the most frequent site. Here we report an extremely rare and aggressive case of the primary gingival SDC. To the best of our knowledge, only 2 cases of SDC with gingiva involvement have been reported in the English-language litera-

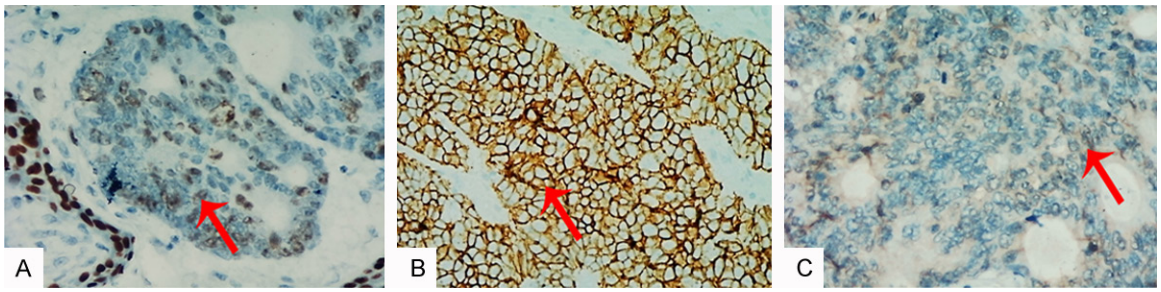


**Figure 4.** Immunohistochemical analysis. (A) Immunopositivity for androgen receptor (AR) is partly seen in the nuclei of the carcinoma cells. (B) Wide and intense positive expression of HER2/neu antigen was detected in the cellular membranes of the tumor cells. (C) Immunopositivity for gross cystic disease fluid protein 15 (GCDFP15) is partly observed in cytoplasm of the carcinoma cells. (A-C, original magnification ×200).

**Table 1.** Summary of clinicopathological characteristics in two cases of salivary duct carcinoma in the gingiva

| Author | Age/ gender | Site | Duration of symptom | Origin | Treatment | Metastasis | Follow up status |
|---|---|---|---|---|---|---|---|
| Bernabe et al. [4] | 67/male | Mandibular buccal attached gingiva | 5 months | Right parotid gland SDC | Biopsy | Mandibular gingiva, skin | Death from complications of a pulmonary metastasis (1 month) |
| Chandrasekar et al. [5] | 60/male | Lower anterior jaw region | 15 days | Primary SDC | Biopsy | Scapula, humerus, pelvic bones and liver | Lost to follow-up |

ture (see **Table 1**) [4, 5]. Compared with the previous cases, SDC in this report was characterized by sound bilateral major salivary glands and intact jaw bone. Thus, the possibilities of SDC originating within the jaw (intraosseous) or metastasizing from other primary lesions were ruled out. SDC in our report might originate from an ectopic minor salivary gland in the attached gingiva of the anterior mandibular region.

SDC exhibits aggressive clinical behavior, characterized by a high rate of regional nodes metastases (53.5-56%) and early distant metastasis (48%) [6, 7]. In the present case, the patient experienced bilateral levels I-V lymph node metastasis at the time of diagnosis, indicative of an adverse outcome. Given gingival SDC is extremely rare, no evidence-based therapeutic recommendations have been developed and treatment is mainly based upon experience with SDC of the major salivary glands. Surgical resection should be radical. Furthermore, adjuvant radiation is performed in most cases considering the aggressive clinical course. Nevertheless, cytotoxic chemotherapy showed limited efficacy in the treatment of SDC, it is often prescribed with adjuvant radiation or offered as palliative therapy in patients with recurrent or metastatic disease [8, 9].

In recent years, there has been an unprecedented advancement in biotherapy for patients with recurrent or metastatic malignancies. In breast cancer, patients receive docetaxel and trastuzumab as the first-line treatment for HER2-positive metastatic breast cancer [10]. Similarly, anti-HER2 monoclonal antibody has been suggested to be contributive as a therapeutic strategy for patients with HER2/neu-positive SDC [11]. Limaye et al. [12] reported long-term survival with complete response at 52 months in a patient with metastatic SDC. Furthermore, about 75% SDCs were characterized by the expression of Androgen receptor (AR) [13]. Anti-androgen therapy (ADT) has demonstrated activity in patients with recurrent or disseminated AR-expressing SDC [14, 15]. Recently, a study on the immune checkpoint ligand, PD-L1, demonstrated its expression in nearly half of 31 SDC specimens, suggesting that anti-PD-1/PD-L1 or other checkpoint inhibitors may exhibit some anti-tumor activity in this malignancy [16]. Pembrolizumab, an anti-PD1 antibody, exhibited 11.5% response rate and 46.2% stable disease rate in a cohort study of 26 advanced patients with salivary gland carcinoma, and 66.7% responders had SDC [17]. As in our case, it partly expressed AR and high expressed HER-2/neu. Regretfully, the patient only got the radical locoregional control

and could not proceed with the following therapies.

Based on the study of SDC of the major salivary gland, the prognostic factors including tumor size, anatomical location, positive infiltrative margin, regional recurrence, nodal metastasis, distant metastasis and overexpression of HER2/neu [11, 18]. However, due to the rarity of the incidence, prognostic data concerning SDC of minor salivary gland origin remains limited. SDCs originating in minor salivary glands has been described as less aggressive than those arising in major ones [19]. However, as for our research, the primary gingival SDC might exhibit a more aggressive progression, and followed by a poor prognosis.

In summary, this report describes an extremely uncommon occurrence of gingival SDC. The case sheds light on the aggressiveness and poor prognosis of this malignancy. The review of potential therapeutic strategies illustrates that surgical resection should be radical and for the advanced and metastatic cases, immunohistochemical staining examination of HER2/neu and AR is recommended for the preparation of probable biotherapies. Furthermore, early diagnosis is crucial in reducing adverse events and improving survival rate.

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## Disclosure of conflict of interest

None.

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