Salivary Duct Carcinoma in Minor Salivary Glands: Report of Two Cases with Different Clinical Behavior

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Abstract

Salivary duct carcinoma (SDC) is a malignant epithelial tumor extremely rare in minor salivary glands. This manuscript describes two cases of SDC of the minor salivary glands with different clinical behaviors. The first patient was an 80-year-old man who had SDC (T1N0M0) in the upper buccal fornix and the second patient was a 64-year-old man with a tumor (T2N2cM0) in the soft palate. Patients were treated with radical surgical resection and none patient underwent postoperative radiotherapy or chemotherapy. Histopathologically, the lesions showed proliferation of ductal cells with varying degrees of nuclear pleomorphism arranged in solid and cribriform structures and prominent comedonecrosis. The patient with SDC in the soft palate developed metastases and died shortly after diagnosis while the patient with SDC in upper alveolar ridge is alive without disease for over 6 years of follow-up. Although SDC is aggressive, anatomical site and precocious diagnosis are relevant factors for better prognosis.

Keywords: Salivary duct carcinoma; Minor salivary gland; Alveolar ridge; Soft palate

Introduction

Salivary duct carcinoma was first described in 1968 by Kleinsasser et al., [1] and it was recognized in the World Health Organization classification of salivary gland tumors in 1991 [2]. SDC is an uncommon and high-grade malignant tumor occurring predominantly in major salivary glands [3,4] with predilection for elderly men [5,6]. SDC is infrequent in minor salivary glands having resemblance to the ductal carcinoma of breast. SDC arises de novo or develops as the malignant component of carcinoma ex pleomorphic adenoma. SDC has invasive growth resulting in early regional and distant metastasis including lungs, liver and bones [4,7], and nearly 50% of the patients die of the disease within 4 to 5 years [8,9].

We report two cases of SDC arising of the minor salivary glands with different clinical behaviors.

Case reports

Case 1

An 80-year-old man was referred to the Oral Diagnostic Clinic for evaluation of a lesion in left upper buccal fornix with two months of evolution. On clinical examination, it was observed a painless ulcerated nodule with 2.0 x 1.0 cm that impeded the proper use of upper prosthesis (Figure 1A).
The patient underwent incisional biopsy and the histopathological examination showed large and polygonal cells with eosinophilic cytoplasm containing prominent nucleoli arranged in cribriform and papillary pattern. Mitotic figures and prominent comedonecrosis were also noted highly suggestive of salivary duct carcinoma (Figure 1C and 1D).

Figure 1C: Island of tumor cells arranged in a cribriform pattern (H&E staining, original magnification 100x).

Figure 1D: Large and polygonal with eosinophilic cytoplasm containing prominent nucleoli, mitotic figures and comedonecrosis (H&E, original magnification 400x).

Absence of hemorrhage and perineural and vascular invasion were observed. No invasion to surrounding tissue was found. Immunohistochemical study confirmed the luminal epithelial nature of the tumor cells with strong staining for CK7, CK8, CK18, CK19 and PSA (Figure 2).

Figure 2: Immunohistochemical study confirmed the luminal epithelial nature of the tumor cells with diffuse strong staining for CK7 (A), CK8 (B), CK18 (C) and CK19 (D) (high magnification 400x).

It was observed negativity for p63. The Ki-67 index in the tumoral cells was 5%.

The patient was referred to the head and neck surgeon who requested chest x-ray, gastrointestinal endoscopy, prostate ultrasound, bone scintigraphy and laboratory tests (PSA), which ruled out the possibility of metastasis or other primary tumors. The patient was staged as T1N0M0 and a maxillectomy was performed. The specimen measured 1.8x1.0 cm and the histopathologic analysis of the surgical specimen confirmed the diagnosis of SDC and showed free surgical margins. The tumor was well delimited. At six years of follow-up, the patient is alive without evidence of recurrence or metastasis.

Case 2

A 64-year-old man was referred complaining of a painless nodule in the palate for five months. Extraoral evaluation revealed cervical lymph nodes bilaterally suggestive of metastasis. On intraoral examination it was observed a nodular lesion involving the soft palate, measuring approximately 3.0x2.5 cm displacing the uvula to the right side (Figure 3A and 3B).

Figure 3A: Arrow showing enlarged lymph node.

Figure 3B: Nodular lesion on the soft palate causing displacement of the uvula.

The patient underwent incisional biopsy and the microscopical findings showed a proliferation of carcinomatous islands and scattered individual cells immersed in a highly hyalinized connective tissue. The neoplastic cells formed solid islands in a ductal pattern. The luminal cells were eosinophilic with hyperchromatic nuclei and conspicuous central nucleoli. The diagnosis was of invasive adenocarcinoma.

The patient was referred to head and neck surgeon, who staged the patient as T2N2cM0 (TNM system) through image examination (CT). The surgeon performed a radical tumor resection with bilateral neck dissection. The histopathological analysis of surgical specimen...
revealed that the tumor consisted of solid and cribriform cell nests with ductal structures, comedonecrosis, frequent mitoses and intense neural and vascular invasion allowing the final diagnosis of SDC (Figure 3C).

The immunohistochemical findings were the same case 1: positivity for CK7, CK8, CK18, CK19 and PSA, negativity for p63 and Ki-67 index in the tumoral cells was 10%.

However, the patient died after one month.

**Discussion**

Salivary duct carcinoma is uncommon and aggressive adenocarcinoma that occurs almost exclusively in the major salivary glands. Reports of SDCs involving minor salivary glands of the oral cavity are rare (Table 1) [1,5,6,10-29].

<table>
<thead>
<tr>
<th>Author</th>
<th>Age/ Gender</th>
<th>Site</th>
<th>Size (cm)</th>
<th>Clinical (UICC)</th>
<th>Treatment</th>
<th>Follow-Up</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kleinsasser et al. [1]</td>
<td>57/M</td>
<td>Hard palate</td>
<td>“Hazelnut in size”</td>
<td>NI</td>
<td>Extirpation</td>
<td>NI</td>
</tr>
<tr>
<td>Chen [10]</td>
<td>60/F</td>
<td>Tongue</td>
<td>“Lump”</td>
<td>NI</td>
<td>Wide excision</td>
<td>NED 5 years</td>
</tr>
<tr>
<td>Zohar et al. [12]</td>
<td>47/M</td>
<td>Upper vestibule</td>
<td>1</td>
<td>NI</td>
<td>Wide excision</td>
<td>NED 2 years</td>
</tr>
<tr>
<td>Watatani et al. [13]</td>
<td>60/F</td>
<td>Tongue</td>
<td>0.4</td>
<td>T1N0M0</td>
<td>Wide excision</td>
<td>NED 4 years</td>
</tr>
<tr>
<td>Kumar et al. [14]</td>
<td>NI (2 cases)</td>
<td>Maxilla</td>
<td>NI</td>
<td>NI</td>
<td>NI</td>
<td>Ni</td>
</tr>
<tr>
<td>Delgado et al. [15]</td>
<td>42/M</td>
<td>Hard palate</td>
<td>3</td>
<td>T2N0M0</td>
<td>Maxillectomy</td>
<td>DOD 5.2 years</td>
</tr>
<tr>
<td>Epivatianos et al. [16]</td>
<td>80/M</td>
<td>Upper vestibular sulcus</td>
<td>2.5</td>
<td>T2N0M0</td>
<td>Maxillectomy</td>
<td>Ni</td>
</tr>
<tr>
<td></td>
<td>74/M</td>
<td>Lower vestibular sulcus</td>
<td>4</td>
<td>T2N2cM0</td>
<td>Wide excision-ND</td>
<td>DOD 2 years</td>
</tr>
<tr>
<td></td>
<td>58/M</td>
<td>Hard palate</td>
<td>4</td>
<td>T2N2bM0</td>
<td>RT</td>
<td>DOD 6 months</td>
</tr>
<tr>
<td></td>
<td>60/M</td>
<td>Buccal sulcus</td>
<td>3</td>
<td>T2N0M0</td>
<td>Maxillectomy-ND-RT</td>
<td>NED 4 years</td>
</tr>
<tr>
<td>Yoshimura et al. [5]</td>
<td>62/M</td>
<td>Buccal mucosa</td>
<td>3.1</td>
<td>T2N2bM0</td>
<td>Radical surgery-RT</td>
<td>Alive after 1.6 years with multiple metastases</td>
</tr>
<tr>
<td>Tatemoto et al. [6]</td>
<td>58/F</td>
<td>Hard palate</td>
<td>1</td>
<td>T1N0M0</td>
<td>Local resection</td>
<td>NED 2.5 years</td>
</tr>
<tr>
<td>Guzzo et al. [17]</td>
<td>NI</td>
<td>Cheek</td>
<td>NI</td>
<td>TxN0M0</td>
<td>Enucleated</td>
<td>Alive with disease (54 months)</td>
</tr>
<tr>
<td>Suzuki &amp; Hashimoto [18]</td>
<td>56/M</td>
<td>Mandible</td>
<td>4</td>
<td>NI</td>
<td>Excision</td>
<td>NED 5 years</td>
</tr>
<tr>
<td>Lopes et al. [19]</td>
<td>63/M</td>
<td>Hard palate</td>
<td>6</td>
<td>T4N2bM0</td>
<td>Hemimaxillectomy-ND-RT</td>
<td>DOD 11 months</td>
</tr>
<tr>
<td>Huh et al. [20]</td>
<td>61/M</td>
<td>Hard palate</td>
<td>5</td>
<td>T3N0M0</td>
<td>Hemimaxillectomy-ND-RT</td>
<td>NED 9 months</td>
</tr>
<tr>
<td></td>
<td>54/M</td>
<td>Hard palate</td>
<td>5</td>
<td>T3N0M0</td>
<td>Hemimaxillectomy</td>
<td>NED 15 months</td>
</tr>
<tr>
<td></td>
<td>23/F</td>
<td>Hard Palate</td>
<td>4</td>
<td>T4N0M1</td>
<td>Patient denied further treatment</td>
<td>DOD 7 months</td>
</tr>
<tr>
<td>Van Heerden et al. [21]</td>
<td>53/F</td>
<td>Hard palate and right alveolar ridge</td>
<td>14</td>
<td>T4N-M0</td>
<td>Patient refused treatment</td>
<td>Lost to follow-up</td>
</tr>
</tbody>
</table>

Figure 3C: Tumor cell with comedonecrosis (H&E, original magnification 100x).
To the best of our knowledge, only 37 cases of SDC originating in the intraoral minor salivary glands have been reported in the English-language literature. The most frequent site is the hard palate (14 cases). We related the first case of SDC in the buccal fornix and the second case of SDC in the soft palate. SDC most frequently affects older male patients in the fifth or sixth decade of life [30]. The mean age of the current patients was 72 years (64 and 80 years) and both patients were male.

Salivary duct carcinoma can occur de novo or as the malignant component of carcinoma ex pleomorphic adenoma [31]. SDC can be classified into three subtypes, according to intraductal or infiltrative predominance: 1) predominantly intraductal, where 90% of the tumor is intraductal; 2) predominantly infiltrative, when less than 20% of the tumor is intraductal; or 3) infiltrative, when the tumor is entirely desmoplastic. Angiolymphatic, perineural and bone invasion are prominent comedonecrosis [33]. The stroma is densely fibrous or desmoplastic. Angiolymphatic, perineural and bone invasion are common [4,36,37].

Immunohistochemical studies can confirm the luminal epithelial nature of the tumor cells [38]. SDC is immunoreactive for low- and high-molecular-weight cytokeratin. It was shown by immunohistochemical analysis performed in case 1 of the current study. Tumor cells had diffuse strong reactivity for cytokeratin CK7, CK8, CK18 and CK19. In addition, SDC is immunoreactive for Carcinomembryonic Antigen (CEA), strong nuclear reactivity for Androgen Receptors (AR) stage II (n=1), stage IV (n=4), and metastatic. Immunohistochemical analysis of the 2 presented cases, we noted that both cases were predominantly intraductal corresponding to the more frequent subtype.

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Site</th>
<th>Stage</th>
<th>Treatment</th>
<th>Follow-up</th>
</tr>
</thead>
<tbody>
<tr>
<td>71/M</td>
<td>Hard palate and buccal sulcus</td>
<td>5</td>
<td>T4N-M0</td>
<td>Patient refused treatment</td>
</tr>
<tr>
<td>77/M</td>
<td>Hard palate</td>
<td>5</td>
<td>T4N-M0</td>
<td>Patient refused treatment</td>
</tr>
<tr>
<td>63/F</td>
<td>Hard palate</td>
<td>7</td>
<td>T4N-M0</td>
<td>Hemimandibleectomy-ND-RT</td>
</tr>
<tr>
<td>47/M</td>
<td>Hard palate</td>
<td>5</td>
<td>T4N-M0</td>
<td>Patient still considering surgical treatment</td>
</tr>
<tr>
<td>Cheuk et al. [22]</td>
<td>Buccal mucosa</td>
<td>1.2</td>
<td>T1N0M0</td>
<td>Local excision</td>
</tr>
<tr>
<td>Ide et al. [23]</td>
<td>Retromolar gingiva</td>
<td>1.5</td>
<td>T1N0M0</td>
<td>Local excision</td>
</tr>
<tr>
<td>Jaehe et al. [24]</td>
<td>NI (5 cases)</td>
<td>NI</td>
<td>stage II (n=1), stage IV (n=4)</td>
<td>NI</td>
</tr>
<tr>
<td>Ponniah et al. [25]</td>
<td>26/M Hard palate</td>
<td>3</td>
<td>T2N0M0</td>
<td>Local excision</td>
</tr>
<tr>
<td>Suzuki et al. [26]</td>
<td>64/F Tongue</td>
<td>1.5</td>
<td>T1N0M0</td>
<td>Partial glossectomy</td>
</tr>
<tr>
<td>Kikuchi et al. [27]</td>
<td>62/M Mandible</td>
<td>ND</td>
<td>stage III</td>
<td>Hemimandibleectomy-ND-RT-ChT</td>
</tr>
<tr>
<td>Dhanuthai et al. [28]</td>
<td>NI Alveolar mucosa</td>
<td>NI</td>
<td>NI</td>
<td>NI</td>
</tr>
<tr>
<td>Thamilselvi et al. [29]</td>
<td>35/F Soft palate</td>
<td>5.5</td>
<td>T3N0M0</td>
<td>Local excision</td>
</tr>
<tr>
<td>Present cases</td>
<td>80/M Buccal fornix</td>
<td>1</td>
<td>T1N0M0</td>
<td>Hemimandibleectomy</td>
</tr>
<tr>
<td>64/M Soft palate</td>
<td>3</td>
<td>T2N0cM0</td>
<td>Radical tumor resection-ND</td>
<td>DOD 1 month</td>
</tr>
</tbody>
</table>

ChT, chemotherapy; DOD, died of disease; F, female; M, male; N/A, not available; ND, neck dissection; NED, no evidence of disease; RT, radiotherapy; NI, no information.

Table 1: Salivary duct carcinoma in minor salivary gland in the English-language literature

The main microscopic finding includes an intraductal component, comprising proliferating ductal cells with varying degrees of nuclear pleomorphism arranged in architectural patterns including solid, “Roman bridge”, papillary and cribriform structures, often with prominent comedonecrosis [33]. The stroma is densely fibrous or desmoplastic. Angiolymphatic, perineural and bone invasion are common [4,36,37].
50-70%, [4,17] and the more common sites are lungs, bone, brain, skin, liver and thyroid gland [46-48]. Approximately 50% of the patients die of the disease within 4 to 5 years [8,9,49]. In the case 2, the patient developed bilateral cervical lymph node metastasis probably because the size and the site of primary tumor affecting the soft palate close to the midline. These facts favored the tumor spread and consequently a poor prognosis.

Carcinomas of minor salivary glands are staged (TNM system) according to their anatomic site of origin, similar to other carcinomas [50]. Spiro et al. (1991) [51] have applied the criteria used for squamous cell carcinoma to mucoepidermoid carcinoma of minor salivary glands. Thus, the patients reported were classified as Stage I or T1N0M0 (case 1) and Stage IVA or T2N2cM0 (case 2).

In the current study, both patients were treated with radical surgical excision. The patient of the case 1 diagnosed with SDC in upper buccal forni had no local or distant metastases and is free of disease with T1N0M0 (case 1) and Stage IVA or T2N2cM0 (case 2).

Local invasion, frequent lymphatic and hematogenous metastasis, and poor prognosis characterize the biologic behavior of salivary duct carcinoma. Several studies have described some correlation of prognosis to tumor size (less than 3 cm indicated a better prognosis) [2]. Zohar et al. (1988) showed the highly aggressive biological behavior of the tumor when occurring in the major salivary glands, in contrast to the benign course of the salivary duct carcinoma in the minor salivary gland.

In summary, SDC is an uncommon tumor in minor salivary glands. Although, it is aggressive and has high possibility of developing local and distant metastasis, besides several factors, anatomical location and clinical stage of the tumor are relevant and may interfere with the clinical course of the tumor.

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References


