An extremely rare salivary gland tumor: intraductal carcinoma of the buccal mucosa

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Abstract Intraductal carcinoma of the salivary gland is a rare, indolent neoplasm characterized by intraductal malignant cell proliferation but lacking invasiveness, in contrast to conventional salivary duct carcinoma, a clinically aggressive neoplasm with invasive characteristics. The tumor affects the major salivary glands much more frequently than the minor salivary glands. This report describes an extremely rare intraductal carcinoma arising from the buccal mucosa in a 61-year-old man who presented with a painless mass in the left buccal mucosa, which he had had for 1 month. A biopsy of the tumor indicated it was most likely an adenocarcinoma, but accurate preoperative diagnosis was difficult. The tumor was completely removed, along with sufficient margins. Histological examination revealed that the lesion was composed of proliferating epithelial cells surrounded by an intact myoepithelial layer, with no evidence of invasion. The final diagnosis was intraductal carcinoma of the salivary gland. No recurrence has been observed for over 3 years. In conclusion, the difficulty in preoperatively diagnosing this rare entity suggests that complete surgical excision with sufficient margins remains the best treatment option.

Keywords Intraductal carcinoma · Salivary gland neoplasm · Salivary duct carcinoma · Buccal mucosa

Introduction

Conventional salivary duct carcinoma (SDC) is one of the most aggressive malignancies, usually presenting as a rapidly growing tumor in the parotid gland. SDC resembles high-grade ductal carcinoma of the breast, with both intraductal and widely invasive components [1]. In 1983, a patient was described with an intra-lingual minor salivary gland carcinoma, thought to represent a pre-invasive phase of infiltrating SDC. This tumor, an intraductal carcinoma of the salivary gland, lacked both the aggressive morphologic features and clinical behavior of high-grade SDC [2]. Although not recognized as an entity by the 2005 WHO classification, intraductal carcinoma was found to be a rare, indolent malignant neoplasm characterized by an intraductal proliferation of malignant cells, similar to ductal carcinoma in situ of the breast [3]. Subsequent reports of similar tumors [4–12] have shown that they affect the major salivary glands more frequently than the minor salivary glands. Owing to the rarity of intraductal carcinoma in the minor salivary glands, appropriate therapy has not been determined. This report describes a patient with an intraductal carcinoma arising from the buccal mucosa, which was treated by complete surgical excision.

Case report

A 61-year-old man presented with a painless mass in the left buccal mucosa, which he had had for 1 month. The mass measured 15 × 10 mm; was elastic, hard and non-fixed; and

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Fig. 1 Intraoral appearance of the left buccal tumor. The tumor, which measured 15×10 mm, was hard but not fixed to the underlying structure (*open circle*)

was minimally exposed to the mucosal surface (Fig. 1). T2-weighted magnetic resonance imaging (MRI) showed a high-intensity cystic mass of the left buccal mucosa, with no obvious invasion of the surrounding tissue (Fig. 2a–c).

The tumor was not detected by positron emission tomography–computed tomography. Because a biopsy indicated the tumor was most likely an adenocarcinoma, it was completely excised, with margins of 10 mm, and ipsilateral neck dissection was performed. Subsequently, the surgical defect was reconstructed by a free radial forearm flap. Histological examination of the resected specimen revealed that the primary lesion was a subepithelial unit continuous with the overlying squamous epithelium. The proliferating epithelial cells in the lesion formed tubular and small cystic structures, consisting of two layers of epithelial and myoepithelial cells (Fig. 3a, b). No vascular or perineural invasion was observed. Immunohistochemical analysis showed that tumor islands of S-100 protein positive

epithelial cells were surrounded by a single layer of myoepithelial cells strongly expressing p63 (Fig. 3c, d). Because the tumor cells were negative for androgen receptor and revealed only limited reactivity for gross cystic disease fluid protein 15, SDC was excluded. Based on these histopathological findings, the tumor was diagnosed as an intraductal carcinoma.

After a follow-up period of more than 3 years, there has been no evidence of tumor recurrence or new relevant symptoms.

Discussion

Intraductal carcinoma of the salivary gland was initially defined as an in situ ductal carcinoma with an intact myoepithelial cell layer around all tumor islands [2]. Subsequently, several other such tumors, called low-grade salivary duct carcinomas, have been reported [4–12]. Intraductal carcinoma of the salivary gland has been described as a precursor of SDC [5]. Although both tumor types are characterized by ductal proliferative architecture, their biologic behavior differs substantially, suggesting a lack of relationship between these types. In the patient described here, the tumor was entirely confined within the salivary duct and no infiltrating component was present, resulting in a diagnosis of intraductal carcinoma of the salivary gland.

Most intraductal carcinomas arise from the major salivary glands, with only four patients reported to have intraductal carcinomas of the minor salivary glands, two with tumors of the tongue [2, 9] and one each with tumors of the hard palate [8] and the buccal mucosa [5]. The patient described here may therefore be the second with an intraductal carcinoma of the buccal mucosa.

Fig. 2 Axial MRI of the oral cavity. **a** T1-weighted image showing a heterogeneous low-intensity lesion (*arrow*), measuring $12 \times 25 \times 23$ mm, close to the buccal fat tissue (*arrow heads*) in the left buccal region. **b** T2-weighted image shows several high-intensity areas in the

lesion, which may represent cystic portions (*small arrows*). **c** T1-weighted contrast-enhanced image showing no obvious invasion of the surrounding tissues (*small arrows*)

Fig. 3 Histopathological findings of the resected specimen. **a** Picture of the lesion at its maximum dimensions. The subepithelial lesion did not disrupt the continuity of the overlying squamous cell epithelium. (Hematoxylin and eosin staining, original magnification $\times 12.5$). **b** Photomicrograph at higher power, showing that epithelial cells formed structures with tubular and small cystic patterns. (Hematoxylin and eosin staining, original magnification $\times 100$).

c Immunohistochemical staining for S100 protein, showing proliferation of S100-positive atypical cells and their formation of epithelial islands in the lesion. (Staining with antibody to S100 protein, original magnification $\times 600$). **d** Immunohistochemical staining for p63, showing p63-positive non-neoplastic myoepithelial cells are evenly wrapped around all the epithelial islands. (Staining with antibody to p63, original magnification $\times 600$)

The characteristics of the four previously described patients with minor salivary gland intraductal carcinoma, together with the patient described here, are listed in Table 1. Wide excision of these tumors was associated with a favorable prognosis.

The morphologic features of pure intraductal carcinoma may overlap with those of low-grade cribriform cystadenocarcinoma (LGCCC), although the relationship of these two types remains unclear [4, 12, 13]. However LGCCCs usually occur in the parotid gland and are

Table 1 Characteristics of patients with minor salivary gland intraductal carcinoma

Authors	Age/gender	Nationality	Site	Symptom	Preoperative diagnosis	Final diagnosis	Size (cm)	Treatment	Prognosis
Chen [2]	60/F	USA	The tongue	Painless mass	Carcinoma	Intraductal carcinoma	NA	Wide excision	NED 5 years
Watani et al. [9]	60/F	Japan	The tongue	Painless mass	Undifferentiated squamous cell carcinoma	Intraductal carcinoma	4	Wide excision	NED 4 years
Tatemoto et al. [8]	58/F	Japan	The hard palate	Painless mass	Benign salivary gland tumor	Low malignant Intraductal carcinoma	1	Wide excision	NED 2.5 years
Cheuk et al. [5]	44/F	Hong Kong	The buccal mucosa	Painless mass	NA	Intraductal carcinoma	1.2	Wide excision	NED 4 years
Current case	61/M	Japan	The buccal mucosa	Painless mass	Adenocarcinoma	Intraductal carcinoma	1.5	Wide excision	NED 3 years

NA not available, NED no evidence of disease

characterized by a dominant cribriform structural pattern [5, 14, 15], a pattern not observed in the patient described here. Differential diagnosis should also include cystadenocarcinoma, a tumor characterized by a complex papillary architecture with infiltrative growth and absence of myoepithelial cells [16]. In our patient, however, p63-positive myoepithelial cells were distributed around the epithelial islands.

Many similarities have been observed between breast and salivary malignancies [16]. Histologically, intraductal carcinoma of the salivary glands is characterized by intraductal epithelial proliferation, resembling atypical ductal hyperplasia to high-grade ductal carcinoma in situ of the breast. Architecturally, salivary tumors range from cribriform to solid with central comedo necrosis [10]. Axillary dissection of intraductal carcinoma of the breast [17] shows lymph node metastasis in up to 2 % of patients, indicating that inadequate sampling of the breast lesion led to failure to identify an invasive component. Similarly, intraductal carcinoma of the salivary gland may also develop into invasive carcinoma. Tumors can recur because of incomplete resection of the invasive carcinoma, which may extend locally more than expected or cervical lymph node metastasis. The defining features of intraductal carcinoma of the salivary gland include preservation of preexisting myoepithelial cells around the epithelial units and absence of an invasive component [5, 13, 18]. Complete excision results in a totally benign clinical course [16]. However, preoperative clinical diagnosis of this entity is impossible because the entire sample is necessary to confirm the absence of local invasion.

In summary, this report describes an extremely rare case of intraductal carcinoma arising from the buccal mucosa. Because all clinical features of this tumor are not clear preoperatively and pathological examination of the entire specimen is required for definitive diagnosis, complete surgical excision with sufficiently large margins is required, followed by long-term follow-up.

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Conflict of interest All authors declare that they have no conflict of interest.

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