A Case of Carcinoma Ex Pleomorphic Adenoma in the Buccal Mucosa: Review of the Literature

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Received: 12 September 2010 / Accepted: 30 March 2011 / Published online: 15 June 2011
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Abstract We present a case of carcinoma ex pleomorphic adenoma on the right buccal mucosa in a 52-year-old Japanese woman. Based on the histopathology, the excised tumor was the non-invasive type, but the majority of the tumor consisted of poorly-differentiated adenocarcinoma cells. We performed proton radiation after the surgery. The patient was well, without evidence of disease, 48 months after surgery. Carcinoma ex pleomorphic adenoma in the buccal mucosa has been reported in only four cases during the past twenty years. Therefore, our case was comparatively rare.

Keywords Carcinoma ex pleomorphic adenoma · Buccal mucosa · Proton radiation

Introduction

Carcinoma ex pleomorphic adenoma (CXPA) is a tumor that includes cancer cells within a benign pleomorphic adenoma, and comprises approximately 12% of all salivary malignancies [1]. CXPA most frequently arises in the parotid gland. In the minor salivary sites, CXPA occurs most commonly in the palate, whereas it is rare in the

buccal mucosa. We report a case of CXPA in the buccal mucosa and present a review of the literature.

Case Report

A 52-year-old Japanese woman had complained of a painless mass in the right-side buccal mucosa for 2 months. There were not any prior history of swelling and any history of trauma to the buccal mucosa. Her past history was unremarkable, and her sister had breast cancer. Her face was asymmetrical due to swelling of the right-side cheek. There were no indications of paralysis, trismus, or swelling of the cervical lymph node. In the oral cavity, there was a 3 cm mass that was elastic hard, mobile and clear of the border in the right buccal mucosa (Fig. 1). There was no tenderness and fluctuation. Magnetic resonance imaging scans showed a large anterointernal mass distinct from the parotid gland. T2-weighted image revealed a mass with high density and inhomogeneous signal inside (Fig. 2). Positron Emission Tomography CT scan showed SUV = 7.4 g/ml, but 18F-fluorodeoxyglucose (FDG) retention was not observed in the cervical lymph node or lung. Laboratory examination was within the normal range. The clinical diagnosis was tumor of the right buccal mucosa. We performed resection of tumor intraorally under general anesthesia. The incision was made in the oral mucosa horizontally. The tumor was located immediately beneath the mucosa and was surrounded by a capsule. The tumor was ablated from the surrounding soft tissue and was extracted. Frozen section examination revealed poorly-differentiated squamous cell carcinoma suspected. Therefore, we performed curettage of the surrounding tissue and treatment with a CO₂ laser. We then tied over the open wound with tamponage. Grossly, the surface of the excised

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Fig. 1 Clinical view of a mass in the right-side buccal mucosa

Fig. 2 T2-weighted horizontal magnetic resonance imaging scans. The high-density area was observed in the part of the arrow

tumor ($3.0 \times 2.0 \times 2.0$ cm) was ovoid, solid and gray-yellow. On section, the tumor exhibited a yellow and white, variegated smooth cut surface (Fig. 3). On pathological examination, the majority of the tumor consisted of poorly-differentiated adenocarcinoma cells (Fig. 4a, b). They exhibited large nuclei, and formed the nests and ducts. A portion of the specimen exhibited hyalinization and typical pleomorphic adenoma cells formed seat and biphasic (Fig. 4c). There was no invasion of the capsule. On

Fig. 3 Excised tumor ($3.0 \times 2.0 \times 2.0$ cm) was ovoid, solid and yellow white

immunohistochemical staining, the tumor cells were positive for cytokeratin 7, vimentin, and carcinoembryonic antigen (CEA), and were partially positive for p53, S-100 protein, and actin antigen, but were negative for glial fibrillary acidic protein (GFAP) antigen. Ki-67 was positive, and the labeling index was 14.8%. The pathological diagnosis was CXPA. Seven weeks after the surgery, the patient underwent proton radiation (65GyE) at the Hyogo Ion Beam Medical Center. The patient was well, without evidence of disease, 48 months after the surgery (Fig. 5).

Discussion

CXPA is defined as a pleomorphic adenoma from which an epithelial malignancy is derived. In the 2005 WHO classification of salivary tumors, CXPA was classified as a malignant epithelial tumor, and they comprise approximately 3.6% of all salivary tumors, 12% of all salivary malignancies, and 6.2% of all pleomorphic adenomas [1]. The most frequently affected site is the parotid gland, and the submandibular gland is secondary. In the minor salivary gland, these tumors most often arise from the palate. CXPA from the buccal mucosa is extremely rare, and only four cases [2–5] have been reported (Table 1). Many cases of CXPA have been reported in women [2, 3, 6]. The onset of CXPA has been reported to occur at 60–80 years of age [6], with an average age of 60 years [7, 8]. Frequent clinical symptoms include a painless mass, but pain, facial nerve palsy, ulcer, and swallowing disorder have been reported with CXPA in the major salivary gland [7, 8]. The reported duration from onset to diagnosis has been variable, from several months [6, 7] to over 20 years [6, 8]. Diagnosis is easily made due to the confirmation of both pleomorphic adenoma cells and cancer cells in the tumor on pathology. Based on the histopathology, CXPA can be subclassified as follows (a) non invasive, (b) minimally invasive (≤ 1.5 mm penetration of the malignant component into the extracapsular tissue), and (c) invasive (>1.5 mm of invasion from the tumor capsule to the adjacent tissues). Groups (a) or (b) typically have an excellent prognosis, but those in group (c) exhibit

Fig. 4 **a** The tumor was composed of pleomorphic adenoma (#) and adenocarcinoma areas (*). (H & E, $\times 50$), **b** poorly-differentiated adenocarcinoma cells (H & E, $\times 250$), **c** typical pleomorphic adenoma cells was seen peripheral area of the tumor. (H & E, $\times 250$)

Fig. 5 There was no recurrence of the tumor

significant recurrence and metastasis. While tumor size and grade are also significant prognostic indicators [1], intracapsular CXPA of the parotid gland with metastasis to cervical lymph node has been reported [9]. The treatment of CXPA is commonly through surgery and radiation therapy [1, 7]. Adenoma cells exhibit low sensitivity for

irradiation, and radiation can affect surrounding structures, while heavy ion radiotherapy shows a specific effectiveness in local control of tumors in the paranasal sinuses and salivary gland [10]. Olsen et al. [8] reported local recurrence in 23%, regional metastasis occurred in 56%, and 5 year survival was 30%. Another described that the rate of local recurrence in the rare submandibular and minor salivary gland CXPA (42%) is twice the rate of local recurrence in the parotid. Cervical metastasis occurs in 10–20% of CXPA cases, and distant metastasis occurs in 30% of patients. Wahlberg et al. [6] reported that 311 CXPA patients of parotid gland and 47 patients of submandibular gland had prognosis with a 5 year survival of 76 and 71%, a 10 years survival of 73 and 62% respectively.

In present case, the clinical diagnosis was benign tumor such as pleomorphic adenoma. However, we were not able to deny the possibility of the malignant tumor because SUV showed a high value in PET scan. The treatment was made during the early stage, because the painless mass had increased rapidly, and the tumor was subclassified as the non-invasive type. However, the majority of the tumor was comprised of carcinoma cells, which existed close to the capsule. Therefore, we performed proton radiation. Immunohistochemically, as an epithelial marker (Keratin), a mesenchyme filament marker (Vimentin), and

Table 1 Carcinoma ex pleomorphic adenoma (CXPA) in the buccal mucosa

	Kawano et al. [2]	Takahashi et al. [3]	Toida et al. [4]	Yih WY et al. [5]	Present case
CXPA buccal/total	1/9	1/10	1/2	1/2	1/1
Age and sex	Unknown	Unknown	A 67 year-old man	A 37 year-old man	A 52 year-old woman

carcinoembryonic antigen (CEA) were positive. Indicators of neurofilaments (S-100 protein), myoepithelial cells (Actin) and p53 were partially positive. We therefore considered that this tumor originated from myoepithelial cells. Ki-67 is considered to be an accurate marker of the proliferative stage of tumor cells. Because Ki-67 labeling index of this tumor was 14.8%, they exhibited moderate proliferative ability. While the patient was well without recurrence or metastasis 48 months after surgery, we consider that long-term follow-up is necessary.

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