Basal Cell Adenocarcinoma Arising in a Minor Salivary Gland of the Mandible

Hideo Yoshida*, Masato Okamoto*, Koji Harada*, Jun Kusaka*, Tokuyuki Yuuki*, Masayuki Azuma*, Yoshiaki Yura*, Mitsunobu Sato*, Hironori Hamano** and Yoshio Hayashi**

*The Second Department of Oral and Maxillofacial Surgery and **The Department of Oral Pathology, Tokushima University, School of Dentistry, 3 Kuramoto-cho, Tokushima 770, Japan

Yoshida H, Okamoto M, Harada K, Kusaka J, Yuuki T, Azuma M, Yura Y, Sato M, Hamano H and Hayashi Y. Basal cell adenocarcinoma arising in a minor salivary gland of the mandible. *Oral Med Pathol* 1996;1:97~102. ISSN 1342-0984.

Basal cell adenocarcinoma is a relatively recently described rare type of malignant salivary gland tumor found most often in the parotid gland. We present a case report of minor salivary gland basal cell adenocarcinoma arising in the mandible. Histologically, tumor islands composed of epithelial cells with two morphologic forms and mitotic figures were frequently observed, and tumor cells invaded alveolar bone. Ultrastructurally, tumor cells had secretory granules, mitochondria desmosomes, tonofilament bundle, and basement membrane. Immunohistochemically, the tumor cells showed positive-immunoreactivities with S-100 protein, CEA, EMA, and keratin.

Key words: basal cell adenocarcinoma, minor salivary gland, immunohistochemistry

Hideo Yoshida, The Second Department of Oral and Maxillofacial Surgery, Tokushima University, School of Dentistry, 3 Kuramoto-cho, Tokushima 770, Japan

Introduction

Basal cell adenocarcinoma is a rare type found most often in the parotid gland (1). There has been only one previous report of this tumor originating in a minor salivary gland (2). This tumor is relatively recently described (1, 3-6). Therefore, there are only a few reports of this tumor in the literature. The differential diagnosis between basal cell adenocarcinoma and basal cell adenoma or many other tumors is very important for treatment. A case of minor salivary gland basal cell adenocarcinoma, including immunohistochemical and electron microscopic findings is reported in a 43 year-old Japanese man.

Case Report

A 43-year-old Japanese man visited a dental clinic after three months of left side lower molar buccal gingival swelling and mass formation. He underwent sectional extraction of the mesial root of the first molar in December of 1990. The extraction wound healed, but the mass recurred with slow growth, so he visited in our hospital in March of 1991. The patient's past medical history was unremarkable, with the exception of a history of appendectomy at age 39. On oral examination, a slightly reddish, round swelling measuring 25 mm was observed in the left lower buccal gingiva between the second premolar and the first molar. The swelling was non-inflammatory in nature and presented a firm consistency without tenderness (Fig. 1). Regional lymph nodes were palpable at the ipsilateral level. The dental radiogram showed a diffuse extraction wound of the mesial root of

Fig. 1: Intraoral photograph showing tumor in the buccal gingiva of the left mandible at initial examination

the first molar and bone destruction of the interdental alveolar bone (Fig. 2). The biopsy specimen was histopathologically diagnosed as malignant minor salivary gland tumor. Therefore, these lesions, including the segmental mandible, were surgically excised, and a left side total neck dissection performed. He was followed for

58 months with no sign of recurrence or metastasis.

Methods

Light and electron microscopy

Fig. 2: Periapical radiograph in the left mandiblar premolar and molar teeth. The radiograph shows an ill-defined radiolucency of extraction socket.

Most of the surgical material was fixed in 0.1M phosphate-buffered 5% formalin and embedded in paraffin. The deparaffined sections were stained with hematoxylin-eosin, alcian blue, mucicarmine, periodic acid Schiff(PAS) and reticulin silver stainings. For electron microscopy, a small part of the tumor tissue was fixed in

Table 1: Summary of immunohistochemistry

Antibody	Reaction
S-100 protein	(++)
S-100 protein β chain	(++)
CEA	(++)
EMA	(+)
Keratin	(+)
Vimentin	(-)
Lactoferrin	(-)
Secretory component	(-)
GFAP	(-)
Lysozyme	(-)

Fig. 3: Ordinary microscopic appearance
a: Low power view of tumor, showing cribriform, tubular, focal cystic growth(HE. $\times 90$).
b: showing infiltrative growth to alveolar bone(HE. $\times 90$).
c: High power view showing two forms of epithelial tumor cells and a few mitoses(arrow) (HE. $\times 360$).
d: Tumor cell islands are surrounded by fibrovascular stroma(silver impregnation, $\times 180$).
e: PAS-positive hyalinized material present in the cytoplasm(PAS. $\times 180$)

Fig. 4: Electron microscopic appearance

a: showing two types of tumor cells, polygonal nuclei with high density cytoplasm and oval nuclei with low density cytoplasm ($\times 6,700$)

b: which contains prominent secretory granules and mitochondria ($\times 18,200$)

c: showing slightly thick basement membrane ($\times 9,500$)

d: showing prominent desmosomes and tonofilament bundles ($\times 12,700$).

P: polygonal nuclei cell; O: oval nuclei cell, S: secretory granule, M: mitochondria, B: basement membrane, D: desmosome, T: tonofilament bundles.

2.5% glutaraldehyde in 0.1M phosphate buffer, pH 7.2, containing 5mM calcium chloride for 2 hours and then dissected into 2mm pieces. After washing with phosphate buffered saline(pH7.2), these materials were post-fixed in 2% osmium tetroxide for 1 h, dehydrated with ethanol, and embedded in Epon 812. Ultrathin sections were cut on an LKB ultramicrotome and stained with uranyl acetate and lead hydroxide. The finished preparations were observed under a Hitachi Model H-500 electron microscope.

Immunohistological methods

Sections from formalin-fixed, paraffin-embedded tumor tissue were used for immunohistological staining by the avidine-biotin-peroxidase complex(ABC) method. A commercially available Vectastain ABC Kit(Vector Laboratories, Inc.) was used according to the procedures indicated. The first antibodies used in this study were rabbit polyclonal antibody to S-100 protein(Dako Japan Co., Ltd.), mouse monoclonal antibody to S-100 protein β chain(Otuka Assay Laboratory), vimentin(Dako), epithelial membrane antigen(EMA : Enzo Biochem Inc.), carcinoembryonic antigen(CEA : Enzo), keratin(Zymed Laboratories, Inc.), lactoferrin(Dako), secretory component(Zymed), glial fibrillary acidic protein (GFAP : Zymed). All controls treated with normal rat serum instead of the first antibodies gave negative results.

Result

Light microscopic findings

The specimen consisted of a seemingly well circumscribed tumor expandable to the gingiva and mandible bone of the region from the second premolar to the first molar, but the tumor invaded in part into the alveolus. The cut surface of the tumor was pinkish-white in color and solid. Microscopically, the tumor showed cribriform, tubular, and focal cystic growth(Fig. 3-a). In part, the tumor cells invaded alveolar bone(Fig. 3-b). Many of the tumor islands were composed of epithelial cells with two morphologic forms. One type consisted of small round to oval cells with scanty cytoplasm and dark blue nucleus. The second type was polygonal and larger with eosinophilic cytoplasm and pale nuclei. Swirls of dark cells and squamous eddies were present in foci. Many of the clear cell groups showed peripheral palisading. Mitotic figures were frequently observed(Fig. 3-c). The tumor cell islands were surrounded by a small amount of fibrovascular stroma positively stained by the silver impregnation stain (Fig. 3-d). PAS-positive hyaline like materials were seen in the cytoplasm of clear cells (Fig. 3-e).

Electron microscopic findings

At low power view(Fig. 4-a), two types of tumor cells

Fig. 5: Immunostaining using the avidine-biotin-peroxidase complex technique.
a: tumor cells are positive for S-100 protein (polyclonal antibody) ($\times 180$)
b: positive for S-100 protein β chain ($\times 180$)
c: slightly positive for EMA ($\times 180$)
d: positive for CEA ($\times 180$)

were observed; one type contained oval nuclei and low electron density cytoplasm, and the other contained polygonal nuclei and high density cytoplasm. At high power view(Fig. 4-b,c,d), secretory granules, mitochondria, endoplasmic reticulum, tonofilament bundles, intercellular lumens, and distinct desmosomes were seen in the cytoplasm.

Immunohistological findings

Table 1 summarizes the immunohistological findings in this case. The cytoplasm of tumor cells showed strong immunoreactivities with S-100 protein (Fig. 5-a,b) and CEA.(Fig. 5-d) Some of the tumor cells were positive for EMA(Fig. 5-c) and keratin. No immunoreactivity was seen with other antibodies.

Discussion

Basal cell adenocarcinomas of the salivary gland are rare tumors. The first edition of the World Health Organization's Histologic Classification of Salivary Gland Tumors, published in 1972, had no description of these tumors(7). The first case report of a basal cell adenocarcinoma was by Klima *et al.* in 1978(8). They described a parotid gland tumor arising in a 57-year-old man with morphologic similarities to basal cell adenoma, but containing frequent mitoses and growth characteristics associated with malignant neoplasms. The largest series of basal cell adenocarcinoma of the salivary glands was reported by Ellis *et al.* in the Armed Forces Institute of Pathology(AFIP) (1). They reported the clinicopathologic features of 29 cases of basal cell adenocarcinoma. In 1991, they extended in this series and reported 43 such tumors(5) 39 of which occurred in the parotid gland, and only 4 in the submandibular gland. None of these cases involved minor salivary glands. They also pointed out that basal cell adenocarcinomas have occurred in about 2 % of malignant epithelial salivary gland tumors in the registry of AFIP. No sex differences was observed in the occurrence of this tumor. All of the patients have been adults ranging in age from 27 to 92, with an average age of 60. The first case of basal cell adenocarcinoma originating from the minor salivary gland was reported by Lo *et al.* in 1992(2), in a 28-year-old woman, which arose in the palate. It is well known that minor salivary gland tumors develop most commonly in the palate. The present case is the first report of the basal cell adenocarcinoma arising in the minor salivary gland of the mandible. According to the histologic criteria defined by the second edition of WHO's Histological Classification of Salivary Gland Tumors, this tumor has cytological characteristics of basal cell adenoma in addition to a morphological growth pattern indicative of malignancy(3). It is known that two forms of epithelial cells are present in basal cell adenoma. One is a small, round cells with scanty cytoplasm and a dark basophilic nucleus. The other is a larger, polygonal to elongated cell with eosinophilic or amphophilic cytoplasm and a larger, pale basophilic nucleus. Swirls of cells and squamous

eddies are present in some cases. PAS-positive hyalinized basal lamina is often present. Basal cell adenocarcinoma has been divided into four histologic patterns: solid, trabecular, tubular and membranous. Subtyping in this neoplasms is based on the predominant growth pattern. The solid type is the most common subtype. Basal cell adenocarcinoma consists mostly of solid cell nests, less frequently of trabecular or tubular structures. Basal membranous structures are usually observed on the outside of tumor cell nests. The differential diagnosis from basal cell adenoma is controversial. Frequent mitoses and infiltrative growth are distinctive signs in which contrast with basal cell adenoma. The present tumor has many mitotic cells and invade alveolar bone. Moreover, the solid type of adenoid cystic carcinoma may also be confused with basal cell adenocarcinoma. There have been few reports of electron microscopic studies of basal cell adenocarcinoma. McCluggage *et al.* examined the ultrastructural appearance of this tumor and confirmed its epithelial nature (9). The closely packed, principal cell type frequently contains apical secretory vacuoles and well-formed desmosomes associated with tonofilaments, which are sometimes seen in cytoplasmic aggregates. The cytoplasm contains moderately prominent cisternae of rough endoplasmic reticulum and rounded mitochondria. The second cell type displays the features of myoepithelial cell differentiation. The cytoplasm of these cells contains variable amounts of actin-like filament bundles with focal densities. Ultrastructurally, present case show secretory granules, mitochondria, desmosome, basement membrane and tonofilament. Immunohistochemical investigations of basal cell adenocarcinoma were reported by Williams. *et al.* (10). They examined the immunoreactivity of cytokeratin, S-100 protein, GFAP, CEA, EMA, smooth muscle actin(SMA), vimentin, glycosylated mucin B72.3, cell membrane glycoprotein Ber-EP4, and milk fat globulin(MFG) on 23 basal cell adenocarcinomas compared with 11 basal cell adenomas using the files of AFIP. Both tumors showed immunohistochemical patterns indicative of ductal epithelial and myoepithelial differentiation. The immunoreactivities with cytokeratin, CEA, SMA, vimentin, MFG and GFAP were nearly identical in the two tumors. Anti- S-100 protein was present in two thirds of the basal cell adenomas, but in only one half of the basal cell adenocarcinomas. Anti-EMA antibody reacted positively with 18% of basal cell adenomas, but with 74% of basal cell adenocarcinomas. It is possible that immunohistochemical diversity is present between the two groups of tumors. The present tumor positively stained for S-100 protein, CEA and EMA, and mitotic figures were frequently observed. In addition, it was clear that the tumor invaded to alveolar bone. From these results, we can conclude that the present tumor is basal cell adenocarcinoma originating from a minor salivary gland of the gingibobuccal mucosa of the mandible.

References

1. Ellis GL and Wiscovitch JG. Basal cell adenocarcinomas of the major salivary glands. *Oral Surg Oral Med Oral Pathol* 1990; **69**: 461-9.
2. Lo AK, Topf JS, Jackson IT, et al. Minor salivary gland basal cell adenocarcinoma of the palate. *J Oral Maxillofac Surg* 1992; **50**: 531-4.
3. Seifert G, Brocheriou C, Cardesa A, et al. WHO International histological classification of salivary gland tumors. Tentative histological classification of salivary gland tumors. *Path Res Pract* 1990; **186**: 555-81.
4. Seifert G and Sobin LH. Histological Typing of Salivary Gland Tumours. In: World Health Organization. International Histological Classification of Tumours. Springer-Verlag, Berlin, Heidelberg, New York, London, Paris, Tokyo, Hong Kong, Barcelona, Budapest. 1991.
5. Ellis GL and Auclair PL. Basal cell adenocarcinoma. In: Willis GL, Auclair PL, Gnepp DR ed. Surgical Pathology of the Salivary Glands, W.B. Saunders Co. Philadelphia. 1991; 441-54.
6. Seifert G. Histopathology of malignant salivary gland tumors. *Oral Oncol, Eur J Cancer* 1992; **28B**: 49-56.
7. Thackray AC and Sobin LH. Histological classification of salivary gland tumors. In: World Health Organization. International Histological Classification of Tumors. Geneva. The Organization, 1972.
8. Klima M, Wolfe SK and Johnson PE. Basal cell tumors of the parotid gland. *Arch Otolaryngol* 1978; **104**: 111-6.
9. McCluggage G, Sloan J, Cameron S, et al. Basal cell adenocarcinoma of the submandibular gland. *Oral Surg Oral Med Oral Pathol* 1995; **79**: 342-50.
10. Williams SB, Ellis GL and Auclair PL. Immunohistochemical analysis of basal cell adenocarcinoma. *Oral Surg Oral Med Oral Pathol* 1993; **75**: 64-9.

(Accepted for publication March 23, 1996)