CASE REPORT

Adenoid cystic carcinoma arising the anterior lingual gland (Blandin–Nuhn gland)

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Summary The present case describes a rare example of adenoid cystic carcinoma (ACC) arising the Blandin-Nuhn gland. A 75-year-old Japanese woman took a partial glossectomy, hemimandiblectomy, excision of the hypoglossal nerve and a skin grafting. The tumor tissue consisted of tubular type of ACC and perineural invasion. The tumor cells were immunoreactive for S-100, keratin, α-smooth muscle actin (α-SMA) and PCNA. Numbers of PCNA and α-SMA positive cells were higher in modified or perineural tumor cells than that in tubular tumor cells. Biological roles of ACC invasion might be related to exist of PCNA and actin.

KEYWORDS
Adenoid cystic carcinoma; Blandin–Nuhn gland; Immunohistochemical analysis; α-actin; PCNA

Introduction

The present case is a rare example of adenoid cystic carcinoma (ACC) arising the anterior lingual gland (Blandin–Nuhn gland). ACC occurs frequently in the minor salivary gland, but the oral tongue is uncommon. Previous papers have been reported without special attention for tumor cell invasion mechanism and metastatic potential. In the present case, tumor cell invasion was found in hypoglossal nerve. We dealt with a rare case of ACC arising the anterior lingual gland with histopathologic orientation and evaluated to tumor cell invasion in perineural tissue with the use of immunohistochemical methods. The present case is first described for tumor cell invasion in perineural tissue by immunohistochemical analysis of α-actin and PCNA.

Report of a case

A 75-year-old Japanese woman was referred to outpatient clinic in our hospital. The painful swelling at anterior tongue had been noted 6 months before the first medical examination. Oral examinations revealed 2 cm mass, tender, fixed, existed in the anterior tongue (Fig. 1A). Enhanced T1-weighted magnetic resonance image revealed a well-defined mass in the anterior tongue (Fig. 1B). Under general anesthesia, a partial glossectomy was performed. The strand was 3–4 mm in diameter, existed in the right floor of the mouth following the mass and continued to the direction of the mandibular angle. The tumor mass with the
sublingual gland and the resectable strand were excised. A histological diagnosis in paraffin sections was tubular type of ACC.

Microscopic features of the tumors

Paraffin sections were examined histologically and immunohistochemically. Tumor tissue separated from the sublingual glands, and it was associated with anterior lingual glands (Fig. 2A). The tumor tissue consisted of tubular ACC (Fig. 2B). At the border area between anterior lingual gland and ACC, there were duct like structures, degenerated acinar cells and a little inflammation (Fig. 2A). Tumor tissue consisted of tubular ACC and strand or cord like tissue in periphery of the tumor. In perineural tumor invasion, there were invaded tubular tumor cells (Fig. 2C). Tubular structure composed of modified or neoplastic cells.

Immunohistochemical methods

The deparaffinazed sections were blocked endogenous peroxidase with 0.3% H2O2/methanol. They were incubated at 4°C overnight with following antibodies: S-100, keratin, α-smooth muscle actin, vimentin and PCNA. Microwave pre-treatment was performed in PCNA. Histofine Simple Stain MAX-PO (MULTI) kit (Nichirei, Tokyo) as streptavidin-biotin (SAB) was used for colorization.

Immunohistochemical features

Immunohistochemical expression in the normal anterior lingual gland: keratin was existed markedly in ductal cells and vimentin in stromal tissue; α-smooth muscle actin (α-SMA) was confined to myoepithelial cells and to the smooth muscle zone in vessels, and S-100 protein was limited to terminal nerve fibers.

Immunohistochemical features in ACC: keratin immunoreactivity was positive in neoplastic cells of tubular tumor cells, and irregular reactive in other cells. S-100 protein was strongly positive in nervous fibers, and irregular in neoplastic cells. Neoplastic or modified myoepithelial cells were devoid of the S-100 protein (Fig. 2E). α-SMA reaction was characteristically expressed in modified myoepithelial cells and in strand and cord tumor cells which invaded into perineural connective tissue (Fig. 2F). PCNA positive tumor cells were usually arranged in peripheral tumor cells and also in strand and cord structures (Fig. 2D). Numbers of PCNA positive cells were higher in modified or neoplastic tumor cells than that in central tumor cells, and also higher frequency of PCNA positive cells were observed in small tubular structures at perineural tissue (Table 1).

Discussion

ACC is characterized by a slow-growing and tends to recur locally, metastasis rates are high.
and long-term survival rate is poor. ACC are high invasive rate in perineural structure, however such biologic mechanism or processes have not been well described. Tumor cell type of ACC has been reported to classified histopathologically into intercalated duct, myoepithelial, secretory and pluripotent reserve/stem cells, and also tumor structures were classified into 3 patterns as solid, cribriform and tubular type, and also cribriform, basaloid and trabecular type. Ultrastructure
classification of ACC has been reported to classified into neoplastic myoepithelial and secretory cells. Chisholm et al. had used the stereological analysis of ACC that tumor cell population was composed of duct type (75%), myoepithelial (3%), acinar cells (2%) and other tissues (22%). Among those different tumor cell population, no detailed concept for, what kind of tumor cells indicated an invasion or metastasis, and also those neoplastic cells in ACC have a specific histochemical properties or not, has been asserted. The present study was conducted possible mechanism of perineural invasion of ACC cells with the use of immunohistochemical expression of actin and PCNA. Immunohistochemical studies for exploration of different cell population in ACC have been described to distinguish cytoskeletal proteins and other markers. In ACC, S-100 positive cells were also limited to modified myoepithelial cells. From the present case, α-SMA and PCNA reaction expressed at periphery of the tubular structures and strand and cord cells which invaded into perineural tissue. Numbers of PCNA positive cells were higher in modified or neoplastic tumor cells in peripheral foci than that in centrally tumor cells. This immunohistochemical feature might indicate that peripheral tumor cells may have a high migration and active locomotion. Recently, practicable solution for tumor cell invasion and metastases in ACC has been discovered as scattering factor, hepatocyte growth factor (HGF), suggesting HGF/c-MET may play a significant role for tumor cell invasiveness. Possible mechanism of tumor cell invasion might involve phenotypic change in ACC cells as revealing smooth actin expression, higher reactivity to PCNA and positive reaction of HGF/c-MET.

Salivary gland tumors in the tongue are frequently arisen in the basal tongue and they are uncommon in the anterior tongue. It has previously been reported such clinical analysis. The present study was recognized the histologic origin of ACC in anterior tongue (operated material), indicating tubular ACC arose from the Blandin–Nuhn gland, and also neural invasion of ACC cells in long distance from the primary tumor mass was firstly described with detailed histopathological examinations as well as immunohistochemistry for α-actin and PCNA.

### References


### Table 1 The antibodies used for immunohistochemical analysis and immunoreactivity of ACC

<table>
<thead>
<tr>
<th>Antibodies</th>
<th>Clone</th>
<th>Source</th>
<th>Dilution</th>
<th>Tubular</th>
<th>Perineural</th>
<th>Nerve</th>
<th>Stromal</th>
</tr>
</thead>
<tbody>
<tr>
<td>S-100</td>
<td>N/A</td>
<td>NICHIREI</td>
<td>×1</td>
<td>–</td>
<td>+</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Vimentin</td>
<td>V9</td>
<td>DAKO</td>
<td>×1</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>+</td>
</tr>
<tr>
<td>Keratin</td>
<td>N/A</td>
<td>DAKO</td>
<td>×1</td>
<td>–</td>
<td>+</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>α-SMA</td>
<td>1A4</td>
<td>DAKO</td>
<td>×500</td>
<td>+</td>
<td>–</td>
<td>++</td>
<td>–</td>
</tr>
<tr>
<td>PCNA</td>
<td>PC10</td>
<td>NICHIREI</td>
<td>×1</td>
<td>+</td>
<td>–</td>
<td>++</td>
<td>–</td>
</tr>
</tbody>
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Note: –, negative reaction; +, focally or weak positive reaction; ++, strongly positive reaction.