Tubular-Trabecular Type Basal Cell Adenoma of the Parotid Gland: A Patient Report

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Basal cell adenoma (BCA) is an uncommon benign salivary gland neoplasm that includes isomorphic basaloid cells. We report on a female patient with BCA that developed in the right parotid gland in her 50s. The present patient demonstrated a few tumor nests in the fibrous capsule, and her tumor was larger than usual. These facts made us suspect of malignancy. Histopathologically, the tumor was characterized by multiple duct-like structures and tubular-trabecular masses composed of small isomorphic cells with hyperchromatic, round nuclei and an eosinophilic cytoplasm. It was difficult to determine whether the ductal structures noted in the tumor capsule were invasive. By immunohistochemistry, tumor cells of the tubular nests were positive for cytokeratin 7 and that the outer cells of tubular nests were positive for alpha smooth muscle actin (αSMA) and calponin. Tumor cells were immuno-negative for S-100 protein and glial fibrillary acidic protein. The Ki-67 labeling scores of the cells were extremely low (< 1%). We could achieve an accurate diagnosis of BCA by immunohistochemistry with MIB-1 and other markers.

Key words: basal cell adenoma; immunohistochemistry; parotid gland

Salivary gland tumors are uncommon and constitute 2.0% to 6.5% of all head and neck tumors (Leegaard and Lindeman, 1969; van der Wal et al., 1992). Salivary gland tumors are histologically diverse and include various types and subtypes. Therefore, the accurate diagnosis of salivary gland tumors is difficult in some patients. The majority of salivary gland tumors are located in the parotid gland (Satko et al., 2000; Ito et al., 2005; Gnepp, 2009), and benign tumors predominate over malignant tumors (Satko et al., 2000). Pleomorphic adenoma is the most common salivary gland tumor with an incidence ranging from 60% to 65% (Evenson and Cawson, 1985; Barnes et al., 2005; Gnepp, 2009). On the other hand, basal cell adenoma (BCA) accounts for only 1% to 3% of all salivary gland tumors and demonstrates a female predominance of 2:1 (Luna and Mackay, 1976; Satko et al., 2000; Vargas et al., 2002; Barnes et al., 2005; Gnepp, 2009). BCA was recognized as a distinct disease entity in 1991 by the World Health Organization (Seifert and Sobin, 1991). BCA tumors have been histopathologically classified into solid (monomorphic), trabecular, tubular and membranous types (Ellis and Auclair, 1996). However, basal cells are found in various primary salivary gland tumors either as a component of the tumor or as pure basal cell neoplasms. In this regard, the distinction between true BCA and other primary tumors mimicking the basal cell features of the

Abbreviations: BCA, basal cell adenoma; CK, cytokeratin; GFAP, glial fibrillary acidic protein; αSMA, alpha smooth muscle actin
salivary gland sometimes causes diagnostic difficulties (Seifert, 1996).

Here, we report on a female patient with BCA occurring in the parotid gland in her 50s. Immunohistochemistry provided useful information that allowed an accurate pathological diagnosis to be achieved in this patient.

**Patient Report**

**Clinical summary**

A Japanese woman in her 50s was admitted to the Clinic of Otorhinolaryngology at San-in Rosai Hospital in 2009 due to a painless swelling in her right parotid gland. A physical examination revealed a hard-circumscribed nodule of 4 cm in diameter. The lesion was first noticed in 2001 and had gradually enlarged without pain. Computed tomography showed a round, well-circumscribed heterogeneous mass measuring 3.6 × 4.3 cm in the right parotid gland. No calcification or cystic component was seen in the tumor. Neck magnetic resonance imaging also revealed a heterogeneous, well-demarcated mass in the right parotid gland. On a T1-weighted image, the tumor was heterogeneously isointense to muscle (Fig. 1a). On a T2-weighted image, the tumor demonstrated a heterogeneous moderate intensity. The signal intensity of the tumor on the T2-weighted image was higher than that of the muscle (Fig. 1b).

Initially, her disease was clinically suspected as pleomorphic adenoma. However, the probability of malignancy could not be ruled out so the patient underwent surgery. There has been no recurrence for 7 months after surgery.

**Pathological findings**

Histopathologic examination revealed that the tumor, which was encapsulated with fibrous tissue, was characterized by multiple duct-like structures or solid and trabecular masses composed of small isomorphic cells with hyperchromatic, round nuclei and an eosinophilic cytoplasm (Figs. 2a and b). There was no cartilage formation, mucous stroma or necrosis in the tumor. The tubular portion of the tumor demonstrated a two-layered ductal structure. Mitotic figures were extremely rare (× 400/high power field). Nuclear atypia and mitotic figures were not prominent. In some sections, there were tumor cells in the wall of the capsule (Fig. 2c).

An immunohistochemical examination showed that the inner cells of the tubular components were positive for cytokeratin (CK) 7 and negative for alpha smooth muscle actin (αSMA) and calponin (Figs. 3a and b). On the contrary, the outer cells were negative for CK7 and positive for αSMA and calponin. Tumor cells were immuno-
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Discussion

BCA is a rare, benign epithelial neoplasm of the salivary gland. According to the literature, malig-

Fig. 2. Histopathology of the basal cell adenoma (hematoxylin and eosin stain).

a: The tumor cells demonstrate a tubular structure. Bar = 50 μm.
b: Trabecular tumor cells and tumor cell nest formation. Bar = 50 μm.
c: Trabecular tumor cell nests are noted in the fibrous capsule of the tumor, mimicking infiltration. Bar = 100 μm.

Fig. 3. Immunohistochemistry of the basal cell adenoma.

a: The tumor cells show immunoreactivity for cytokeratin 7. Bar = 50 μm.
b: Alpha smooth muscle actin immunoreactivity is noted in the outermost layer of the tubular type tumor cells. Bar = 50 μm.

negative for S-100 protein and glial fibrillary acidic protein (GFAP). The stromal cells showed immunoreactivity for αSMA, but not for S-100 protein or glial fibrillary acidic protein. In addition, the frequency of Ki-67 positive tumor cells was extremely low, being less than 1%. From these findings, the tumor was diagnosed as a tubular-trabecular BCA.
nant transformation occurs in 4.3% of BCA (Nagao et al., 1997). BCA frequently occurs in people of over 50 years of age as a unilateral tumor with a well-circumscribed round or oval appearance. A painless, slowly enlarging mass is the most common clinical symptom (Nagao et al., 1982; Jang et al., 2004). BCA tumors are usually smaller than 3 cm. In the present patient, the site of occurrence, past history, age and sex were compatible with those written in previous reports, but the tumor size was not compatible. Microscopically, the tumor was histopathologically classified as BCA of the tubular-trabecular type.

The cellular type of pleomorphic adenoma is difficult to distinguish from BCA; however, myxoid or cartilage formation characteristic of pleomorphic adenoma was not observed in the present patient (Ellis and Auclair, 1996; Minicucci et al., 2008). In addition, immunohistochemical staining of the tumor cells was negative for S-100 protein and GFAP. Previous reports have shown that the outer tumor cells in pleomorphic adenoma exhibit a very heterogeneous distribution or the simultaneous presence of S-100 protein and GFAP (Mori et al., 1990; Ogawa et al., 1990; Shida et al., 2005).

Basal cell adenocarcinoma shares common clinical and histological similarities with BCA (Klijanienko et al., 1999; Machado de Sousa et al., 2001). Cytology differences, infiltration and perineural invasion help distinguish basal cell adenocarcinoma from BCA. The present patient demonstrated a few tumor nests or glands in the fibrous capsule. However, nuclear atypia and mitotic figures were not prominent. Moreover, no necrosis or hemorrhaging was observed. We considered that tumor cells in the capsule were not of the invasive origin but a part or component of fibrous tissues.

It is difficult to differentiate between BCA with a two-layered tubular structure and the tubular type of adenoid cystic carcinoma because atypical tumor cells are relatively scarce in both types of tumor. The Ki-67 labeling index is a useful marker of cell proliferation (Murakami et al., 1992; Nagao et al., 1998). The Ki-67 labeling indices of adenoid cystic carcinoma have been reported to range from 13.6% to 34.7%. On the other hand, we found a Ki-67 labeling index of less than 1% in the present patient.

We present a patient with BCA classified as a rare benign tumor that was difficult to differentiate from other tumors with a two-layered structure. We emphasize the importance of immunohistochemistry for obtaining an accurate diagnosis of BCA, particularly because BCA has the potential to be malignant.

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