Yonago Acta medica 2010;53:65–69

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

Motoki Nakabayashi*†, Kohei Shomori*, Shuichi Kiya‡, Tatsushi Shiomi*, Kanae Nosaka* and Hisao Ito*

**Division of Organ Pathology, Department of Microbiology and Pathology, Tottori University Faculty of Medicine, Yonago 683-8503, †Division of Oral and Maxillofacial Biopathological Surgery, Department of Medicine of Sensory and Motor Organs, Tottori University Faculty of Medicine, Yonago 683-8504 and ‡Clinic of Otorhinolaryngology, Sanin-Rosai Hospital, Yonago 683-8605, Japan*

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.

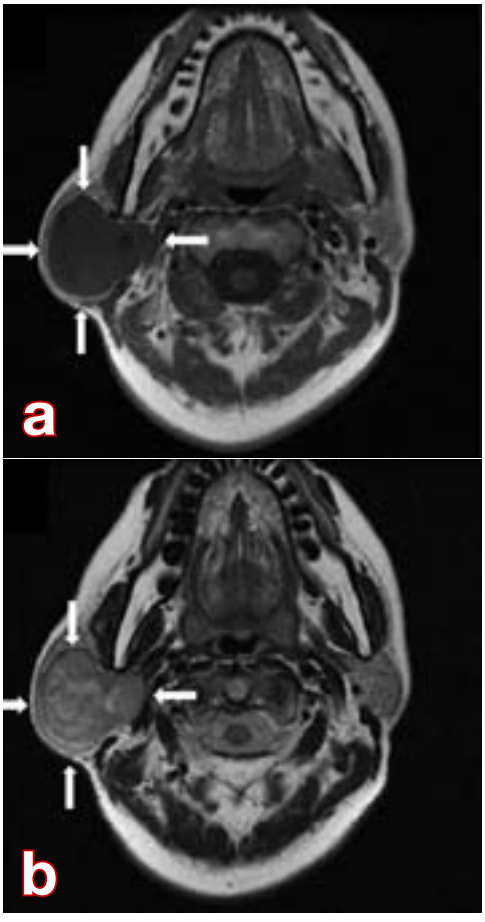

Fig. 1. Contrast-enhanced magnetic resonance scans showing homogeneous moderate enhancement of the mass (arrow). Capsule-like enhancement is seen. **a:** T1-weighed image. **b:** T2-weighed image.

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-

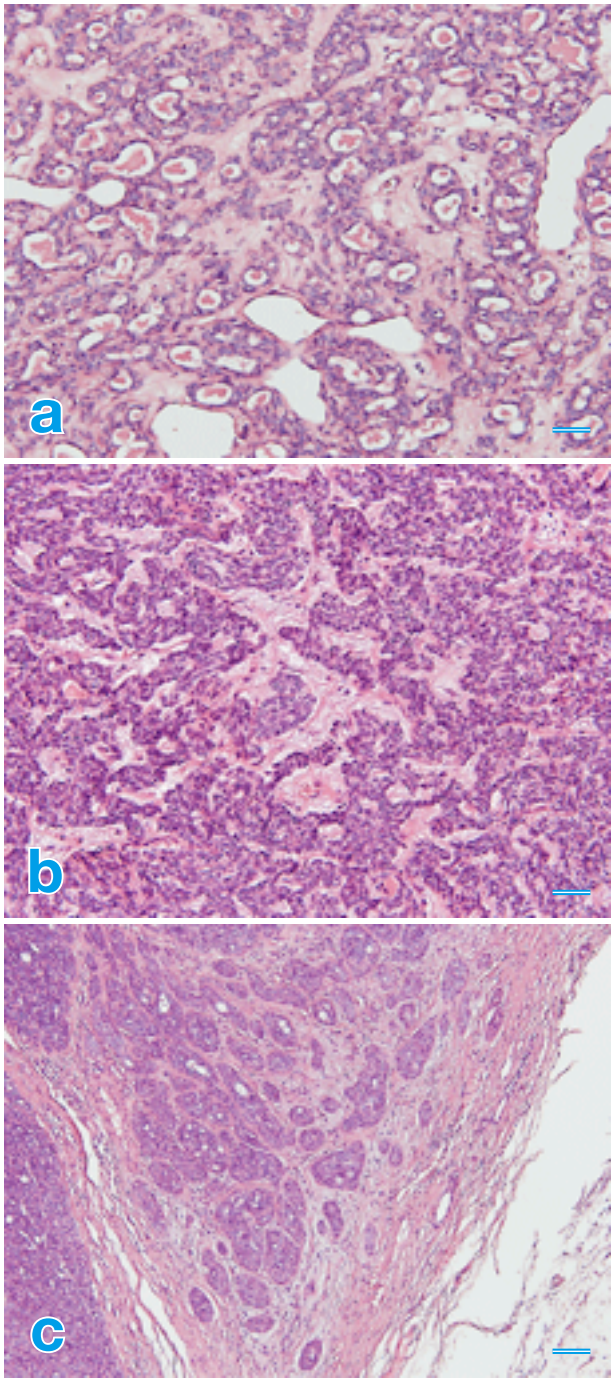

Fig. 2. Histopathology of the basal cell adenoma (hematoxylin and eosin stain).

- **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.

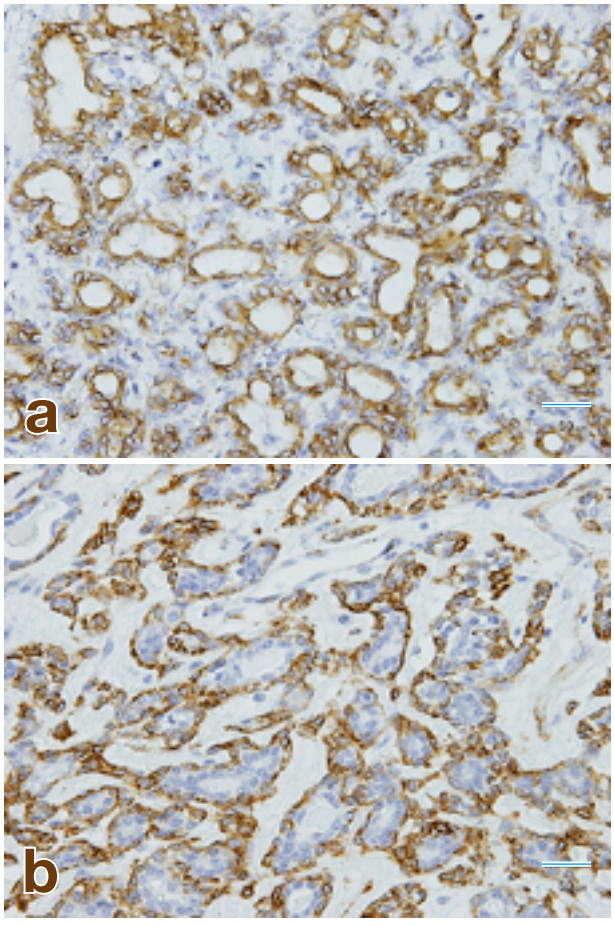

Fig. 3. Immunohistochemistry of the basal cell adenoma.

- **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.

Discussion

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

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.

Acknowledgments: We thank Mr. Norihisa Itaki and Ms. Chie Yamazaki for their technical support.

References

1 Barnes L, Eveson JW, Reichart P, Sidransky D. World Health Organization classification of tumours. Pathology and genetics of head and neck tumours. Lyon: International Agency for Research on Cancer Press; 2005. p. 261–262.
2 Dardick I, Daley TD, van Nostrand AW. Basal cell adenoma with myoepithelial cell-derived "stroma": a new major salivary gland tumor entity. Head Neck Surg 1986;8:257–267.
3 Ellis GL, Auclair PL. Tumor of the salivary glands. Atlas of tumor pathology. Washington DC: Armed Forces Institute of Pathology; 1996. p. 90–94.
4 Evenson JW, Cawson RA. Tumours of the minor (oropharyngeal) salivary glands: a demographic study of 336 cases. J Oral Pathol 1985;14:500–509.
5 Gnepp DR. Diagnostic surgical pathology of the head and neck. London: W. B. Saunders; 2009. p. 351–365.
6 Ito FA, Ito K, Vargas PA, de Almeida OP, Lopes MA. Salivary gland tumors in a Brazilian population: a retrospective study of 496 cases. Int J Oral Maxillofac Surg 2005;34:533–536.
7 Jang M, Park D, Lee SR, Hahm CK, Kim Y, Kim Y, et al. Basal cell adenoma in the parotid gland: CT and MR findings. AJNR Am J Neuroradiol 2004;25:631–635.
8 Klijanienko J, el-Neggar AK, Vielh P. Comparative cytologic and histologic study of fifteen salivary basal-cell tumors: differential diagnostic considerations. Diagn Cytopathol 1999;21:30–34.
9 Leegaard T, Lindeman H. Salivary-gland tumors. Clinical picture and treatment. Acta Otolaryngol Suppl 1969;263:155–159.
10 Luna MA, Mackay B. Basal cell adenoma of the parotid gland. Case report with ultrastructural observations. Cancer 1976;37:1615–1621.
11 Machado de Sousa SO, Soares de Araujo N, Correa L, Pires Soubhia AM, Cavalcanti de Araujo V. Im-

munohistochemical aspects of basal cells adenoma and canalicular adenoma of salivary glands. Oral Oncol 2001;37:365–368.
12 Minicucci EM, de Campos EB, Weber SA, Domingues MA, Ribeiro DA. Basal cell adenoma of the upper lip from minor salivary gland origin. Eur J Dent 2008;2:213–216.
13 Mori M, Yamada K, Tanaka T, Okada Y. Multiple expression of keratins, vimentin, and S-100 protein in pleomorphic salivary adenomas. Virchows Arch B Cell Pathol Incl Mol Pathol 1990;58:435–444.
14 Murakami M, Ohtani I, Hojo H, Wakasa H. Immunohistochemical evaluation with Ki-67: an application to salivary gland tumors. J Laryngol Otol 1992;106:35–38.
15 Nagao K, Matsuzaki O, Saiga H, Sugano I, Shigematsu H, Kaneko T, et al. Histopathologic studies of basal cell adenoma of the parotid gland. Cancer 1982;50:736–745.
16 Nagao T, Sugano I, Ishida Y, Matsuzaki O, Konno A, Kondo Y, et al. Carcinoma in basal cell adenoma of the parotid gland. Pathol Res Pract 1997;193:171–178.
17 Nagao T, Sugano I, Ishida Y, Hasegawa M, Matsuzaki O, Konno A, et al. Basal cell adenocarcinoma of the salivary glands: comparison with basal cell adenoma through assessment of cell proliferation, apoptosis, and expression of p53 and bcl-2. Cancer 1998;82:439–447.
18 Ogawa I, Nikai H, Takata T, Miyauchi M, Ito H, Ijuhin N. The cellular composition of basal cell adenoma of the parotid gland: an immunohistochemical analysis. Oral Surg Oral Med Oral Pathol 1990;70:619–626.
19 Satko I, Stanko P, Longauerova I. Salivary gland tumors in the stomatological clinics in Bratislava. J Craniomaxillofac Surg 2000; 28:56-61.
20 Seifert G, Sobin LH. Histological typing of salivary gland tumors. World Health Organization International Histological Classificationof Tumors. 2nd ed. Berlin: Springer-Verlag; 1991. p. 20–21.
21 Seifert G. Classification and differential diagnosis of clear and basal cell tumors of the salivary glands. Semin Diagn Pathol 1996;13:95–103.
22 Shida H, Tanaka A, Fukuda M, Shigematsu H, Kusama K, Sakashita H. [A case of basal cell adenoma in the parotid gland.] Nippon Kokugeka Gakkai Zasshi 2005;51:352–355 (in Japanese with English abstract).
23 van der Wal JE, Snow GB, van der Wal I. Histological reclassification of 101 intraoral salivary gland tumours (new WHO classification). J Clin Pathol 1992;45:834–835.
24 Vargas PA, Gerhard R, Araujo Filho VJ, de Castro IV. Salivary gland tumors in a Brazilian population: a retrospective study of 124 cases. Rev Hosp Clin Fac Med Sao Paulo 2002;57:271–276.

Received July 6, 2010; accepted, July 23, 2010

Corresponding author: Kohei Shomori, MD