Case Report

Basal Cell Adenoma of the Parotid Gland: A Case Report and Review of the Literature

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Basal cell adenoma (BCA) is a rare benign biphasic epithelial neoplasm of salivary gland composed of basaloid cells and inner ductal epithelial cells. Here, we present a case of a 25-year-old man with a long-standing history of swelling of the left side of the cheek. The specimen was sent for intraoperative frozen section consultation. The tumor appeared to be solid and cystic with a thin capsule and was composed of a biphasic basaloid cells forming tubular and trabecular glands, and fibromyxoid stroma. The differential diagnosis in this case encompasses a broad spectrum of biphasic salivary gland epithelial neoplasms, including benign basal cell adenoma, pleomorphic adenoma, and malignant adenoid cystic carcinoma and basal cell adenocarcinoma. To enhance our proficiency in intraoperative consultation and final diagnosis of biphasic basaloid neoplasms of the salivary gland, we present this rare case along with a comprehensive review of the literature.

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Key Words: *Basal cell adenoma, Parotid gland, Differential diagnosis*

INTRODUCTION

Basal cell adenoma (BCA) is a rare benign biphasic basaloid neoplasm of the salivary gland and is also called monomorphic adenoma or basaloid salivary gland adenoma. It comprises 1-3.7% of all salivary gland neoplasm.[1] The tumor is more frequently seen in elderly adults between the fifth and seventh decades and is uncommon in young adults.[2] It has a female predilection (2:1) except for the membranous type, which bears an equal M:F distribution. BCAs almost always arise in the parotid gland, with the submandibular gland being a distant second; other sites are exceptionally rare.[3,4] Differentiating BCA from a pleomorphic adenoma, adenoid cystic carcinoma, basal cell adenocarcinoma, and ex-carcinoma pleomorphic adenoma is often challenging, yet vitally important.

CASE REPORT

A 25-year-old man presented to the Department of Otolaryngology with a chief complaint of swelling of the left cheek. On examination, a single firm, non-tender swelling nodule was palpable in the left parotid region. An excisional biopsy of the nodule with the superficial parotid gland was performed and sent to pathology for frozen section diagnosis. The nodule was grossly well-circumscribed with a thin capsule and was 2.5 x 2.5 x 2.0 cm in size. Microscopically, the nodule was a solid growth neoplasm with small cystic areas (**Figure 1A**), composed of cellular biphasic basaloid glands in an admixed trabecular and tubular patterns with an outer layer of small basaloid myoepithelial cells, inner layer of ductal epithelial cells, and a distinct basal membrane (**Figure 1B**). The differential diagnoses of this low-grade salivary gland neoplasm included pleomorphic adenoma, adenoid cystic carcinoma, and basal cell adenoma. A definitive diagnosis was deferred to permanent sections. Subsequently, the parotic tissue surrounding the tumor was surgically excised. On examination of the permanent hematoxylin and eosin (H&E) stained sections, the tumor demonstrated a biphasic basaloid solid and cystic neoplasm, comprised of bland glands with abluminal basal-myoepithelial cells and luminal ductal epithelial cells with a distinctive basal membrane and fibromyxoid stroma (**Figure 1C**). Some glands contained eosinophilic secretions in the lumen (**Figure 1D**). No significant cytological atypia, increased mitotic activity, necrosis, perineural invasion, lymphovascular invasion, or destructive infiltrative growth was identified. Immunohistochemical staining was performed for classification of the tumor and results are as follows: Beta-catenin diffusely stained the cytoplasmic membrane of the inner epithelial cells and the cytoplasm and nuclei of the basal-myoepithelial cells (**Figure 2A**), CD117 stained the cytoplasmic membrane of the inner epithelial cells (**Figure 2B**), Dog1 was expressed on the cytoplasm and cytoplasmic membrane of the myoepithelial cells (**Figure 2C**), P63 was diffusely positive with myoepithelial nuclei (**Figure 2D**), P53 showed a wild-staining pattern (**Figure 2E**), and Ki67 demonstrated a low-proliferative index of < 5% (**Figure 2F**).

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In addition, CK AE1/AE3 and CK7 were diffusely positive for the cytoplasm of the inner epithelial cells. GFAP and EMA were negative for basal-myoepithelial cells and ductal epithelial cells. S100 showed focal and weak expression of nuclear positivity of occasional stromal cells. A final diagnosis of basal cell adenoma was rendered based on the morphologic features and immunostaining pattern. This final diagnosis was concurred by an outside expert.

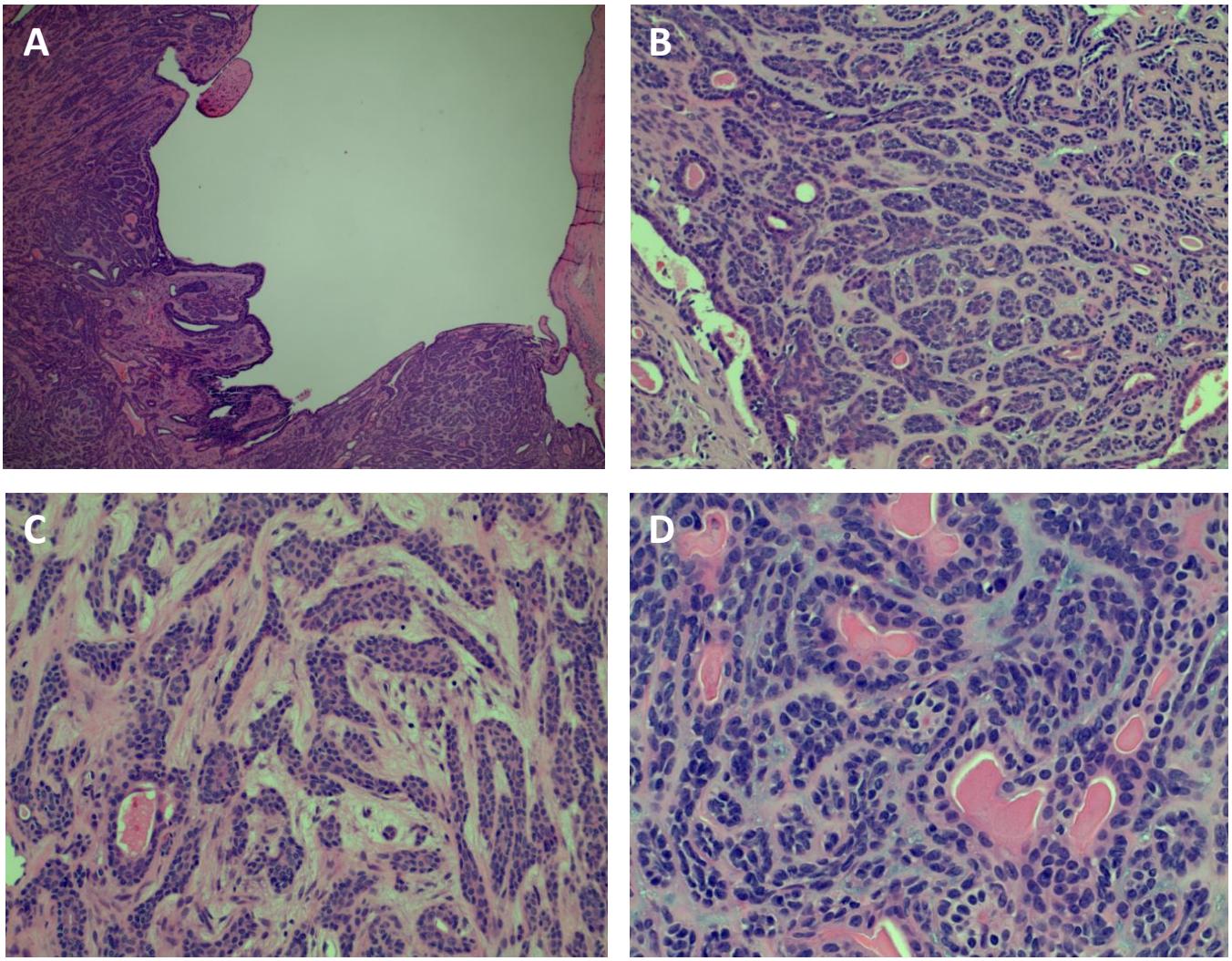

Figure 1. (A) Solid tumor with cystic area (original magnification 40x, H&E). **(B)** A cellular biphasic basaloid tumor with trabecular and tubular architectures (original magnification 100x, H&E). **(C)** Bland appearing abluminal basal-myoepithelial cells and admixed luminal ductal epithelial cells with distinctive basement membrane in a background of fibromyxoid stroma (original magnification 200x, H&E). **(D)** Biphasic basaloid cells with small glands containing eosinophilic secretion. No significant cytologic atypia or increased mitotic activity (original magnification 400x, H&E).

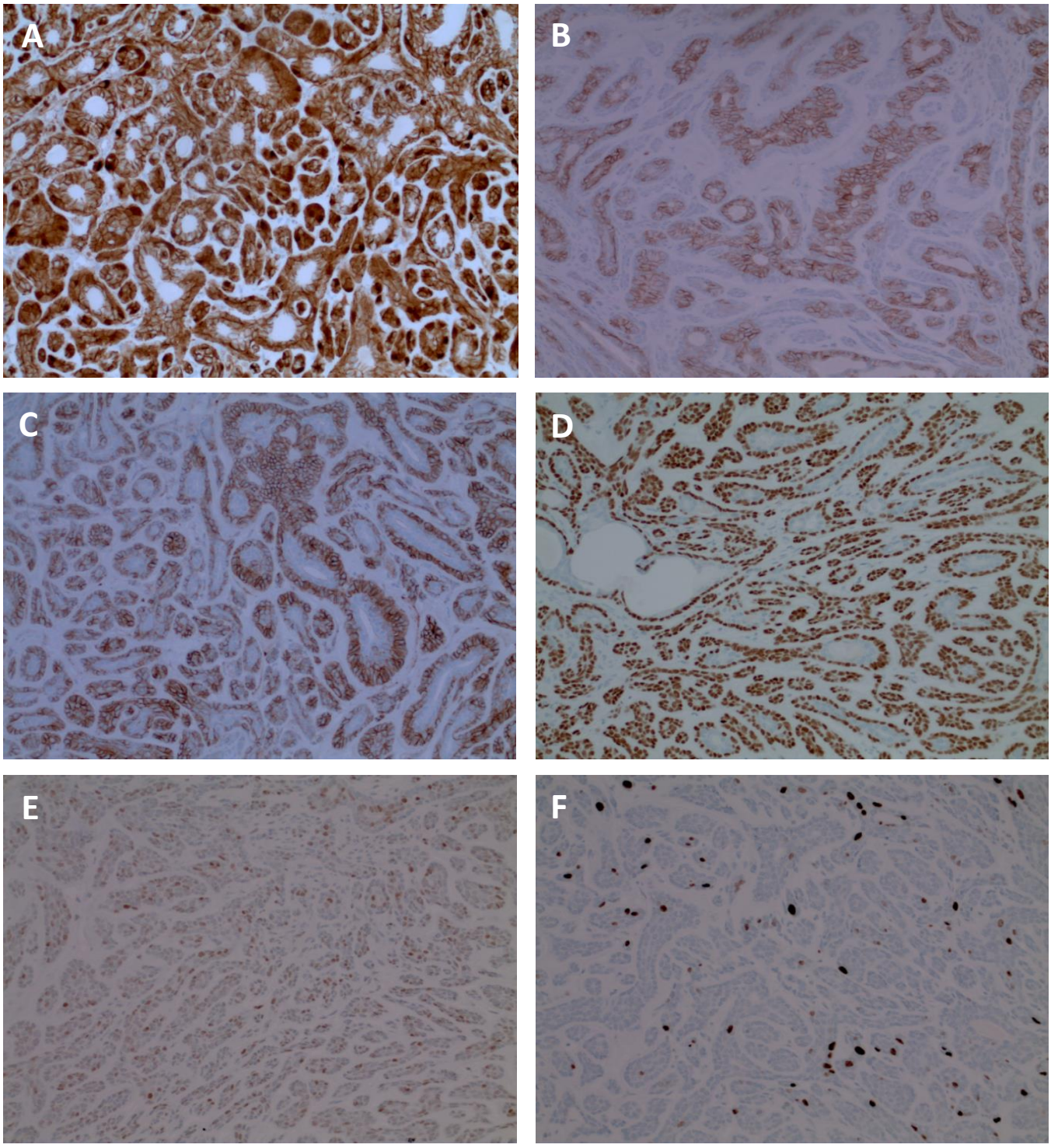

Figure 2. Immunohistochemical staining pictures. Original magnification 200x A-F. **(A)** Beta-catenin shows strong and diffuse expression of the cytoplasmic membrane of the inner epithelial cells and the cytoplasm and nuclei of the myoepithelial cells. **(B)** CD117 stained the cytoplasmic membrane of the inner ductal epithelial cells**. (C)** Dog1 shows expression of myoepithelial cytoplasm and cytoplasmic membrane**. (D)** P63 shows diffuse positivity of myoepithelial nuclei. **(E)** P53 shows a wild staining pattern. **(F)** Ki67 demonstrates a low-proliferative index of < 5%.

DISCUSSION

Basal cell adenoma (BCA) is a rare benign epithelial tumor of the salivary gland displaying monomorphic basaloid cells and luminal epithelial cells without a myxochondroid component. BCA is synonymous with monomorphic adenoma, basaloid salivary gland adenoma and membranous adenoma, also called dermal analogue tumor.[1,2] Patients diagnosed with BCA are usually adults, with 67% being female with a mean age 58 years. Although BCA resembles an embryoma, it is rarely congenital.[3,4] More than 80% of BCAs arise in the major salivary glands, mainly the parotid gland (specifically in the superficial lobe), followed by the submandibular gland (5%) and 6% in found in various intraoral locations, with the upper lip being the most common site, followed by the buccal mucosa.[5,6] BCA usually appears as a firm, mobile, slow growing, and asymptomatic mass. 65% of BCAs showed various degrees of cystic changes. They have characteristic numerous, endothelial-lined vascular channels with prominent small capillaries and venules, which can explain why BCAs are well-enhanced.7 Pathological examination is regarded as the most accurate method for diagnosing BCA.[6,7]

Histologically, BCA is divided into four subtypes based on morphologic patterns: solid, trabecular, tubular, and membranous, and is often with admixed two subtypes. Solid variants are the most common type, and membranous BCAs are normally expected to be non-encapsulated, multicentric, and multilobular.[8,9] Other primary salivary gland tumors, such as pleomorphic adenoma, adenoid cystic carcinoma, and basal cell adenocarcinoma can simulate its basal cell features, making it difficult to differentiate those entities.

However, BCAs often demonstrate diverse growth patterns with diverse cell types. The outer layer has peripheral palisading with dark small cells, scant cytoplasm, and dark but still vesicular nuclei which is the hallmark of all BCAs, regardless of subtype. Central to these cell layers is the luminal cell layer, which consists of small cuboidal cells with scant eosinophilic cytoplasm that form compressed tubules. Additionally, in all types of BCA, there may be mature squamous and sebaceous elements present. The abluminal cell layer is basal-myoepithelial and is positive for both muscle markers and basal markers such as P63, calponin, and high molecular weight keratins. Dog1 is expressed in cytoplasm and the cytoplasmic membrane of basal-myoepithelial cells. The luminal cell layer stained positive for C-kit and lower molecular weight keratins such as CK7. The presence of CTTNB1 mutations in BCAs result in BCA expression of Beta-catenin by immunohistochemistry. The membranous subtype of BCA is unique in that they may coexist with dermal cylindromas or trichoepitheliomas and are associated with Brooke-Spiegler syndrome. As such, even sporadic tumors show CYLD1 mutations and loss. BCAs have a low recurrence rate (2%) and rarely undergoes malignant transformation, the exception being the membranous type, which demonstrates a higher rate of local recurrence (25%) and 4% malignant transformation.[7-9] All BCAs are managed by local excision of the involved lobe, though the membranous type may require more extensive surgery due to a high rate of recurrence and occasional malignant transformation.[10-11]

It is challenging to differentiate BCA from other potential differential diagnoses, namely biphasic salivary tumors such as pleomorphic adenoma (PA), adenoid cystic carcinoma (ACC), basal cell adenocarcinoma (BCAC), epithelial-myoepithelial carcinoma (EMCA), and carcinoma ex-pleomorphic adenoma (CXPA).

Pleomorphic adenoma (PA) is sometimes misdiagnosed as BCA. PA is the most commonly occurring tumor, constituting up to two-thirds of all salivary gland neoplasms, and presents most frequently as a benign neoplasm of the salivary gland. Histological presentation of PA shows a variable pattern of epithelium in a loose fibrous stroma of myxoid, chondroid, or mucoid types. The tumor has three components: an epithelial, myoepithelial cell, and mesenchymal component, and diagnosis of PA require the identification of these three components. Myoepithelial cells are polygonal in shape with a pale eosinophilic cytoplasm.[11-12] Cellular PA is biphasic and bilayers but well demarcated, consisting of abluminal myoepithelial cells and luminal ductal cells. The abluminal myoepithelial cells are small, less distinct, and characteristically “stream” into a chondromyxoid stroma. PA is negative for Beta-catenin immunostaining.[10-12] In contrast, BCAs lack a chondromyxoid stroma and show the presence of a distinctive basal membrane.

Adenoid cystic carcinoma (ACC) bears the most histologic resemblance to BCA. ACC most frequently occurs in submandibular gland, with perineural invasion in 73% of cases.[13] ACC is a biphasic tumor with abluminal myoepithelial cells and luminal ductal cells, and both cell components of ACC consist of angulated hyperchromatic nuclei with scant cytoplasm.[14,15] ACC is more infiltrative and tubules will cleft from the basement membrane. C-kit is commonly used as it is preferentially expressed in ACC (mainly the ductal component). ACC is negative for Beta-catenin immunostaining.[16-18]

Basal cell adenocarcinoma (BCAC) is a rare malignancy most commonly seen in the salivary glands and is considered to be the malignant counterpart of BCA. It represents 1-2% of salivary gland neoplasms and presents about one decade later than BCA. BCAC may arise from BCA, though it is often a de novo malignancy. It is indolent, with a local recurrence rate as high as 50%, but has a low metastatic and mortality rate. Histologically, BCAC may appear similar to BCA, but typically displays a distinct morphology including a multinodular, focal infiltrating pattern, cytological atypia, perineural invasion (documented in about one-third of cases of BCAC), increased mitosis (> 4 mitoses per 10 HPFs), a ki-67 proliferation index of > 5%, and local invasion, which are not seen in basal cell adenoma.[9,19]

Epithelial-myoepithelial carcinoma (EMCA) is a rare malignant neoplasm that occurs most frequently in the major salivary glands and accounts for approximately 1% of all salivary gland neoplasms, predominating in the sixth decade with a slight female predilection (3:2). The characteristic growth pattern of EMCA consists of a multinodular permeative border with variable hyaline sclerosis. Classically, this is a clear cell tumor consisting of tubular, glandular, and solid growth patterns with abluminal clear polygonal myoepithelial cells rich in glycogen (diastase sensitive PAS+) and compressed tubules with scant eosinophilic or oncocytic cytoplasm. Occasional papillary and cystic areas may be seen.[9,20]

Carcinoma ex-pleomorphic adenoma (CXPA) is an aggressive malignancy. It is traditionally difficult to diagnose as the mixed tumor component is small and overlooked, and the malignant component may be difficult to classify. Tumors that invade beyond the capsule into the surrounding tissue by less than 1.5 cm are known as minimally invasive; these patients have an excellent prognosis. Tumors that go beyond 1.5 cm are considered invasive and are commonly associated with perineural invasion, angiovascular invasion, and necrosis. Perineural invasion, lymph node metastasis, and positive margins are all poor prognostic factors. Diagnosis of CXPA may require identification of a small mixed tumor in a salivary gland carcinoma. Additionally, it was reported that immunoreactivity for P53 can be used to differentiate pleomorphic adenoma and CXPA.21

CONCLUSION

BCA is an uncommon benign salivary gland tumor. As the tumor often presents in the fifth and seventh decades of life, a high index of suspicion is necessary to differentiate it from a malignant tumor arising from the same location. It is a diagnosis of exclusion, and it is necessary to rule out more common biphasic salivary gland tumors including adenoid cystic carcinoma, pleomorphic adenoma, basal cell adenocarcinoma, epithelial-myoepithelial carcinoma, and carcinoma ex-pleomorphic adenoma.

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CONFLICT OF INTEREST
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