Basal cell adenoma of salivary glands with a focal cribriform pattern: clinicopathologic and immunohistochemical study of 19 cases of a potential pitfall for diagnosis

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Original Contribution

1. Introduction

Basal cell adenoma (BCA) was first described by Kleinsasser and Klein in 1967 [1]. It's a rare benign neoplasm characterized by the basoloid appearance of the tumor cells [2]. Nagao [3] first reported that some BCAs have cribriform patterns, pseudocysts of amorphous, basophilic material characteristic of adenoid cystic carcinoma (AdCC), which is a very difficult problem for differential diagnosis. Then Dardick [4] described this kind of adenoid cystic pattern or solid-cribriform type of BCA in 1992. Recently, 18 cases of cribriform BCA (cBCA) were reported having most of the clinicopathologic features of conventional BCA [5]. However, because of its rarity, more extensive review of this pattern is necessary.

The aims of this study were to analyze the clinicopathologic features and prognosis of cBCA with cribriform component and to compare the microscopic characteristics of cribriform pattern between cBCA and AdCC using matrix metalloproteinase-9 (MMP9), calponin, SMA, S100, P63, CD117, and laminin antibodies. It would allow clinicians to better understand the intrinsic quality of cBCA and choose an appropriate treatment.

2. Materials and methods

The patients fulfilling the following criteria were included in our study: (i) a well-circumscribed tumor composed of the peripheral-palisading basoloid cells. (ii) cribriform patterns accounted for more than 30% in the tumor. Thus, a group of 19 cases from a total of 261 cases diagnosed as cBCA was retrieved from the files of Oral Pathology Department, Peking University School and Hospital of Stomatology from 1985 to 2012. All tissues were obtained in accordance with the protocols approved by Ethics Committee of Peking University Health Science Center. The surgical specimens were fixed in formalin, routinely processed, and embedded in paraffin. The histologic materials from the tumors were reviewed on the hematoxylin-eosin-stained sections by two experienced pathologists to confirm the accuracy of the diagnosis. The investigated parameters included the age at the time of diagnosis, the anatomical location, the imaging findings, the histological type, the treatment and the prognosis. Additionally, 10 cases of AdCC were chosen as contrasts.
The immunohistochemical staining was performed using a standard streptavidin-biotin-peroxidase complex method. Calponin, SMA, S100, MMP9, P63, CK8&18, CD117, and laminin antibodies were purchased from Zymed Laboratories (South San Francisco, CA, USA) (Table 1). The antibodies of MMP9, CK8&18, SMA, S100, and laminin were used for single staining by LAB-SA kit. Calponin (only myoepithelial cell is positive to) and P63 (both myoepithelial cell and basaloid cell are positive to) antibodies were used for the double staining by Polink DS-MR-Hu A1 kit, a simultaneous polymer double staining kit for mouse and rabbit antibody with DAB and AP-Red Plus. We purchased LAB-SA kit and Polink DS-MR-Hu A1 kit from Golden Bridge International Labs (Mukilteo, WA, USA). Two experienced pathologists respectively judged the immunohistochemical results.

3. Results

3.1. Clinical data

Nineteen cases of cBCA included 15 women and 4 men. The age at the time of diagnosis ranged from 24–71 years (average, 48 years). They all affected the parotid glands. The clinical symptom was only local swelling without pain. The enhanced CT revealed a well-defined solid mass that was rich in vascular (Fig. 1). The complete surgical removal with an extracapsular limit was performed. Grossly, the sizes of the tumors ranged from 0.8 to 5cm with the complete encapsulations (Fig. 2).

The follow-up data were available for all 19 patients ranging from 5 months to 276 months, with a median of 67 months (Table 2). The patient had a satisfactory postoperative period, and presented no sign of local recurrence after surgery until this paper was summarized (March, 2013).

3.2. Microscopic findings

The gross specimen of cBCA showed a well-encapsulated mass with a varied pattern. Generally, the well-defined capsules were very evident, and some of the tumors tended to separate entirely from the capsule after dissection. Not any kind of perineural or perivascular invasion was presented in the tumor (Fig. 3A, B).

As far as AdCC was concerned, it exhibited an invasive growth capacity consistent with aggressive clinical behavior. These tumors were typically unencapsulated or poorly defined, and infiltrative (Fig. 3D). They could invade the surrounding muscle tissue (Fig. 3E). The perineural or even intraneural invasion could be observed in AdCC (data not shown). The proliferating cell was a
small cuboidal cell with a round hyperchromatic nucleus and scant cytoplasm. Mitotic activity, pleomorphism, and cellular atypia were not usually presented (Fig. 3F). The cells were arranged in various patterns that had been described as cribriform, tubular, and solid. In order to compare in parallel with cBCA, the cribriform pattern predominated in these series of AdCC, but the tubular or solid area may coexist in the same tumor. In the cribriform area, islands of cells formed pseudocystic spaces which were surrounded by basophilic, mucinous, or hyalinized material representing replicated basal lamina. The tubular pattern showed the cells in ductal arrangement with a single lumen. The solid pattern had broad sheets and solid islands of the small, dark-staining cells. The stroma in AdCC was fibrous.

3.3. Immunohistochemical findings

Immunohistochemically, all cells around the cribriform structures showed no reactivity for MMP9 (Fig. 4A). P63-positive and calponin-negative cells were found in the cribriform pattern of cBCA, although the tumor cells exhibited some degree of myoepithelial cell participation (calponin-positive) in other areas such as solid and trabecular-tubular area. The cells around the cribriform structure in cBCA were almost devoid of staining with calponin, SMA, S100, and CK8&18 (Fig. 5A-D). Lamin protein was faintly or negatively expressed in the cribriform patterns of cBCA (Fig. 6A).

In contrast, the cells around the cribriform structure in AdCC were partially MMP9-positive (Fig. 4B). Calponin and P63 protein were both detected in the cribriform pattern (Fig. 5E). However, SMA and S100 were faintly or negatively expressed there. Some SMA/S100-positive nests appeared in the solid area (Fig. 5F,G). The inner layer of the cribriform pattern in AdCC showed positive immunoreactivity for CK8&18 (Fig. 5H). The substrate-like substances were revealed clearly by the lamin stain (Fig. 6B). CD117 was expressed strongly in some AdCC but no staining in cBCA (Fig. 7).

4. Discussion

Basal cell adenoma is the third most common of the benign parotid tumors, although its incidence is as low as accounting for 1% to 4% of all salivary gland tumors [7]. Nagao [3] reported that the incidence of BCA was 7.5% among 531 cases of primary epithelial tumors of the parotid gland, and adenoid cystic pattern accounted for 10% in BCA. Our data suggested that the percentage of cBCA was 7% (19/261). Basal cell adenoma can occur at any age but it happens most commonly in middle-aged and older adults with prevalence in the seventh decade of life [8]. Our data showed that cBCA had a female tendency.

The characteristics of BCA such as the integrity of the basal layer, decreased number of mitoses, and slow growth pattern are the typical characteristics of a benign lesion. From our findings, we could
conclude that the cribriform pattern was not the differential points for cBCA and AdCC. The distinction points between cBCA and AdCC were the intactness of the capsule and the outer palisaded cells in cBCA as well as the invasive growth pattern in AdCC. Additionally, the vascular-rich appearance of enhanced CT was also valuable for the diagnosis. True invasion must be distinguished from both multinoularity with a pushing type of growth pattern and multifocal origin in adjacent salivary lobules.

It was reported that BCA exhibited some degree of myoepithelial cell participation [8] with the periductal, epithelioid, and spindled (stromal-like) morphologic structures [9]. We did find the myoepithelial marker-positive cells in other areas of cBCA except the cribriform area. But the cells around the cribriform patterns of cBCA were almost devoid of staining with the calponin, SMA, S100, and CK8&18, suggesting that they were composed largely of basaloid cells. We speculated that these cells originated from the basal layers of the intercalated duct or the terminal duct.

Distinction of BCA with cribriform areas and AdCC of salivary glands can be problematic. In this study we have found that the most reliable features that help separate the two conditions include good
circumscription and lack of invasive properties in cBCA and absence of staining for MMP9 and laminin in the cells around the cribriform spaces in cBCA, and of calponin, SMA, or S100 in the cribriform areas in contrast with AdCC.

References


Fig. 7. Most cells around the cribriform pattern in cBCA (A) showed no immunoreactivity for CD117, but some AdCC presented strong positive staining there (B).