“Malignant Pleomorphic Adenoma” in the Palate

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A case of tumor occurring in the palate of a 74-year-old Japanese female is reported. Although histological and immunohistochemical features of the tumor were identical to those of pleomorphic adenoma, except for scarce pleomorphic or “mixed” appearance, diffuse cellular and nuclear pleomorphism and relatively high proliferative cellular activity were observed. However, there was no metastasis or recurrence, indicative of its low-grade malignancy. Pre-existing benign pleomorphic adenoma was not recognized. Due to these characteristics, we consider that the tumor should be diagnosed as “malignant pleomorphic adenoma” or “low-grade malignant mixed tumor” and propose to separate such types of tumor from ordinary types of pleomorphic adenoma and carcinoma in pleomorphic adenoma.

Key words: malignant pleomorphic adenoma, low-grade malignant mixed tumor, salivary gland tumor

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Introduction

Pleomorphic adenoma (PA) is the most common benign tumor of the salivary glands. Although the risk of recurrence and malignant transformation of PA is higher than that of other benign salivary gland tumors, the cytologic features are usually benign. There are rare tumors that show histologic features of PA and morphologic atypia, such as enlarged, pleomorphic or hyperchromatic nuclei and frequent or abnormal mitoses. They do not show any foci of pre-existing benign PA.

We report such an unusual tumor arising in palatal

gland and discuss the differential diagnosis.

Case Report

A 74-year-old Japanese female was referred to our hospital for a gradually enlarging mass in the palate, which had been noticed for one year.

Oral examination revealed a mass on a left portion of the hard palate, measuring 18mm x 17mm, with a clear boundary. Formation of ulcer and submucosal hematoma due to a biopsy in an other hospital (histological diagnosis: PA) was observed (Fig. 1). A panoramic radiograph showed that the tumor pushed up the floor of the nasal cavity. At surgery, resorption of palatal bone was observed, so the tumor was excised along with the palatal bone. There were no signs of recurrence or metastasis at follow-up for two years.

Histopathologic findings

Microscopically, the tumor was separated from surrounding tissues by a fibrous connective tissue, and invasive growth was not apparent (Fig. 2). The tumor was mainly composed of tubular structures showing a biphasic growth pattern characterized by tubule-lining cells and non-luminal cells (Fig. 3). Trabecular and solid nests were also observed. The stroma was hyalinized with marked hemorrhage. Although myxomatous or chondroid areas as seen in typical PA were not found, the non-

Fig. 1: Clinical view of the tumor in the palate.

Fig. 2: The tumor is well-circumscribed and surrounded by a fibrous capsule (H-E, ×40).

Fig. 5: Tumor cells show diffuse cellular and nuclear pleomorphism including atypical mitosis (arrow) (H-E, ×200).

Fig. 3: The tumor is mainly composed of tubular structures showing biphasic growth pattern characterized by tubule-lining cells and non-luminal cells (H-E, ×150).

Fig. 6: Non-luminal cells strongly express GFAP (streptavidin-biotin method, ×200).

Fig. 4: Hyalinized stroma with occasional isolated tumor cells ("mixed" appearance) (H-E, ×200).

Fig. 7: The tumor cells are frequently positive for PCNA (streptavidin-biotin method, ×200).

luminal cells focally showed isolation into the hyaline matrix (Fig. 4). The tumor cells diffusely exhibited nuclear pleomorphism and hyperchromatism (Fig. 5). Mitotic figures were not so numerous but were detectable. There were no obvious sarcomatous components in this tumor. Pre-existing PA was also absent.

For immunohistochemical staining, the strep-

tavidin-biotin peroxidase complex method (Histofine, SAB-PO kit, Nichirei) was employed on paraffin sections. Primary antibodies against S-100 protein (1: 500, DAKO), vimentin (1: 10, DAKO), glial fibrillary acidic protein (GFAP) (1: 100, DAKO) and proliferative cell nuclear antigen (PCNA) (1: 100, Novocastra Lab.) were used for this examination. The non-luminal cells exhib-

ited positive reactivity for vimentin and S-100 protein in addition to frequent expression of GFAP (Fig. 6). Many PCNA-positive tumor cells were present throughout the specimen (Fig. 7). Based on these histological and immunohistochemical findings, the tumor was diagnosed as "malignant PA".

Discussion

We have experienced several cases arising in the minor or major salivary glands resembling the present case. Their histological and immunohistochemical features are in accordance with those of PA, but in the tumors, characteristics indicative of low-grade malignancy such as incomplete encapsulation, diffuse cellular and nuclear pleomorphism and relatively high proliferative activity were more or less detected (1, 2). Pre-existing benign PA was not observed, indicating *de novo* development. Carcinomatous and/or sarcomatous components or metastases were not observed.

Because these cases were mainly composed of biphasic tubular structures consisting of inner-luminal and outer-myoe epithelial cells without obvious mesenchymal-like structures, they have to be differentiated from tubular type of adenoid cystic carcinoma (ACC), basal cell adenoma/adenocarcinoma and epithelial-myoe epithelial carcinoma. Although, based on the histological findings by hematoxylin-eosin staining only, they could possibly be distinguished from these well-defined tumor types, the immunohistochemical findings are of confirmative value for the differential diagnosis. In ACC and basal cell adenoma/adenocarcinoma, S-100 protein is occasionally expressed by the luminal cells but not by the outer myoe epithelial/basal cells. That is quite different from the findings of the present case. Although the im-

munoreactivity of epithelial-myoe epithelial carcinoma is similar to that of PA, significant positivity for GFAP and vimentin in outer myoe epithelial cells favors the diagnosis of PA.

According to the present WHO international classification of salivary gland tumors (3), the malignant counterpart of PA is carcinoma in PA (malignant mixed tumor). Within the heading of carcinoma in PA included are three different clinical and pathologic entities: carcinoma in PA, carcinosarcoma and metastasizing PA. Therefore, the type of tumors as in the present case could not fit into any entities of carcinoma in PA in the present WHO classification. Although the histological and cytological findings indicate low-grade malignancy of these tumors, it is necessary to analyze a large number of cases with long follow-up in order to evaluate the precise prognosis. For this purpose, it may be appropriate at present to separate these tumors from ordinary types of PA and carcinoma in PA by naming this entity "malignant PA" or "low-grade malignant mixed tumor".

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