Carcinoma ex Pleomorphic Adenoma of the Palate
- A Case Report -

A case of squamous cell carcinoma ex pleomorphic adenoma in a palate is presented and comments on diagnostic criterias are described. The patient was 36-year-old male presenting with an ovoid elevated palate mass for 6 months. The tumor located in the junctional area of soft and hard palate. The mucosa was diffusely ulcerated and the mass focally tightly adherent to adjacent tissue. The initial cytologic and pathological diagnosis by fine needle aspiration biopsy and open biopsy was benign pleomorphic adenoma. After total removal, histologic examination revealed that tumor was composed partly of benign pleomorphic adenoma and partly of an squamous cell carcinoma component with areas of necrosis and capsular invasion. Immunohistochemical staining in the carcinoma area revealed positive reaction for low and high molecular weight cytokeratin, and epithelial membrane antigen, but negative for desmin, actin, GFAP and S-100 protein. In situ hybridization using biotinylated Epstein-Barr virus probe was done and the neoplastic cells were negative. Our case is an unusual partially encapsulated carcinoma ex pleomorphic adenoma in the palate and is not related to EBV infection. *(JKMS 1997; 12: 63~6)*

Key Words : *Carcinoma ex Pleomorphic Adenoma, Hard Palate, Immunohistochemistry*

Kyoung Mee Kim, M.D., Anhi Lee, M.D., Sun Ho Yoon, M.D.*, Jin Han Kang, M.D., and Sang In Shim, M.D.**

Department of Clinical Pathology, Otolaryngology* and Pediatrics**, Catholic Uneversity Medical College

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Address for correspondence
Kyoung Mee Kim, M.D., Department of Clinical Pathology, Our Lady of Mercy Hospital, Catholic University Medical College, Pupyongdong, Pukgu, Inchon, Korea. 403-016
Tel : 032-510-5500, Fax : 02-744-8994

INTRODUCTION

Malignant mixed tumors of salivary gland origin are uncommon neoplasm and may be of three types. The majority arise as carcinomas within benign pleomorphic adenomas. Carcinoma ex pleomorphic adenoma contains elements of a benign pleomorphic adenoma and a frankly malignant epithelial component(1). It accounts for approximately 2~5% of all pleomorphic adenomas(2). It has been reported that the most frequently affected site is the parotid gland, while the incidence rates in minor salivary gland are much lower(2). The carcinoma which develops in a pleomorphic adenoma is most frequently an adenocarcinoma and second most common is undifferentiated carcinoma. Less frequently the malignancy will be a squamous cell carcinoma(3). We report a case of squamous cell carcinoma ex pleomorphic adenoma in the palate and the immunohistochemical staining findings and in situ hybridization results are described with comments on diagnostic criterias.

CASE REPORT

A 36-year-old man came to our hospital due to flat elevated oval shaped mass on the palate for 6 months. The patient complained of disturbance of his speech. Laboratory examination revealed normal range except idiopathic thrombocytopenia(44,000/mm^3). The bone marrow biopsy specimen showed mildly increased megakaryocytes. Head and neck CT showed 2cm sized round soft tissue mass in the palate(Fig. 1). The palate bone in the posterior margin showed discontinuity in a midportion and there was diffuse, symmetrical thickening in the mucosal space of pharyngeal wall with resultant narrowing of airway. The radiologic diagnosis was lymphoma or other lymphoproliferative disease. Examination on fine needle aspirated material revealed only a few small clusters of bland epithelial cells. The initial pathological diagnosis by open biopsy was benign pleomorphic adenoma. After plasmapheresis, excision biopsy of the palate mass and skin graft was done. At operation, 3cm sized flat ovoid elevated mass was noted on the right side of the hard and soft palate(Fig. 2). The postoperative course was uneventful and the patient has been well for 9 months and the idiopathic thrombocytopenia was corrected mysteriously and spontaneously after operation.

Grossly, the surface of the excised tumor (3.4×3.0×2.5cm) was ovoid, solid and gray white. On section, it has yellow and gray, variegated smooth cut surfaces. On microscopic examination, the majority of the tumor consisted of a typical pleomorphic adenoma, while malignant areas showed moderately differentiated squamous

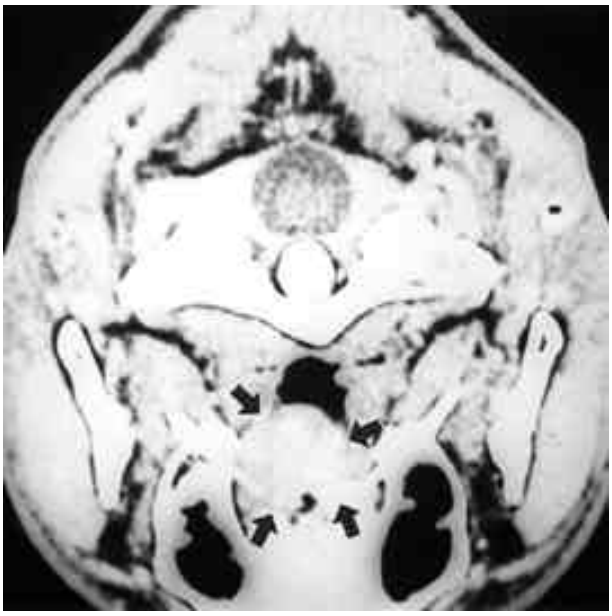

Fig. 1. Head and neck CT scan revealed about 2cm sized, round, soft tissue mass in the palate(arrow)

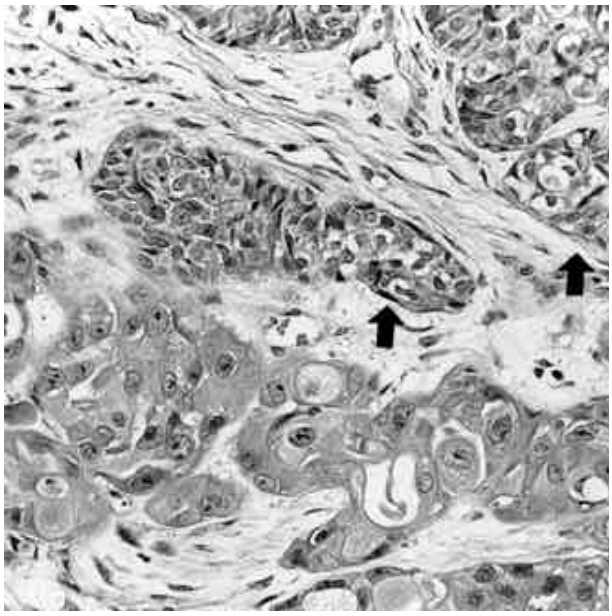

Fig. 3. The tumor was composed of pleomorphic adenoma area (arrow) and moderately differentiated squamous cell carcinoma area (Hematoxylin & eosin, ×200).

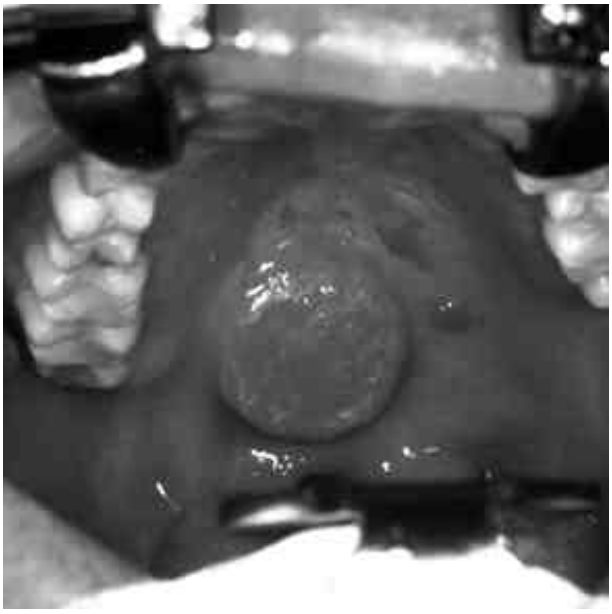

Fig. 2. A 3cm sized flat, ovoid, ulcerated and elevated mass in the right side of palate.

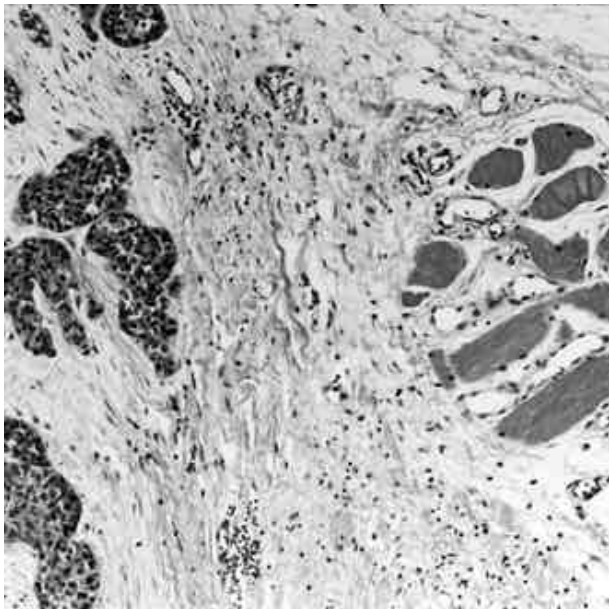

Fig. 4. Tumor cell nests outside the capsule infiltrating into adjacent normal fibromuscular tissue(Hematoxylin & eosin, ×100)

cell carcinoma with severe desmoplasia (Fig. 3). The cells comprising the carcinoma were polygonal in shape and showed prominent nucleoli, occasional mitosis and cellular pleomorphism. In this malignant area, minute areas of necrosis and calcification were also noted. There was focal capsular invasion and tumor cell infiltration into adjacent normal tissue (Fig. 4). Immunohistochemical staining was done using low and high molecular weight cytokeratin, desmin, actin, GFAP, S-100 protein and epithelial membrane antigen. The squamous cell carcinoma area showed positive reaction for low and high molecular weight cytokeratin and epithelial membrane antigen. The tumor cells were negative for desmin, actin, GFAP and S-100 protein, so we could conclude that the

myoepithelial cells had disappeared. In situ hybridization was performed on paraffin embedded tissue using biotinylated Epstein-Barr virus probe (Research genetics, USA) and the neoplastic cells were negative.

DISCUSSION

Carcinoma ex mixed tumor, also known as carcinoma ex pleomorphic adenoma or carcinoma arising in a mixed tumor, is a mixed tumor in which a second neoplasm develops from the epithelial component that fulfills the criteria for malignancy. However, the term 'malignant mixed tumor' should be divided into four different clinical and histological entities : invasive carcinoma ex pleomorphic adenoma, true malignant mixed tumor (carcinosarcoma) (1, 4), so-called benign metastasizing pleomorphic adenoma (5) and non-invase carcinoma ex pleomorphic adenoma (6).

Carcinoma in pleomorphic adenoma may be rather uncommon and their incidence in total epithelial parotid gland tumors has variously been reported to be 1.5% to 6.0% (7). The scarcity of well documented cases and the lack of generally accepted histopathologic criteria has led to poor understanding of this form of salivary gland cancer. Histological evidence for carcinomatous transformation in pleomorphic adenoma is as follows : (a) unusual destructive and infiltrative growth ; (b) abnormal nuclear changes with mitoses ; (c) necrosis ; (d) hemorrhage ; (e) dystrophic calcification ; (f) vascular or neural invasion, or both ; and (g) local and distant metastasis (1, 7). Gnepp and Wenig (8) defined the criteria of malignancy as invasiveness, destruction of normal tissues, cellular anaplasia, cellular pleomorphism, atypical mitoses, and abnormal architectural patterns, such as back-to-back glands and sheets of tumor cells. Beahrs et al.(9) referred to a major criterion for malignancy to the finding that neighboring myoepithelial cells are destroyed by atypical epithelial cells due to an active proliferation of the latter. Gerughty and his colleagues (7) suggested that the histologic evidence of an invasive growth pattern, neural or vascular invasion, necrosis, and focal calcification implied a poor prognosis. Then it is thought that cellular pleomorphism with mitosis, necrosis and infiltrative growth are the main clues in the diagnosis of carcinomatous transformation in pleomorphic adenoma. As described in the recently published book by Cawson and Eveson (6), non-invasive carcinoma ex pleomorphic adenoma is one of the definite disease entity comprising carcinoma ex pleomorphic adenoma. In agreement with Cawson and Eveson's concept (6), and according to the diagnostic criterias proposed by Gerughty et al.(7), we think that our case is a carcinomatous transformation in the pleomorphic adenoma. Our case had only necrosis among several pathologic prognostic factors and he has been well for 9 months without any evidence of recurrence or metastasis. Livolsi and Perzin (4) stated that lesions of the palate had a better prognosis as compared to tumors of the major salivary glands, perhaps because of their relatively small size when discovered clinically. However Spiro et al.(10) reported that carcinoma ex pleomorphic adenoma of the palate developed high recurrence rates. Because the number of cases are very small, there is no distinct tendency as to the rate of recurrence and rate of formation of metastasis.

There is no definite sex incidence for this tumor. Beahrs et al.(9) reported the predominance of males whereas Evans and Cruickshank (11) showed that carcinoma ex pleomorphic adenoma are more common in the females than males. It has been reported that the size of carcinoma ex pleomorphic adenoma is larger than that of other benign tumors (12). Nagao et al.(13) showed that 50% of the carcinoma ex pleomorphic adenoma of the parotid gland were greater than 5cm in size. On the other hand, Livolsi and Perzin (4) stated that this tumour, arising in a minor salivary gland, is smaller than that arising in a major salivary gland. In the palate, the neoplasms tended to be more small (75% were 2cm or less). However the tumor size of our case was large and measured 3.4cm.

It has been reported that pleomorphic adenoma is the most common neoplasm arising in a minor salivary gland of the palate. In malignant palatal tumors, mucoepidermoid carcinoma and adenoid cystic carcinoma are frequently found(14~16). When compared with these tumors, carcinoma ex pleomorphic adenoma arising in the palate is rare. Waldron et al.(16) reported only four cases out of 181 palatal tumors. Da-Quan and Guangyan (14) also reported 19 cases out of 160 cases, but Regezi et al.(15) failed to report any cases out of 109 cases.

Immunohistochemistry was believed to be of potential assistance in the diagnosis of salivary gland tumors and in prediction of histogenesis (15). In our case, immunohistochemical staining in carcinoma area showed negative reaction for desmin, actin, GFAP and S-100 protein and diffuse strong positive reaction for high molecular weight cytokeratin. In a pleomorphic adenoma area desmin, S-100 protein, actin, high molecular weight cytokeratin were focally positive.

So immunohistochemistry proved the disappearance of myoepithelial cells in carcinoma area. In situ hybridization was performed on paraffin embedded tissue using biotinylated Epstein-Barr virus(EBV) probe to look at whether this disease is associated with the EBV. The

tumor cells were all negative for EBV. So our case is a rare carcinoma ex pleomorphic adenoma occurred in the minor salivary gland of a palate and is not related to EBV infection.

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