CASE REPORT

A case of squamous cell carcinoma ex pleomorphic adenoma in the palate: Immunohistochemical analysis and chromosomal alteration by comparative genomic hybridization

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Summary Carcinoma ex pleomorphic adenoma (CXPA) is an uncommon tumor of salivary gland; moreover, histologically, squamous cell carcinoma (SCC) is exceedingly rare. This report documents a case of CXPA arising in the hard palate, which showed transformation from pleomorphic adenoma (PA) to SCC reacted to Ki-67 immunostaining. Other immunohistochemical stains also demonstrated different immunoreactivities between PA cells and SCC cells. Comparative genomic hybridization identified a chromosomal imbalance. Gain regions of the PA were 8q11–22 and 8q24 and the loss region was 13q32–34 in PA; additionally, in SCC, regions characterized by increased DNA copy number were 8p, 8q and 12q12–15.

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KEYWORDS
CXPA; Squamous cell carcinoma; Hard palate; Malignant transformation; Immunostain; Comparative genomic hybridization

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Introduction

Carcinoma ex pleomorphic adenoma (CXPA) is a rare malignant neoplasm of salivary gland accounting for approximately 2 ~ 5% of all pleomorphic adenoma (PA). CXPA is the most frequently occurring malignancy in the parotid gland; furthermore, incidence in the minor salivary gland is very low. The present report documents a rare example of squamous cell carcinoma (SCC) ex pleomorphic adenoma originating in palatal minor salivary gland. Immunohistochemical staining and comparative genomic hybridization (CGH) methodology were employed to identify the tumor characteristics and chromosomal imbalances. In addition, correlation of chromosome copy number alterations between CXPA and PA was discussed.

Case report

A seventy two-year old man presenting with a multi-year history of a mass on the left side of the palate was referred to our facility. Physical examination revealed an elastic-hard mass, 20 × 20 mm, with a 12 × 12 mm epithelial defect (Fig. 1). Lymphadenopathy in the cervical region was not palpable. Magnetic resonance imaging scans disclosed a clearly definite mass in the palate (Fig. 1). Initial pathological diagnosis by biopsy was PA comprised of myoepithelial-type cells; evidence of malignancy was not apparent. The tumor was removed surgically with a sufficient safety margin; subsequently, the resected tumor was examined histologically in terms of finer detail. The majority of the tumor consisted of myoepithelial-type and ductal epithelial-type cells identical to those observed in the biopsy sample; however, moderately differentiated SCC located in the area of epithelial defect was identified. These cells exhibited large nuclei, prominent nucleoli and polygonal shape in comparison with PA cells; moreover, myoepithelial-type cells of PA clearly transformed to SCC (Fig. 2). Immunohistochemical reaction for Ki-67 displayed positive readings in more than 40% of SCC cells; in contrast, only 1% of PA cells were stained. Finally, diagnosis of CXPA was rendered.

Additional immunohistochemical staining was conducted. In the presence of keratin, SCC cells were immunoreactive for AE1/AE3, whereas ductal epithelial-type cells were positive for both AE1/AE3 and CK7; myoepithelial-type cells were focally positive. No cell type exhibited immunoreactivity for CK20. SCC and ductal epithelial-type cells were focally positive for EMA and CEA. Although PA consisting of ductal epithelial-type and myoepithelial-type cells was immunoreactive for S-100 protein, SCC cells were not stained.

In order to examine the genetic relationship between SCC cells and myoepithelial-type cells, CGH was conducted employing techniques described previously. As a result, PA demonstrated increased copy number at 8q11–12 and 8q24, whereas SCC displayed increased copy number at 8p, 8q and 12q12–15. On the other hand, 13q32–34 in PA and SCC was the common region of decreased copy number (Table 1).

Discussion

Numerous CXPA subtypes have been described in previous reports. In CXPA, SCC cells exhibited large nuclei, prominent nucleoli and polygonal shape in comparison with PA cells; moreover, myoepithelial-type cells of PA clearly transformed to SCC. In contrast, PA cells were immunoreactive for S-100 protein, whereas SCC cells were not stained. CGH was conducted employing techniques described previously. As a result, PA demonstrated increased copy number at 8q11–12 and 8q24, whereas SCC displayed increased copy number at 8p, 8q and 12q12–15. On the other hand, 13q32–34 in PA and SCC was the common region of decreased copy number (Table 1).
pleomorphic adenoma is rare as noted by Peel and Gnepp. In differential diagnosis, it is important to distinguish SCC and squamous cell metaplasia. In this case, squamous cell metaplasia was suspected. Differential diagnosis was relatively easy, because cells positive for Ki-67 immunostaining, a cell proliferation marker, were greater in the SCC field than in the PA field. Zhu et al. indicated that Ki-67 staining can discriminate between benign and malignant tumors of parotid gland. Thus,

**Figure 2** (Left) Squamous cell carcinoma (upper portion) and pleomorphic adenoma (lower portion) (H&E, ×40). (Right) Transition from pleomorphic adenoma to squamous cell carcinoma. No border zone is present between these neoplasms (×100).

**Table 1** Immunohistochemical stain and CGH analysis

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<td>CGH Loss</td>
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the immunostain of Ki-67 facilitated the differential diagnosis of SCC from squamous cell metaplasia in the current patient.

PA consisted of two components, ductal type and myoepithelial type; moreover, based on histological findings, it appeared that SCC developed from myoepithelial type. Ten kinds of immunostaining were performed according to the report from myoepithelial type. Ten kinds of immunological findings, it appeared that SCC developed and myoepithelial type; moreover, based on histological diagnosis of SCC from squamous cell metaplasia.

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The loss region at 13q32–34 was evident in both PA and SCC; however, tumor suppressor genes are not located in this region to the best of our knowledge. In summary, this investigation suggests that copy number gains of the 8q11–22 and 8q24 regions might be essential for development of PA. In addition, the gain in the 12q12–15 region may be required for progression from PA to SCC.

References