A Case of Oral Adenoid Squamous Cell Carcinoma: Histopathological and Immunohistochemical Studies

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We reported a case of adenoid squamous cell carcinoma manifested in the tongue of a 66-year-old man along with its histopathological and immunohistochemical findings. Histopathological examination revealed that almost the entire part of the neoplasm was characterized by pseudoglandular structures lined by cuboidal cells lacking intercellular bridges, keratinization, or other features of a squamous growth. Alcian blue (AB), mucicarmin (MC), and periodic acid schiff (PAS) stains failed to demonstrate epithelial mucin in the cytoplasm of the cuboidal cells or intraluminal substance. Immunohistochemical staining showed positive reactions against antibodies to cytokeratin (CK) and vimentin (VM), and no reaction with antibodies to epithelial membrane antigen (EMA) and factor VIII related antigen (FVIII). These findings suggested that this tumor involved the acantholysis and degeneration of a squamous cell carcinoma.

Key words: Adenoid squamous cell carcinoma/Tongue/Histogenesis/Immunohistochemical study

Introduction

Adenoid squamous cell carcinoma is a well-recognized variant of squamous cell carcinoma that was first described by Lever¹ in 1947. Although adenoid squamous cell carcinoma is most frequently found on sun-exposed skin, this tumor very rarely occurs in the oral cavity²⁻⁵. There are several histopathological, immunohistochemical, and ultrastructural
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studies as to this tumor[1]. However, its histogenesis and nature are still controversial.

We report a case of adenoid squamous cell carcinoma of the tongue and discuss the histogenesis of this tumor based on the histopathological and immunohistochemical findings.

Case report

A 66-year-old man visited to our department (Oita Red Cross Hospital) with the chief complaint of a painful mass on the right side of the tongue. He had firstly noticed the painless mass about two months earlier. When he visited his dentist because of a rapid increase in size and pain of this lesion, he was advised to undergo a complete examination and was referred to our oral surgery clinic. On his first visit, laboratory tests and examination of his general condition showed no abnormalities.

Oral examination revealed a fingertip sized, opaque, elastic hard mass, and ulcerated lesion in the right posterior portion of the tongue. The size of the mass was a circular nodule measuring 25 × 15 mm (Fig. 1). The suspected clinical diagnosis was a malignant tumor. After making a diagnosis of undifferentiated carcinoma by biopsy, the tumor was widely resected together with the surrounding tissues en bloc under general anesthesia. The postoperative course has been uneventful, and no recurrence has occurred for about 1.5 years after the operation.

The removed tumor was a nodular, nearly oval-shaped tumor measuring 25 × 15 × 10 mm. It was elastic and slightly hard. The cut surface was solid and yellowish-white.

Histopathological findings: The tissue specimens obtained on surgical excision were fixed in 10% neutral formalin saline. The mass was cut into two parts, and routine paraffin sections were made. Four micrometer-thick paraffin sections were cut and stained with hematoxylin–eosin (HE). In addition, specimens were stained with alcian blue (AB), mucicarmine (MC), and periodic acid shiff (PAS) with and without diastase digestion.

Most parts of the tumor were composed of an alveolar or solid structure of cuboidal cells lacking intercellular bridges, keratinization, or other features of squamous growth. Cystic degeneration of the epithelial islands with the formation of pseudoglandular structures was noted in portions of the neoplasm. The ductal structures were lined by a cuboidal layer of cells showing nuclear pleomorphism, hypercromatism, and mitosis. Furthermore, these cells exhibited loss of cytoplasmic eosinophilia with the assumption of an amphophilic to basophilic cytoplasm, enhancing the gland-like appearance. The surrounding fibrous connective tissue consisted of loosely or densely arranged collagen fibers interspersed with fibroblasts and scattered chronic inflammatory cells. PAS staining showed focal intracytoplasmic glycogen that was removed with diastase predigestion. Mucin stains (AB, MC) failed to demonstrate epithelial mucin in the cytoplasm of the cuboidal cells and intra luminal substance (Figs. 2 and 3).

Immunohistochemical findings: Deparaffinized sections were also prepared for immunohistochemistry. Primary antibodies against Cytokeratin (CK), epithelial membrane antigen (EMA), vimentin (VM), and factor VIII related antigen (FVIII) were purchased from DAKO.
(Glostrup, Denmark). To detect the antigens, the labeled streptavidin biotin (LSAB) method was used. The endogenous peroxidase activity was blocked with 3% H2O2 for 5 minutes, and the sections were incubated with normal bovine serum for 5 minutes to reduce non-specific antibody binding. The sections for CK (dilution, 1:200), EMA (dilution, 1:100), VM (dilution, 1:200), and FVIII (dilution, 1:12,000) immunostaining were incubated for 20 minutes at room temperature. The second antibody was biotinylated mouse IgG, and the sections were incubated with it for 10 minutes at room temperature. Peroxidase activity was developed using 3,3'-diaminobenzidine tetrahydrochloride (Sigma, Deisenhofen, Germany) containing 0.3% H2O2 for 20 minutes. Each step was followed by a wash with phosphate-buffer saline and then light staining with Mayer's hematoxylin. In negative controls, the primary antibody was replaced with non-immune serum. The immunohistochemical expression of CK, EMA, VM, and FVIII was evaluated by light microscopy.

CK and VM were moderately positive in the cytoplasm and nuclei of tumor cells. There was no immunoreactivity for EMA and FVIII in the tumor cells. The negative controls for each antibody were not stained (Figs. 4–6).

Discussion

Lever\(^1\) first described adenoid squamous cell carcinoma in 1947. Since then, some authors have reported in head and neck skin\(^2\)–\(^4\) and have discussed the histogenesis of this tumor\(^5\)–\(^11\). There is considerable evidence that the tumor originates from the pilosebaceous structures, although it probably also arises in area of senile keratosis with acantholysis. Throughout the body, it often occurs in and under the skin\(^2\)–\(^4\). In the oral cavity, it has been reported to occur in the lip, tongue, buccal mucosa, and other tissues\(^1\)–\(^15\).

Adenoid squamous cell carcinoma of the oral cavity often occurs in the sixth decade of life\(^1\)–\(^15\). This tumor has also been reported to occur more frequently in males, with a ratio of about 5:1\(^11\)–\(^13\). The majority of cases are reported as ulcerated or keratotic, whereas other lesions are described as nodular, exophitic, or indurated\(^11\)–\(^15\). The clinical appearance resembles squamous cell carcinoma or basal cell carcinoma.

The diagnostic criteria\(^2\) of adenoid squamous cell carcinoma are as follows: 1) basic cell of the keratinizing squamous cell type, 2) adenoid structure consisting of a rounded space with a definite wall, principally one cell thick, and 3) lumen containing single or grouped dyskeratotic acantholytic cells. Our case met these strict criteria.

The histogenesis of adenoid squamous cell carcinoma is still controversial. Although it is suggested that adenoid squamous cell carcinoma in the sun-exposed areas of the skin originates from pilosebaceous structures\(^5\), the histogenesis of the tumors arising in an exposed location without the pilosebaceous apparatus, such as oral mucosa, remains controversial\(^12\). One interpretation is that the tumor occurs as a consequence of squamous metaplasia of neoplastic glandular cells; in another interpretation, this tumor is considered a variant of squamous cell carcinoma with an origin in nonglandular structures, in which the tubular and alveolar spaces represent pseudoglandular spaces arising from acantholysis.
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Fig. 1 Clinical finding of the tumors lesion in right posterior tongue before surgery.

Fig. 2 Histological finding: Sagittal section of the specimen indicating existence of the tumor (Arrow, HE staining, original magnification $\times 10$).

Fig. 3 Histological finding: Neoplastic squamous epithelium demonstrating transition to characteristic adenoid or ductal structures containing acantholytic epithelial cells (Arrow, HE staining, original magnification $\times 20$).

Fig. 4 Immunohistochemical finding: Cytokeratin staining moderately positive in the cytoplasm of adenoid squamous cell carcinoma (Arrow, CK staining, original magnification $\times 20$).

Fig. 5 Immunohistochemical finding: The tumor cells positive for Vimentin (Arrow, VM staining, original magnification $\times 50$).

Fig. 6 Immunohistochemical finding: The tumor cells stained negatively for epithelial membrane antigen (EMA staining, original magnification $\times 16$).
of squamous cell carcinoma\(^\text{11)}\). Yanagawa et al. (1986)\(^\text{9)}\) stated that the squamous components present in adenoid squamous cell carcinoma arising from the oral mucosa were closely associated with squamous metaplasia of the neoplastic ductal cells arising in the minor salivary gland present in the oral mucosa and that the cells composing the adenoid structure represent the remnants of glandular cells.

Immunohistochemical findings of these tumors have shown strong reactivity for epithelial markers, such as cytokeratin or epithelial membrane antigen\(^\text{10)}\). In our case, mucin stain (alcian blue) failed to demonstrate epithelial mucin in the cytoplasm of the cuboidal cells and intraluminal substance. Therefore, we presume that there was no evidence of glandular differentiation or secretory activity or products. Moreover, the immunohistochemical stain showed positive reactions with antibodies to cytokeratin. These histopathological and immunohistochemical findings suggested that oral adenoid squamous cell carcinoma in our case was derived from acantholysis and degeneration of squamous cell carcinoma.

**Conclusion**

We examined the histogenesis of oral adenoid squamous cell carcinoma based on the histopathological and immunohistochemical findings of a case. We believe that this adenoid squamous cell carcinoma arose as acantholysis and degeneration of a squamous cell carcinoma.

**Reference**


口腔領域に発現した腺様扁平上皮癌の1例:
病理組織学的ならびに免疫組織化学的検討

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66歳、男性の右側舌に発現した腺様扁平上皮癌について、病理組織学的ならびに免疫組織化学的研究な検討を行った。病理組織学的には、細胞間橋、角化や扁平上皮の増殖を示さない立方形の腫瘍細胞が腺管様構造を呈していた。また、アルシアンブルー(AB)染色、ムチカルミン(MC)染色、PAS染色にそれぞれ陰性であった。さらに、免疫組織化学的には、腫瘍細胞はサイトケラチン(CK)、ビメンチン(VM)に陽性であったが、上皮膜抗原(EMA)や第VIII(FVIII)には陰性であった。以上のことから、本腫瘍は扁平上皮癌細胞の変性と棘融解によって生じたものと推定された。

キーワード:
腺様扁平上皮癌/舌/発生起源/免疫組織化学的研究