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CASE REPORT

Sialadenoma Papilliferum in a Female Mongrel Dog

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A B S T R A C T

A 14-year-old female Mongrel dog presented with multiple, cherry-sized, well-circumscribed papillary masses on the right upper hard palate and gingival area. Histologically, the masses contained biphasic components composed of hyperplastic squamous epithelium forming papillary fronds, and underlying tortuous dilated ducts and cysts. Immunohistochemistry demonstrated that both squamous and ducts epithelium were pan-Cytokeratin (pCK) positive, but they were negative of Alpha smooth muscle (α-SMA), Vimentin and Protein 53 (P53). Duct epithelial cells were strong positive of Cytokeratin 8&18 (CK8&18), Ki-67, and weakly positive of S-100, whereas squamous component were strong positive of Cytokeratin 5&6 (CK5&6). Sialadenoma papilliferum (SP) was diagnosed based on clinical sign, gross and histopathological findings, and biochemistry.

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INTRODUCTION

Sialadenoma papilliferum (SP) is a rare, distinctive benign tumor of salivary gland origin in humans (Kubota *et al*., 2012). There are about 50 cases of SP in literature since it was first described in 1969 (Brunnert and Altman, 1990). The average age of occurrence is 59.2 years with a male predilection (Anuradha *et al*., 2012). Clinically SP is presented as a well-circumscribed non-encapsulated, exophytic papillary mass commonly on the oral palate. The histological characteristics are well differentiated papillary hyperplastic squamous epithelium covering ductal component, which forms dilated to cystic spaces lined by cuboidal or columnar epithelium (Ubaidat *et al*., 2001). To the best of authors' knowledge, this is the first documented case of Sialadenoma papilliferum in veterinary medicine.

History: A 14-year-old female Mongrel dog was presented with masses in the mouth. Few months ago, the masses were just small ones, but it became bigger and bigger so that would influence the dog ingestion, and it was going to Beijing Barbie Pet Hospital for diagnosing. The masses were removed through operation.

Clinical examination: The dog was presented with multiple, 1-2 cm in diameter, well-circumscribed, fresh pink nodular masses on the right upper palate, gingival and surrounding the canine and premolar teeth (Fig. 1A). Diffusely, the oral mucosa was red with swollen and hemorrhagic gingival. The masses were surgically removed, fixed in 4% neutral-buffered paraformaldehyde, and submitted to the Department of Veterinary Pathology of the Huazhong Agriculture University for pathological evaluation.

Histologically, protruding from the palate mucosa and extending into the submucosa was a well-demarcated, pedunculated, un-encapsulated neoplasm composed of biphasic components of exophytic stratifies squamous cells and underlying, endophytic glandular to ductal neoplastic cells. The exophytic papillary projections were covered by thick layers of hyperplastic to dysplastic squamous cells with fibrovascular cores. The squamous cells of exophytic papillary were mildly to moderately dysplastic characterized by loss of cell polarity, pleomorphism, and megakaryocytosis. The deeper papillary projections merged with dilated ducts and cysts that were lined by 1 to 3 layers of cuboidal to columnar cells. The neoplastic epithelial cells had indistinctive borders and variable amount eosinophilic cytoplasm. The nuclei had coarse to vesicular chromatin and 1-2 nucleoli. The mitotic figures were rare. There was small amount of fibrovascular stroma with small number of lymphocytes, plasma cells and macrophages (Fig. 1B).

Immunohistochemical staining was performed on 4-μm thick, formalin-fixed and paraffin-embedded tissue sections using a standard streptavidin-biotin method and

diaminobenzidine as chromogen detection with hematoxylin counterstain. The specific antibodies and their concentrations were summarized in (table 1). The second antibodies were anti-mouse immunoglobulins and anti-rabbit immunoglobulins (Boster, China). Both neoplastic squamous and duct epithelial cells were pCK strong positive. The neoplastic squamous epithelial cells were CK8&18 negative, but CK5&6 positive (Fig. 1C). However, the columnar and cubic epithelial cells were CK8&18 (Fig. 1D), Ki-67 and S-100 positive, but CK5&6 negative. Vimentin and α-SMA were detected in the fibrovascular cores and myoepithelial cells. But P53 kept negative in all cells. All positive signals were in the cytoplasm except Ki-67 which was in the nucleus.

DISCUSSION

Sialadenoma papilliferum, a rare tumor of human salivary gland, usually occurs in males older than 50 years as a painless papillary growth at the junction of hard and soft palate. Histopathologically, it is composed of two distinct components: a superficial squamous epithelium making up the exophytic papillomatous part and underlying ductal to cystic component lined by cuboidal to columnar epithelium. Fibrovascular stroma contains many lymphocytes and plasma cells (Mahajan *et al*., 2007). The current case showed the similar features to human SP.

In human medicine, immunohistochemical examination with many specific antibodies has been used in the diagnosis of SP. Myoepithelial cells and fibrovascular cores were strongly labeled by anti-human α-SMA and anti-porcine vimentin, luminal columnar cells were labeled by pCK (AE1/3), CK8&18, and both were stained by S-100. Squamous papillae demonstrated homogenous positivity for AE1/3 and CK5&6 (Anuradha *et al*., 2012, Kubota *et al*., 2012). In this study, basal cells and myoepithelial cells were proved by α-SMA, Vimentin; luminal columnar cells were labeled by pCK, CK8&18, S-100 and squamous papillae were labeled by pCK, CK5&6. On the other hand, Ki-67 is helpful to better predict the risk of recurrence and the sign of positive indicated a higher proliferation index (Pereira *et al*., 2013). P53 showed positive was meaning the tumor cells responsible for malignant progressions (Tarakji *et al*., 2010). In this study, the P53 was negative but Ki-67 was positive which were meaning the tumor have the possible for malignant progressions. And ductal papilloma was divided into sialadenoma papilliferum, inverted ductal papilloma and intraductal papilloma. But in intraductal papilloma, the proliferation was occurred in duct epithelium that arises from a segment of the interlobular or excretory duct and causes unicystic dilatation, and in inverted ductal papilloma, the proliferating epithelium was predominantly epidermoid (Ramaswamy *et al*., 2013).

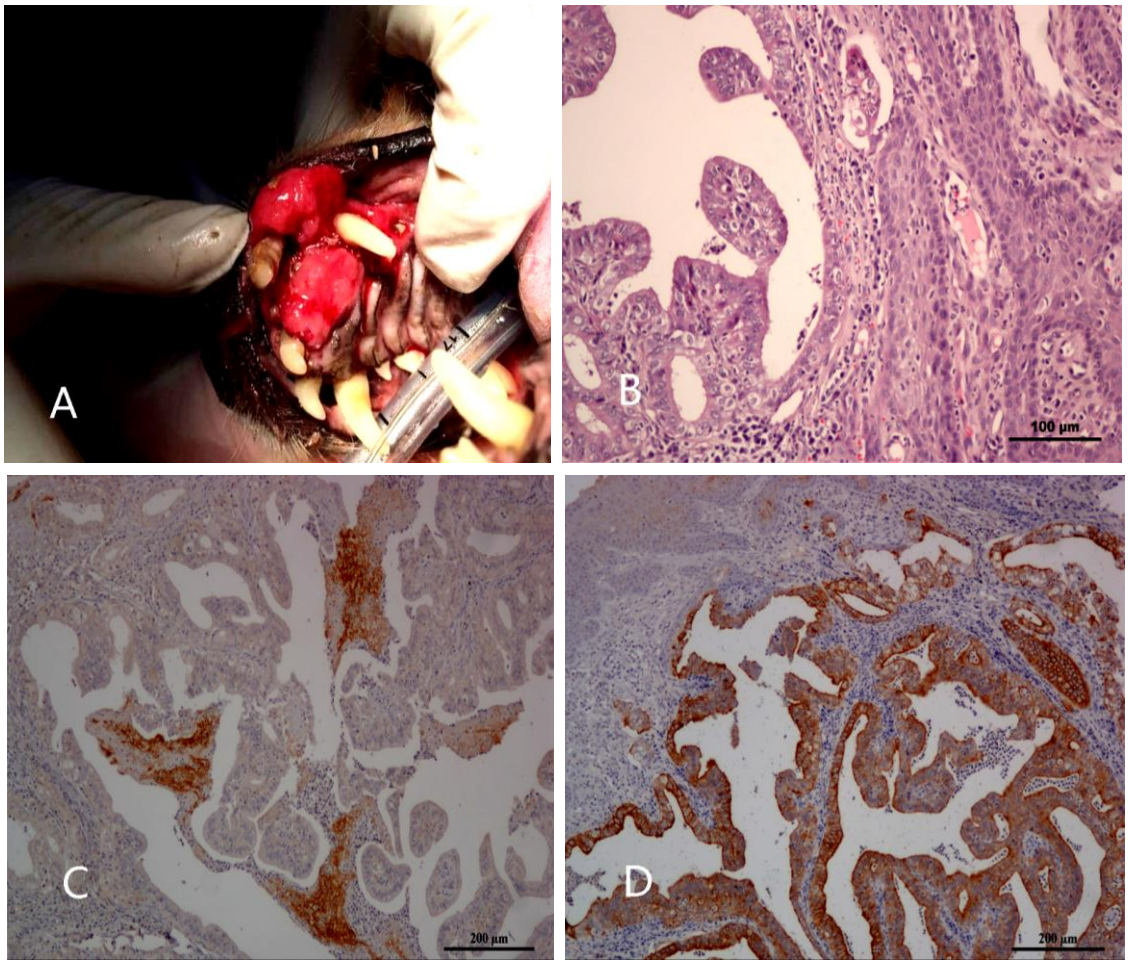

Fig. 1: A) The tumor is cherry size, flesh pink. Papillary projection existed on the right upper gingiva surrounding the teeth. **B)** The neoplastic epithelial cells formed dilated ducts and cysts. Some neoplastic cells formed papillary projections. HE, 200×. **C)** The squamous epithelium cells express positive by CK5&16. IHC, 100×. **D)** The cubic or columnar epithelial cells were present positive by stained with CK8&18. IHC, 100×.

Table 1: Details of immunohistochemical primary antibodies and result

Primary antibody	Type of antibody	Supplier	Result
pCK	mAb	Boster,China	++
CK5&6	mAb	Zhongshan, China	++
CK8&18	mAb	Zhongshan, China	++
S-100	pAb	Boster,China	+
α-SMA	mAb	Boster,China	++
Vimentin	mAb	Boster,China	++
P53	mAb	Boster,China	-
Ki-67	pAb	Boster,China	++

mAb: Monmclonal mouse antibody; pAb: Polyclonal rabbit antibody; ++: Strong positive; +: Weak positive; -: Negative. The primary antibodies were diluted in 1:100.

In canine, salivary tumors are not common, the most frequently are mucoepidermoid tumors, squamous cell carcinoma, mixed tumors, adenoid-cystic carcinoma, acinic cell tumor and adenocarcinomas (Baba and Câtoi, 2007). Mucoepidermoid tumors are characterized by epidermoid and mucusproducing features. The ductular origin was obvious and cystic dilatation of the ducts with retention of a mucoid, faintly fibrillar material. And only squamous cells were proliferated in squamous cell carcinoma (Baba and Câtoi, 2007). In mixed tumors, tumor tissue revealed simultaneous proliferation of both the epithelial and mesenchymal components (Kim *et al*., 2008). Acinic cell tumor has a characterized by a more or less pronounced acinar architecture (Brunnert and Altman, 1990). Adenocarcinomas are included ductular and trabecular adenocarcinomas. The neoplasm was obvious, the ductules being lined by low cuboidal epithelium with occasionally marked papillary projections (Baba and Câtoi, 2007).

Conclusions: The tumor with squamous epithelial and duct epithelial were proliferated in papillary. And through immunohistochemical, both squamous epithelial and duct epithelium were proved as a part of the neoplasm. According the feature of the tumor, it was diagnosed as SP.

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Authors' contribution: In this article, ZQF, JY and XYH conceived and designed the study. BL and LQX executed the experiment and analyzed the tissue samples. XLL, CQG, WPZ and GFC analyzed the slides. All authors interpreted the study, critically revised the manuscript for important intellectual contents and approved the final version.

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