Case Report

CANALICULAR ADENOMA ARISING IN THE UPPER LIP: REVIEW OF THE PATHOLOGICAL FINDINGS

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Abstract

This case report describes a rare case of canalicular adenoma arising in the upper lip of a 61-year-old male patient. Macroscopic examination of the tumor revealed a well-defined, smooth, firm, elastic hard, round nodule with a diameter of 1.0 cm. The cut surface was white. Histopathology showed that the tumor was an encapsulated mass with a complex cellular pattern of anastomosing duct-like or trabecular structures lined by a single layer of tall columnar epithelial cells, which were embedded in a loose, fibrous, and highly vascular connective tissue stroma. The tumor cells were immunoreactive to AE1/AE3, CK19 and S-100, were partially positive for CK7, CK8, GFAP and PCNA, but were negative for SMA, CK13, CK14 and vimentin.

Key words: Canalicular adenoma—Salivary gland tumor—Upper lip—
Immunohistochemistry

INTRODUCTION

Canalicular adenomas are uncommon benign salivary gland neoplasms, which derive from the minor salivary glands. They occur in the upper lip mucosa in about 90% of cases, and the majority arise in patients over 50 years of age^{4,6,8,9,12,14)}. The histological features of canalicular adenomas are similar to, but can be distinguished from, the trabecular type of basal cell adenoma, polymorphous low-grade adenocarcinoma, or other tumors^{1,2,4,5,7)}. This paper reports a rare case

of a canalicular adenoma with immunohistochemical observations and a review of the literature.

CASE REPORT

A 61-year-old male patient noticed a painless swelling on the left side of his upper lip in 2003 and was admitted to the Dental Clinic on September 14, 2004. A macroscopic examination revealed a well-defined, smooth, firm, round nodule with a diameter of 1.0 cm. The

lesion was removed under the clinical diagnosis of a mucous cyst and sent to the clinical laboratory of the Tokyo Dental College for pathological diagnosis. The tumor was elastic hard, and the cut surface was white. The patient had no history of trauma in that region.

HISTOPATHOLOGICAL FINDINGS

After the specimen was fixed with 10% formalin, paraffin sections were prepared for light microscopy and were stained with hematoxylin and eosin using routine methods. The labeled streptavidin-biotin immunoperoxidase staining method was used with primary antibodies to AE1/AE3 (1:50, monoclonal antibody, Dako, CA), CK7 (1:20, monoclonal antibody, Progen, Heidelberg), CK8 (1:25, monoclonal antibody, Dako, CA), CK13 (1:10, monoclonal antibody, Progen, Heidelberg), CK14 (1:10, monoclonal antibody, Progen, Heidelberg), CK19 (1:10, monoclonal antibody, Progen, Heidelberg), vimentin (1:20, monoclonal antibody, Dako, CA), SMA (1:50, monoclonal antibody, Oncogene Research Products, CA), S-100 (1:200, monoclonal antibody, Dako, CA), GFAP (1:100, monoclonal antibody, Dako, CA) and proliferating cell nuclear antigen (PCNA, PC-10, 1:100, monoclonal antibody, Dako, CA). After diaminobenzidine was used as the chromogen, sections were then counterstained with hematoxylin.

Examination of hematoxylin-eosin staining revealed a well encapsulated tumor mass composed of columnar and cuboidal, uniform glandular epithelial elements arranged in anastomosing monolayered duct-like, luminal, or trabecular structures in a "beading" pattern. The stroma consisted of loose fibrovascular tissue with partially thin-walled, dilated blood vessels. All of these features were diagnostic for canaliculal adenoma of minor salivary gland origin (Fig. 1a to c). Furthermore, the tumor cells were immunoreactive to AE1/AE3, CK19 and S-100, and partially positive for CK7, CK8, GFAP and PCNA (Fig. 1d to h). However, they were negative for SMA, CK13, CK14 and vimentin.

DISCUSSION

Canaliculal adenomas are rare neoplasms of the salivary gland. WHO reports that these tumors are localized to the upper lip in 90% of cases, and, in almost all cases, they occur in patients over 50 years of age. An extremely rare case of a multiple canaliculal adenoma was reported by Queiroz *et al.*¹⁰⁾, a canaliculal adenoma arising from the palate was reported by Smullin¹³⁾, one arising from the buccal mucosa was reported by Yamada *et al.*¹⁴⁾, and one arising from the parotid gland was reported by Rossiello *et al.*¹¹⁾; our case is typical of canaliculal adenomas, but still remains a rare case. In our laboratory of Tokyo Dental College, the present case is the only one among 18,093 cases of all lesions from 1996 to 2004.

It is necessary to differentiate the diagnosis of canaliculal adenoma from that of basal cell adenoma, polymorphous low-grade adenocarcinoma, adenoid cystic carcinoma or papillary cystadenocarcinoma. Dardick³⁾ states in his book: "Tubulo-trabecular variants of basal cell adenoma can be a consideration at low power magnification, but closer inspection shows the presence of both basal and luminal cells and a more collagenized stroma compared to canaliculal adenoma." When canaliculal adenomas are resected in a fragmented fashion or are cystic, they are occasionally misdiagnosed as polymorphous low-grade adenocarcinomas. Three main features separate this neoplasm from canaliculal adenoma; infiltration of salivary and adjacent tissues, frequent peri-neural invasion, and heterogeneous histologic growth patterns. The two cell types that differentiate in tumor cell nests of adenoid cystic carcinoma, the intercellular "pseudo-cystic" spaces, the invasive growth pattern, the peri-neural invasion, and the lack of a highly vascularized stroma all serve to distinguish this tumor from canaliculal adenoma. Canaliculal adenomas with a single, rather large cystic space or multiple, smaller cysts, and resulting zones with papillary projections may be confused with papillary cystadenocarcinoma. In addition to

Fig. 1 Histological observations

a,b,c: H-E staining (original magnification a; $\times 2.55$, b; $\times 50$, c; $\times 100$)

d to h: immunohistochemical staining (original magnification $\times 50$) d; AE1/AE3, e; CK19, f; SMA, g; S-100, h; GFAP

the encapsulation, some regions of cystic canalicular adenoma will display typical, rather parallel rows each composed of a layer of columnar cells and mucoid, vascularized stroma. Papillary cystadenocarcinomas are infiltrative, and the epithelium is more uniformly arranged along the surfaces of complex branching or interconnecting fibrovascular cores.

Histological observations have revealed that canalicular adenomas have characteristic rows of columnar epithelial cells in a loose fibrovascular connective tissue stroma¹³⁻¹⁵⁾, and our case also showed that feature. Immunohistochemical staining is of great assistance in the differential diagnosis. In this case, tumor cells were immunoreactive to AE1/AE3, CK19 and S-100 and partially positive for CK7, CK8 and GFAP. However, CK13, CK14 and vimentin were negative. Machado de Sousa *et al.* reported that CK7 and CK13 were positive, and canalicular adenoma cells were partially reactive to CK8, CK14 and CK19⁸⁾. Furthermore, Furuse *et al.* reported that vimentin is an indicator for the differential diagnosis between canalicular adenoma and polymorphous low-grade adenocarcinoma. The tumor cells in our case were not immunoreactive for vimentin⁵⁾. Zabro *et al.* showed that the immunophenotype of canalicular adenomas are intensely stained with an antibody to S-100¹⁶⁾. The S-100 and GFAP positive staining implies that these tumor cells originate from myoepithelial cells, but SMA negativity means the tumor cells originate from the other cells. Furthermore, it has been reported that smooth muscle differentiation identifies the myoepithelial cells¹⁶⁾. Ferreiro⁴⁾ reported that all of 6 cases of canalicular adenoma were immunoreactive for AE1/AE3 and S-100 and that GFAP was reactive in only one case. Zarbo *et al.* reported that the spectrum of salivary gland adenomas with participating cell types, canalicular adenoma and myoepithelioma, is represented by exclusive luminal cell and myoepithelial cell differentiation, respectively¹⁶⁾. The relative participation of the morphologically diverse myoepithelial cells (epithelioid, clear, spindled,

plasmacytoid) and their products (basement membrane, chondroitin sulfate, proteoglycans) appears to blend these adenoma entities¹⁵⁾. Furthermore, myoepithelial cells have been identified by immunohistochemistry with the sensitive markers for smooth muscle differentiation. This case of canalicular adenoma, as well as tumor in the report by Zabro *et al.*¹⁶⁾, did not immunoreact with SMA.

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