

Papillary oncocytic cystadenoma of a palatal minor salivary gland: A case report

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Abstract. Papillary cystadenomas of the salivary gland are uncommon, benign, encapsulated or well-circumscribed, multicystic tumors with intracystic papillations. In a large review, papillary cystadenoma constituted 2% of all minor salivary gland tumors. The present study reports an extremely rare case of a papillary cystadenoma arising from the palate that demonstrated oncocytic features. A 60-year-old man was referred by his dentist to the Second Department of Oral and Maxillofacial Surgery at Osaka Dental University Hospital for the diagnostic evaluation of a mass of the left palate. An incisional biopsy was performed and the microscopic findings were interpreted as consistent with a papillary oncocytic cystadenoma. Therefore, the lesion was excised under general anesthesia. The post-operative course was uneventful and no recurrence had developed 5 years subsequent to surgery.

Introduction

Cystadenoma of the salivary gland is an uncommon benign neoplasm that is further subdivided into papillary and mucinous types (1,2). Cystadenoma accounts for 4.2-4.7% of all benign tumors, and 2% of all minor tumors of the salivary gland, worldwide (3-5). This tumor closely resembles Warthin tumors, but does not demonstrate the lymphoid elements; Warthin tumors are strongly associated smoking and commonly present as asymptomatic slow-growing round masses. They are typically composed of glandular and cystic structures, occasionally with a papillary cystic arrangement. Typically, the tumors are lined by an epithelial bilayer comprised of inner columnar eosinophilic or oncocytic cells surrounded by smaller basal cells and the stroma contains a variable amount of lymphoid tissue with germinal centres (6). The most frequent clinical finding of salivary gland cystadenoma is a painless mass beneath the

mucosa of the palate, lips or buccal mucosa. Oncocytic change can be observed focally or extensively. The majority of cystadenoma cases are treated by simple excision, and recurrence is extremely rare (3). The present study reports an extremely rare case of a papillary cystadenoma arising from the palate, with oncocytic features. Written informed consent was obtained from the patient.

Case report

A 60-year-old man was referred by his dentist to the Second Department of Oral and Maxillofacial Surgery at Osaka Dental University Hospital (Osaka, Osaka, Japan) for the diagnosis of a mass of the left palate in August 2008. This mass had been identified by the dentist approximately one month prior to the diagnosis, and the patient had not identified the tumor previously. Physical examination revealed a mass that was 10 mm in diameter, well-circumscribed, elastic, soft, round and located on the left hard palate (Fig. 1). The surface of the mass was smooth and a normal color. The hematological and biochemical examinations were within the normal limits; white blood cell count, $49.1 \times 10^2/\mu\text{l}$ (normal range, $35.0-80.0 \times 10^2/\mu\text{l}$); red blood cell count, $445 \times 10^4/\mu\text{l}$ (normal range, $380-480 \times 10^4/\mu\text{l}$); hemoglobin level, 13.7 g/dl (normal range, 11.3-15.2 g/dl); hematocrit, 39.1% (normal range, 34.0-43.0%); platelet count, $14.0 \times 10^4/\mu\text{l}$ (normal range, $15.0-35.0 \times 10^4/\mu\text{l}$); aspartate aminotransferase level, 18 U/l (normal range, 7-38 U/l); alanine aminotransferase level, 15 U/l (normal range, 4-44 U/l); alkaline phosphatase level, 178 U/l (normal range, 106-220 U/l); lactate dehydrogenase level, 197 U/l (normal range, 106-345 U/l); C-reactive protein level, 0.05 mg/dl (normal range, 0.00-0.30 mg/dl). Although the platelet count was marginally lower than normal, the level was not significant enough to have an impact on symptoms. Based on the findings of the physical examination, the benign salivary gland tumor was pre-operatively diagnosed, and an incisional biopsy was performed in September 2008. The microscopic findings (magnification, $\times 20$) were interpreted as consistent with a papillary oncocytic cystadenoma. Therefore, the lesion was excised under general anesthesia in November 2008. Subsequent to the procedure, the healing was uneventful. The excised mass was a solid soft-tissue mass 10x9 mm in size, which was white-yellow in color on the cut surface (Fig. 2). Microscopic examination (BX50; Olympus Corporation, Tokyo, Japan) of hematoxylin-stained

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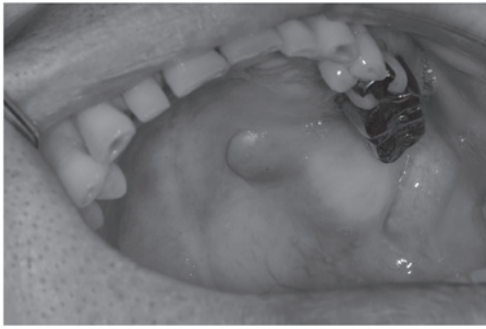


Figure 1. Image of the initial presentation, showing a semifirm painless mass in the palate.

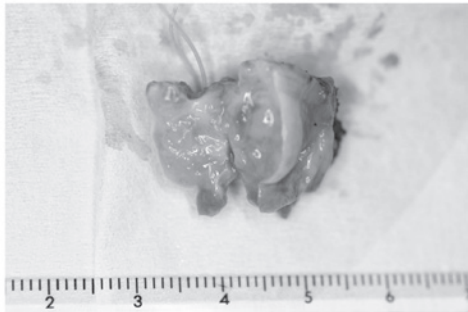


Figure 2. Macroscopic aspect of the cutting surface of the surgical specimen.

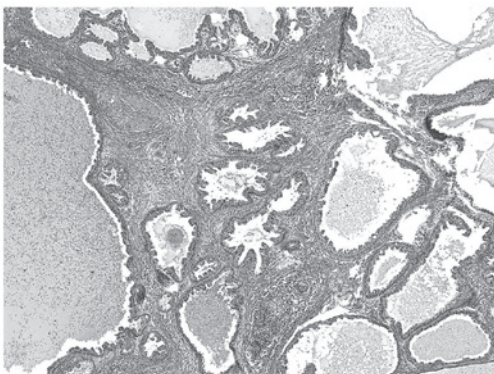


Figure 3. Photomicrograph showing a submucosal adenomatous cystic nodule with papillary intraluminal projections (hematoxylin-eosin stain; original magnification, x4).

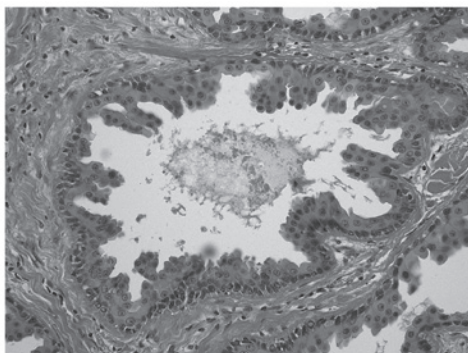


Figure 4. Cystic papillary projections and the major cyst cavity were lined by bilayer oncocytic columnar epithelium (hematoxylin-eosin stain; original magnification, x20).

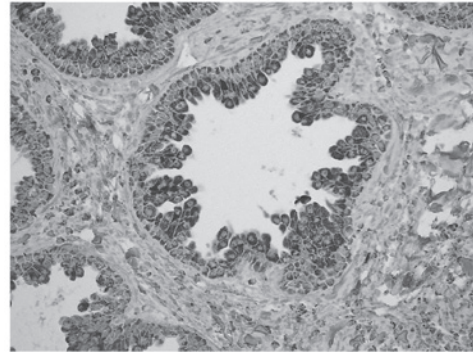


Figure 5. Positive staining for mitochondria was observed in the oncocytic columnar epithelium (anti-mitochondria antibody stain; original magnification, x20).

tissue sections and certain papillary intraluminal projections revealed a submucosal adenomatous cystic nodule (Fig. 3). The latter findings were supported, as the core of the thin fibrous connective tissue lacked lymphocytic components. Cystic papillary projections and the major cyst cavity were lined by bilayer oncocytic columnar epithelium (Fig. 4). Mitotic figures and cytological atypia were not observed. Mitochondria (EMD Millipore, Temecula, CA, USA) were found to be present in the oncocytic columnar epithelium using immunohistochemistry (monoclonal mouse anti-human mitochondria antibody; cat. no. MAB1273; 1:100; EMD Millipore) (Fig. 5). Therefore, the histopathological diagnosis of papillary oncocytic cystadenoma was made. The post-operative course was uneventful, and there has been no evidence of recurrence at 5 years subsequent to the procedure.

Discussion

Cystadenoma of the salivary gland was first subclassified into various types of monomorphic adenoma in the first edition of the World Health Organization Histological Classification of Salivary Gland Tumors (1). In the second edition, which was published in 1991, cystadenomas were more clearly defined as a specific histopathological entity that was further subdivided into papillary and mucinous types (2). However, in the third classification published in 2005, cystadenomas were only subdivided into papillary and mucinous types (6).

The frequency of papillary cystadenoma is extremely low. Toida *et al* (7) reported 1 case of papillary cystadenoma among 82 cases of intraoral minor salivary gland tumors. Chaudhry *et al* (8) reported only 3 cases of the tumor (7.0%) out of 43 cases of intraoral benign minor salivary gland tumors. In addition, out of the 800 benign intraoral minor salivary gland tumors reported in the English language literature between 1927 and 1960, 16 cases of papillary cystadenoma (2.0%) have been reported (3). Due to the rarity of papillary cystadenoma, the cytological features of the lesion have not been well described in textbooks and other publications. The cytological findings of a reported case of papillary cystadenoma from a minor salivary gland revealed cohesive groups of epithelial cells demonstrating a complex folded appearance in a cystic proteinaceous background, and the possibility of salivary gland tumors was raised in the fine

needle aspiration diagnosis (9). Nasuti *et al* (10) reported that the aspiration material was insufficient in the papillary oncocytic cystadenoma.

Microscopically, it has been revealed that the tumors are generally well circumscribed and surrounded by fibrous capsules. Although the extent of solid regions is usually limited, there are cystic regions into which papillae lined by two layers of cuboidal to columnar cells usually project (11). In the majority of cases, the multilocular individual cystic space is separated by a limited amount of interstitial intervention. Lumens, in numerous cases, contain eosinophilic material with scattered epithelial, inflammatory or foamy cells. Oncocytic, mucus, epidermoid and apocrine cells are occasionally present locally, or may be predominant. Oncocytic variants of cystadenomas predominantly consist of oncocytes in a unilayered or two-layer papillary structure, similar to the epithelium of Warthin tumors, but without lymph stroma.

Therefore, papillary cystadenoma closely resembles Warthin tumors, but the present case was distinguished from Warthin tumors by the almost complete lack of lymphoid follicles. Sections of the lesion revealed multiple small cystic spaces or a single large cyst surrounded by lobules of salivary gland or connective tissue. Although the focal variation in epithelial differentiation is typical, a single cystadenoma, a single cell type, is characteristically dominant. Auclair *et al* (12) identified the oncocytic differentiation in 16% of the cases of papillary cystadenomas assessed.

During differential diagnosis, it may be challenging to distinguish between papillary cystadenoma and cystadenocarcinoma, as the tumors demonstrate similar structures (13). The two tumors usually demonstrate papillary proliferation of the epithelial layer, which is composed of cells which possess 'bland-looking' nuclei (5).

Commonly, cystadenoma is treated by simple excision, and recurrence is not observed (4). However, Skorpil (14) and Collins (15) have each reported cases that experienced recurrence.

However, a lack of evidence of locally devastating behavior, the relative quiescence of the tumors, which results in the tumors often being found incidentally, histological evidence of a well-circumscribed tumor lacking mitoses and atypia, and the notable failure of any of these tumors to metastasize all prevent the suggestion of malignant potential. Therefore,

it is likely that recurrences are attributable to incomplete resection or possibly due to a misdiagnosis of a low-grade cystadenocarcinoma (11). For these reasons, the present patient is followed-up at regular intervals, and a similar management plan is recommended for all patients that are diagnosed with papillary cystadenoma.

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