

# Papillary Cystadenoma of Salivary Glands: Report of Two Rare Cases and Review of Literature

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## ABSTRACT

**Introduction:** Papillary cystadenoma is a rare benign salivary gland neoplasm characterized by the presence of multiple cystic spaces with intraluminal papillary projections. It is often a slow-growing painless mass which is treated conservatively by complete excision. The prognosis is good with minimal recurrence rate.

**Case reports:** We present two cases reported within a span of 7 days. A 42-year-old male patient presented with a firm swelling on the right lateral border of tongue and a 9-year-old boy presented with a firm, nodular swelling of 2 cm diameter in the left posterior auricular region. Investigative procedures, including biopsy and histological examination, revealed both cases to be papillary cystadenoma.

**Conclusion:** Though papillary cystadenoma has good prognosis with minimal recurrence rate, its histological picture resembles that of many other lesions. The occurrence of two cases of papillary cystadenoma within a week alerts an oral pathologist to be aware of its histopathology.

**Keywords:** Benign lesion, Papillary cystadenoma, Salivary gland.

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## INTRODUCTION

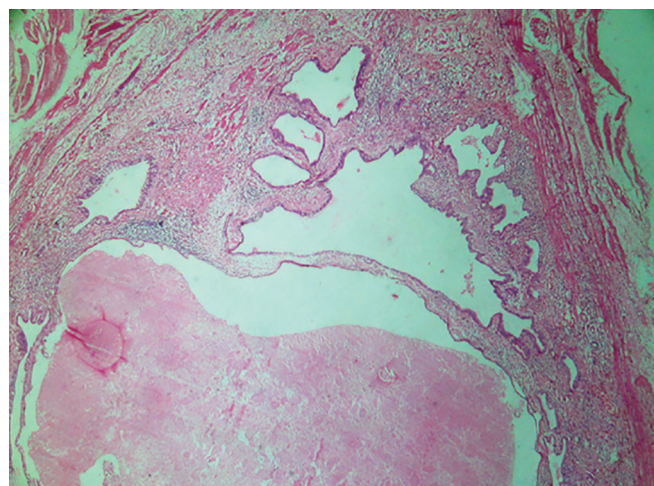
Cystadenomas of the salivary glands are rare benign neoplasms in which the epithelium demonstrates adenomatous proliferation i.e., characterized by the formation of multiple cystic structures.<sup>1</sup> The two major variants of cystadenoma are papillary and mucinous. The epithelial lining is frequently papillary and rarely mucinous. Majority of cases of cystadenomas of the salivary glands occur in the minor salivary glands with 45% occurrence

rate in the parotid glands.<sup>2</sup> Cystadenomas contribute to 0.6 to 4% of the minor salivary gland neoplasms.<sup>3</sup> The various synonyms for cystadenoma include monomorphic adenoma, cystic duct adenoma, Warthin tumor without lymphoid stroma, intraductal papillary hyperplasia, and oncocytic cystadenoma. Cystadenomas of the major glands present as asymptomatic masses, but in the oral cavity they may resemble mucocoeles.<sup>4</sup> Due to its well-circumscribed nature and indolent behavior, the recurrence rate of papillary cystadenoma is low and the prognosis is good.<sup>3</sup> Two cases of papillary cystadenoma of salivary glands that reported to the Department of Oral Pathology and Microbiology, Govt. Dental College, Kottayam, within a span of 7 days are presented here with a brief review of literature.

## CASE REPORTS

### Case 1

A 42-year-old male patient presented with a 1 × 1 cm sized nontender, firm swelling on the right lateral border of tongue in relation to lower right first molar tooth since 3 months. There was no increase in size of the lesion, associated pain, or difficulty in chewing. Cytological examination was suggestive of a cystic lesion. Microscopy revealed apparently normal looking salivary gland parenchyma with cyst-like spaces in the densely collagenous connective tissue stroma (Fig. 1). The cystic spaces were

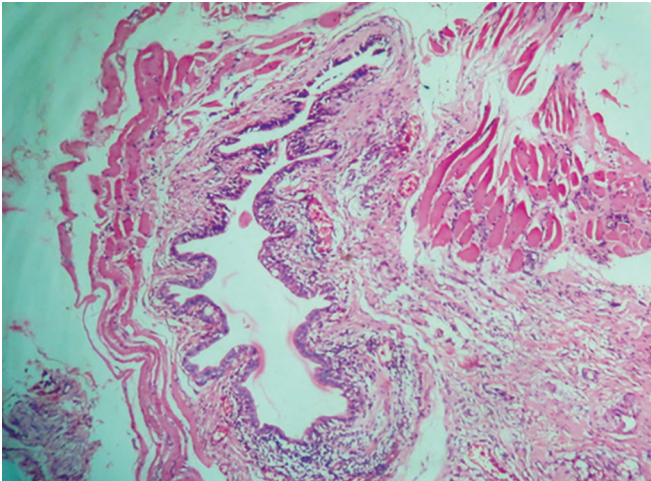


**Fig. 1:** Photomicrograph showing scanner view of multiple cystic spaces of papillary cystadenoma, also note the peripheral compression (H&E 40×)

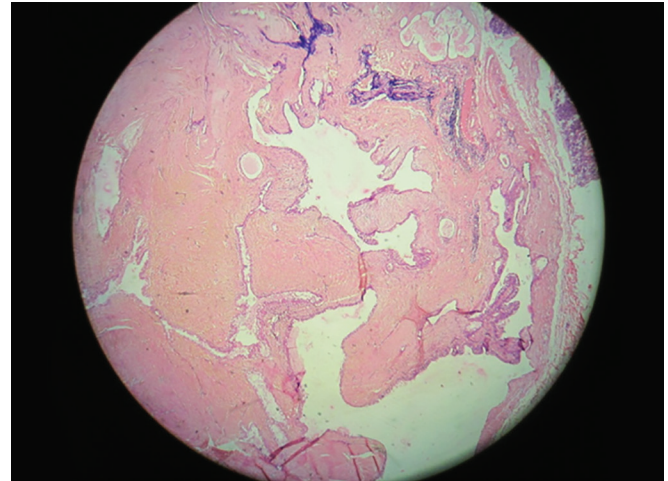
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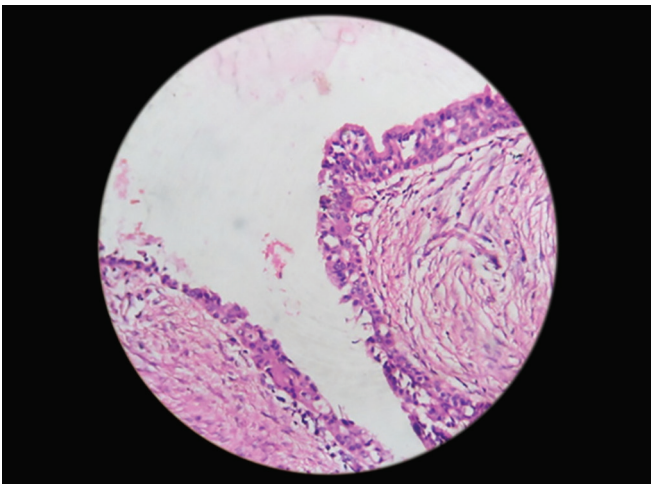
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**Fig. 2:** Photomicrograph showing low power view of papillary cystadenoma with intraluminal papillary projections (H&E 100×)



**Fig. 3:** Photomicrograph of papillary cystadenoma showing multiple cystic spaces (H&E 40×)



**Fig. 4:** Photomicrograph of papillary cystadenoma exhibiting bilayered epithelial lining (H&E 400×)

of varying sizes and lined by pseudostratified columnar epithelium projecting intraluminally in a papillary fashion. In some areas the cyst-like spaces were lined by cuboidal and columnar bilayered epithelium. No cellular atypia was noted. The periphery of the lesion showed partial condensation (Fig. 2). Most of the cyst-like spaces contained amorphous eosinophilic coagulum. The lesion was diagnosed as papillary cystadenoma.

## Case 2

Within a span of 7 days, a 9-year-old boy presented with a nontender, firm, nodular swelling of 2 cm diameter in the left posterior auricular region of 1 month duration. The overlying skin was of normal color and texture. Lesion was not fixed to the underlying tissues and was nonpulsatile. Ultrasonography was suggestive of a solid lesion measuring 5.5 × 3.9 cm in the superficial lobe of left parotid gland. Cytologic examination was suggestive of nonneoplastic cystic lesion of salivary gland. Gross specimen

after superficial parotidectomy was a single pyramidal-shaped soft tissue mass of approximate size 5 × 3.2 × 2 cm. The longitudinally cut section showed cheesy white area at the center. Histopathology revealed many large and small cystic spaces scattered in an apparently normal looking serous salivary gland tissue (Fig. 3). The cystic spaces were lined by predominantly pseudostratified and columnar epithelium. Many areas showed bilayered epithelial lining (Fig. 4). The epithelial lining showed many papillary infoldings into the cystic spaces. The cystic spaces contained homogenous eosinophilic coagulum. A diagnosis of papillary cystadenoma was given.

## DISCUSSION

Although cystadenomas are rare in the salivary glands, they are very common in other sites like ovary, biliary tract, and pancreas. These are the most common neoplasms occurring in the ovaries. Papillary cystadenomas were initially classified as monomorphic adenomas in the first edition of World Health Organization's (WHO) classification of salivary gland neoplasms.<sup>5</sup> But in its second edition, the cystadenoma was considered as a distinct benign neoplasm and was further classified into papillary and mucinous subtypes.<sup>2</sup>

About 4.2 to 4.7% of all the benign neoplasms and 2% of all minor salivary gland tumors worldwide are cystadenomas.<sup>5</sup> In a study conducted by Fabio et al of 546 minor salivary gland tumors, 7.7% were papillary cystadenomas.<sup>6</sup> In another study, out of 713 salivary gland tumors, papillary cystadenoma accounted for 4.2% of the total benign or malignant neoplasms.<sup>7</sup> The most common location for salivary gland cystadenomas are the minor salivary glands.<sup>8</sup> About 45% of cases occur in the parotid.<sup>1</sup> While some authors have reported equal gender predilection<sup>9</sup> for papillary cystadenoma,



the WHO classification of head and neck tumors has found that there is a female predominance for the lesion.<sup>2,10,11</sup> Some other authors have reported a slight male predilection with male to female ratio being 1.23:1. The mean age of incidence is 57 years with a range of 12 to 89 years.<sup>2</sup> The most common site of the lesion is the lips followed by buccal mucosa and palate.<sup>1-3,8</sup>

Cystadenomas of the major salivary glands are usually painless, slow-growing swellings, whereas those of the minor salivary glands are often compressible and may appear as mucocoeles.<sup>4</sup> Initially this lesion was considered as a type of ductal hyperplasia<sup>12</sup> and later after a careful study of the histopathological features, it was classified as a benign neoplasm. Papillary cystadenoma can be identified by the multiple cystic spaces that it forms with intraluminal papillary projections. The lining of the cystic spaces varies from flattened to tall columnar, including cuboidal, mucous, and oncocytic cells.<sup>1-3,8</sup> They are frequently well-circumscribed and may have a thick, encapsulating band of fibrous connective tissue.<sup>3</sup> However, cystic structures are often haphazardly arranged over a background of fibrous connective tissue or salivary gland parenchyma with evidence of encapsulation absent. Most cases are multilocular with individual cystic spaces separated by limited amounts of intervening stroma. The lining epithelium of these cystic structures is mostly columnar and cuboidal. Oncocytic, mucous, epidermoid, and apocrine cells are sometimes present focally or may even predominate.<sup>8,14,18</sup> Goldman<sup>13</sup> has reported a case of papillary cystadenoma where the neoplastic oncocytes showed distinct melanogenesis. Cystadenomas have usually single type of cells, but infrequently can show some variation from site to site.<sup>3</sup> The cells show no cytological atypia.<sup>2,3</sup> The lumen often contains eosinophilic material with scattered inflammatory, epithelial, or foamy cells.

Considering the complexity and histomorphological diversity of salivary gland tumors, the differential diagnosis of papillary cystadenoma would include intraductal papilloma, cystadenocarcinoma, low-grade mucoepidermoid carcinoma (especially the oncocytic type), Warthin tumor, oncocytoma, and cheilitis glandularis.<sup>2,3,14-17</sup>

Intraductal papilloma is a tumor entirely confined within a circumscribed or encapsulated unicystic cavity in contrast to papillary cystadenoma which is multicystic. The papillary projections of intraductal papilloma partially or completely fills the lumen, whereas the papillary projections of papillary cystadenoma usually occupies the lumen to a limited degree.<sup>2</sup>

It is difficult to distinguish papillary cystadenoma from cystadenocarcinoma since both the lesions show papillary proliferation of the epithelial lining into the cystic spaces and the cells show bland cytomorphological

features. Cystadenocarcinoma should be distinguished by the identification of actual infiltration of salivary gland parenchyma or surrounding connective tissue by either cystic or solid epithelium.<sup>14</sup> Review of multiple sections would be helpful.

Low-grade mucoepidermoid carcinoma presents along with the multiple cystic spaces, noncystic epithelial proliferations which consists of epidermoid, mucous, and intermediate cells.<sup>4,17</sup> This being the most characteristic feature of mucoepidermoid carcinoma is the important distinguishing feature between both neoplasms. The features should be diligently scrutinized since mucoepidermoid carcinoma is an infiltrating neoplasm with the growth pattern and involved cell population similar to papillary cystadenoma.<sup>17</sup> Fonseca et al<sup>17</sup> have conducted a study on the expression of p63 on papillary cystadenoma and mucoepidermoid carcinoma. They found the labeling pattern to be restricted only at the basal layer of the cystic spaces of papillary cystadenoma, indicating that the proliferating cells are the luminal cells and the cystic spaces keep the architecture of normal ducts. In mucoepidermoid carcinoma, the labeling pattern was found in all the layers of the epithelium lining the cystic spaces, although not uniformly. Thus the expression of p63 would be a distinguishing feature to identify papillary cystadenoma from mucoepidermoid carcinoma.

Warthin tumor (papillary cystadenoma lymphomatosum) can pose a similar picture to papillary cystadenoma but the predominance of a lymphoid component seen in the former is absent in the latter.<sup>1,2,16,18</sup> Thus the diagnosis of Warthin's tumor should be unmistakable.

Cheilitis glandularis (clinical diagnosis) is an inflammatory disorder and has no consistent diagnostic features at the microscopic level. It may present with various changes in the surface epithelium and submucosal tissue. These changes can be erosion, ulceration, surface hyperkeratosis, hyperemia, atrophy or distention of acini, ductal ectasia, chronic inflammatory infiltration and replacement of glandular parenchyma, and interstitial fibrosis.

Immunohistochemically, the positive staining of papillary cystadenoma for pan cytokeratin and S100 suggests its epithelial origin and rules out other tumors of lymphoid, vascular, and endothelial origin. It stains negative for smooth muscle actin (SMA) and rules out the possibility of myoepithelial carcinoma.<sup>17,18</sup>

Papillary cystadenoma is a benign tumor and it is usually treated conservatively by complete surgical excision.<sup>2,10,18</sup> It is highly unlikely to recur, although cases with recurrences have been reported. Prognosis is good with no malignant transformation of papillary cystadenoma reported although there is a reported case of malignant transformation of mucinous cystadenoma.<sup>18</sup>

## CONCLUSION

Though rare, the occurrence of two cases of papillary cystadenoma within a short span of one week alerts an oral pathologist to be aware of its histopathology. The real test the entity poses is in differentiating the lesion from those with a similar histologic picture.

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