

Keratinizing pleomorphic adenoma: An unusual case report

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Abstract

Pleomorphic adenoma (PA) is the most common benign tumor of major or minor salivary glands. PA exhibits a great histological diversity, such as differentiation into oncocytic, sebaceous, mucinous, squamous, chondroid, osseous or adipose cells. Squamous metaplasia rarely results in the formation of extensive keratin-filled cyst lined by squamous epithelium. Extensive squamous metaplasia can be mistaken for malignancy, including mucoepidermoid carcinoma and squamous cell carcinoma. Here, we report a case of slowly enlarging PA with extensive squamous metaplasia and keratin cyst formations in a minor salivary gland in hard palate and discuss its microscopic features.

Keywords: Keratin, pleomorphic adenoma, squamous metaplasia

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INTRODUCTION

Pleomorphic adenoma (PA) or benign mixed tumor is the most common benign tumor of major or minor salivary glands.^[1] It accounts for 54%–65% of all salivary gland neoplasias and 80% of the benign salivary gland tumors.^[2] PA arises most commonly in parotid gland; about 80% are reported in parotid, 10% in submandibular gland and 10% in the minor salivary glands of the oral cavity, nasal cavity and paranasal sinuses and the upper respiratory and alimentary tracts. Among the minor salivary glands, hard palate is the most common site accounting for approximately 50%–60%, followed by upper lip (15%–20%) and buccal mucosa (8%–10%). The affected patients are between 30 and 50 years of age. There is a slight female predilection.^[3] Histological diversity is the hallmark of PA.^[4] It shows varying combinations of epithelial and myoepithelial cells in a mesenchymal or stromal background.^[5] Extensive squamous metaplasia

with keratin-filled cysts is rarely reported in PA. Here, we present an unusual case of PA with exuberant squamous metaplasia and keratin cysts formations in a minor salivary gland.

CASE REPORT

A 28 year old male patient presented with a chief complaint of a small growth on the palate that had been slowly enlarging over the previous 7–8 years with no pain. Clinical examination showed 1 cm × 1 cm sized, firm swelling with normal overlying mucosa [Figure 1]. The swelling was nontender, nonfluctuant, sessile in appearance with well-defined margins. The patient had no significant medical history. On general and systemic examinations, the patient was apparently healthy. There was no regional lymphadenopathy. The adjacent teeth 25, 26 were carious. Radiological findings revealed localized osteolytic lesion on the left palate. Based on the clinical findings, a provisional

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diagnosis of palatal fibroma was made with a differential diagnosis of PA and lipoma.

Excisional biopsy was performed under local anesthesia, under aseptic condition and the specimen was sent for histopathological examination. Gross specimen comprised of an encapsulated soft tissue mass, measuring 1.5 cm × 1.5 cm × 1 cm, round, gray-white, and firm. Cut surface was firm and gray-white with no areas of hemorrhage, necrosis or cystic change [Figure 2].

Histopathological features

Under low magnification, hematoxylin and eosin-stained sections revealed, a well-circumscribed lesion composed of superficial and deep-seated keratin-filled multicystic spaces of variable size and shape [Figure 3]. On higher magnification, the epithelium enclosing the fibrous mass was parakeratinized stratified squamous epithelium. Within the stroma, a large number of cystic spaces, gland-like tubular structures, tumor islands and mucous cells could be seen

[Figures 4 and 5]. Cystic spaces were of variable size and shape and were dispersed throughout the stroma. Cystic spaces were lined by squamous cells. Most of the cystic spaces contained keratotic lamellae, some contained eosinophilic material and some were empty [Figure 4]. The tumor islands were composed of basaloid cells. The tumor cells, dispersed throughout the stroma, were pleomorphic with shapes being basaloid, plasmacytoid, angular or elongated [Figure 6]. Periodic acid-Schiff staining revealed the presence of mucin in some cystic areas [Figure 7]. The connective tissue stroma was composed of dense collagen fibers, fibroblasts, endothelial-lined blood vessels with extravasated red blood cells and inflammatory infiltrate mainly comprising of lymphocytes. A histopathological diagnosis of PA, with extensive squamous metaplasia was made.

DISCUSSION AND LITERATURE REVIEW

PA is characterized by great histologic diversity. The presence of squamoid or frankly squamous epithelia is



Figure 1: Intraoral swelling on the palate having intact margins

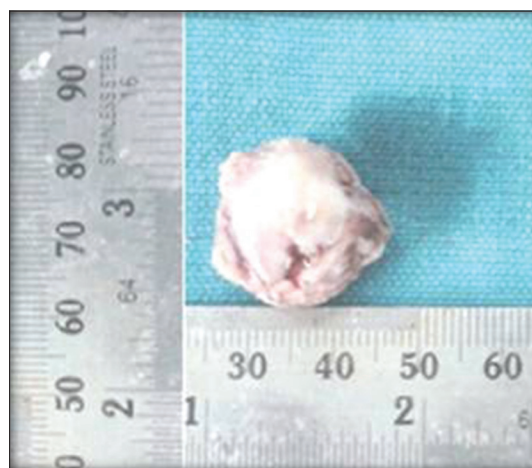


Figure 2: Gross specimen measuring 1.5 cm × 1.5 cm × 1 cm

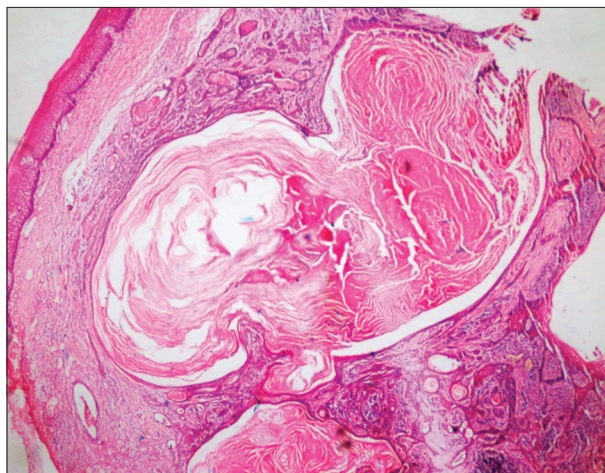


Figure 3: Histopathological image showing a well-circumscribed lesion composed of multiple cystic spaces (H&E, ×40)

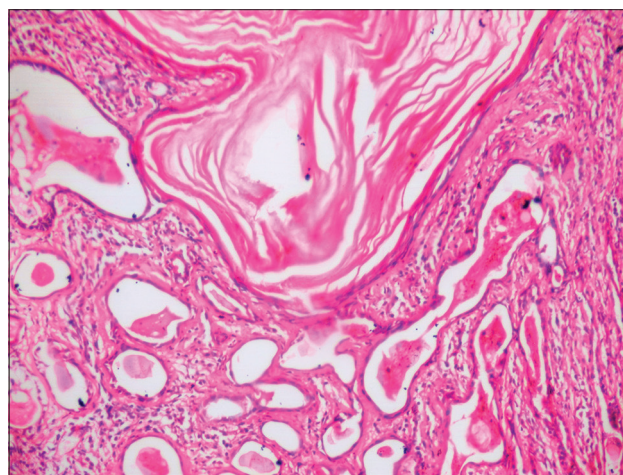


Figure 4: Histopathological image showing tumor stroma showing large number of cystic spaces having keratotic lamellae and lined by squamous cells (H&E, ×200)

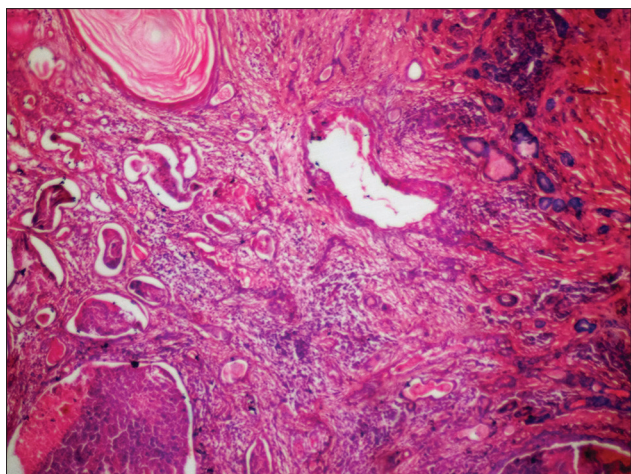


Figure 5: Histopathological image showing tumor stroma having numerous gland-like tubular structures (H&E, x100)

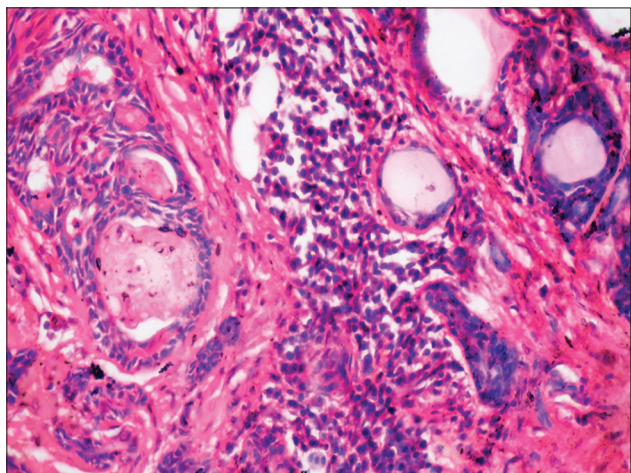


Figure 6: Histopathological image showing tumor stroma showing tumor cells composed of basaloid, plasmacytoid and angular cells (H&E, x400)

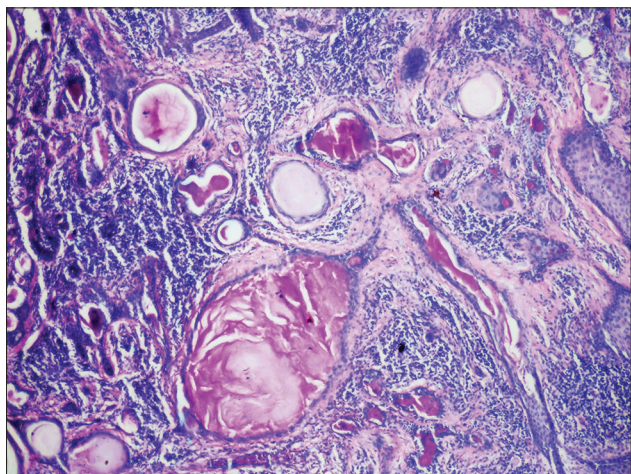


Figure 7: Histopathological image showing presence of mucous cells containing mucin (Periodic acid-Schiff stain, x200)

a common feature of a number of reactive or neoplastic conditions of the salivary glands, such as chronic sialadenitis,

radiation change of salivary glands and necrotizing sialometaplasia, mucoepidermoid carcinoma (MEC), PA, basal cell adenoma and Warthin's tumor. Focal squamous metaplasia in PA can be related to ischemia, repair following infarction, and necrosis of the salivary gland and may be found in about 25% of the PA.^[6] However, PA with extensive squamous metaplasia is rarely reported and can signify a potential pitfall in the histopathological diagnosis.^[7] PA with extensive keratin-filled cysts lined by squamous epithelium is referred to in the literature as "cystic PA with extensive adnexa-like differentiation," since the histologic features mimic cutaneous appendages.^[8]

In the present case, the tumor does not have a capsule. Intraoral PA, especially those within the palate, lack a well-defined capsule.^[9] There was extensive squamous metaplasia by which many glandular cells were transformed into squamous cells, resulting in multiple squamous epithelium-lined cysts containing keratotic lamellae in the deep as well as in the superficial regions. These types of histological features may lead to a misdiagnosis of a benign lesion, such as keratocystoma or malignant lesions, such as squamous cell carcinoma, MEC.^[10] While considering squamous cell carcinoma, there are possibilities of a collision tumor consisting of squamous cell carcinoma arising in the overlying squamous epithelia of PA and squamous cell carcinoma ex PA.^[6]

Keratocystoma or choristoma, is a benign salivary gland tumor resembling a trichoadenoma.^[10] It exhibits solid squamous cell islands, keratinized masses outside the cysts with multinucleated giant cells and focal calcification. It lacks myxochondromatous, myoepithelial or glandular components.^[7]

MEC should have infiltrative borders with the cystic spaces of MEC lined by mucous cells and prominent keratinization is rare.^[5,11] Keratinization, if present in MEC, is found exclusively in the high-grade group, which is characterized by predominantly solid growth, significant nuclear pleomorphism and paucity of mucinous cells.^[12] In fact, among salivary gland tumors, keratinization is much more commonly seen in benign tumors. However, even if the features diagnostic of PA are identified, the differential diagnosis may still include a MEC arising in a preexisting PA. However, MEC ex PA is exceedingly rare and is usually a high grade malignancy.^[13,14]

Different immunohistochemical studies reported that the squamous epithelium lining the keratin cyst formations shows homogeneous positivity for high-molecular-weight (HMW) cytokeratin (CK), while

some cells express low-molecular-weight (LMW) CK (CK7 and CK19) and p63. Luminal cells may also show positive immunostaining for epithelial membrane antigen, S-100 and carcinoembryonic antigen. The pattern of CK expression suggests that the cells expressing Hmw CK have undergone squamous metaplasia, but those expressing Lmw CK and p63 have not yet undergone squamous metaplasia. These morphologically similar squamoid cells are metaplastic squamous cells and ductal epithelial cells showing squamoid features depending on the immunohistochemical and morphologic profiles, respectively.^{16,71} Positive immunostaining for myoepithelial cell markers such as Hmw CKs, p63, S-100, vimentin, and occasionally for smooth muscle actin, muscle-specific actin and glial fibrillary acidic protein (GFAP) was reported in abluminal cells. Immunopositivity, either focal for CK7, CK19, vimentin, GFAP and S-100 or frequent for Hmw CKs was also reported for cells in solid sheets, nests and cords presented.¹⁷¹

Benign nature of this tumor was identified by intact overlying squamous epithelium without atypia, absence of metastasis and tumor necrosis, and minimal cellular proliferative activity and significantly slow growth of the tumor.

Wide local excision is the treatment of choice in these lesions. Although PA has a low proliferative rate, interestingly, the epithelial lining of the large keratin-filled cyst shows a higher proliferative index than the other areas. It may signify that the squamous metaplasia resulting in the large keratin-filled cyst in PA may be clinically significant, probably related to an important growth potential.¹⁷¹ In the present case, the patient was kept on follow-up for 6 months, and there was no signs of recurrence.

CONCLUSION

The diverse histomorphologic presentation of a PA can cause diagnostic confusion. PA in minor salivary gland is rare in occurrence and to prevent misdiagnosis, a careful approach in diagnosis is of utmost importance for a proper treatment and management.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and

other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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