A benign salivary gland tumor of minor salivary gland mimicking an epithelial malignancy

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Abstract

Pleomorphic adenoma (PA) is the most common benign tumor of major or minor salivary glands. Microscopically, PA exhibits a great diversity of morphological aspects. Here, we present an unusual case of PA with extensive squamous metaplasia and keratin-filled cysts in the left retromolar region of a 50-year-old edentulous person whose microscopic finding may represent a diagnostic dilemma for pathologists.

Keywords: Keratin-filled cysts, pleomorphic adenoma, squamous metaplasia

Introduction

Pleomorphic adenoma (PA), the most common salivary gland tumor, accounts for 54-65% of all salivary gland neoplasias and 80% of the benign salivary gland tumors.[1] The incidence of it in intraoral minor salivary glands is 40-50%.[2] PA usually appears as a solitary slowly growing, painless rubbery mass.[3] Histological diversities are the hallmark of PA as its name implies. It is characterized by a wide spectrum of morphological patterns, including squamous cells, mucous cells, oncocytes, sebaceous cells, bone, adipose tissue, and crystalline materials.[4] Focal squamous metaplasia is found in about 25% of PA.[5] Rarely extensive squamous metaplasia with cystic changes are reported. Here, we present an unusual case of PA with extensive squamous metaplasia and keratin-filled cysts formation in a minor salivary gland, with special attention given to the potential sources of diagnostic pitfalls.

Case Report

A 50-year-old man presented with a mass in the right retromolar region that had been slowly enlarging over the previous 2 years with no pain. History was unremarkable. Physical examination revealed a firm mass measuring 1 cm × 1 cm [Figure 1]. A provisional diagnosis of benign tumor of salivary gland or mucocele was made. Complete mass excision was done. Grossly tumor was well-encapsulated, grayish-white, and measured 2 cm × 1 cm × 1.5 cm. The cut surface showed no cystic area, hemorrhage or necrosis [Figure 2]. The specimen was submitted for routine microscopic examination. Histological features showed an encapsulated tumor mass with approximately 70% of the tumor volume composed of superficial and deep-seated keratin-filled multicystic spaces of variable size and shape, lined by metaplastic squamous epithelium. The epithelial component of the tumor showed solid sheets, nests of ductal structures. No dysplastic features or mitotic figures were evident within the squamous cells. Occasional foci of residual chondromyxoid matrix were seen [Figures 3-5]. These microscopic features were suggestive of PA with extensive squamous metaplasia.

Discussion

Tumors originating in the minor salivary glands are infrequent and represent <20% of all salivary neoplasms. The most common benign histological type is PA, in coincidence with different studies that report a variable incidence of between 40% and 72% of all salivary gland tumors.[3] PA is characterized by great histologic diversity; however, PA presenting extensive squamous metaplasia is uncommon and can signify a potential pitfall in the histopathological diagnosis. 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.[5] Rarely extensive squamous metaplasia with cystic changes are reported.

In the present case, many glandular cells were transformed into squamous cells through a process of squamous metaplasia, resulting in multiple squamous epithelium-lined

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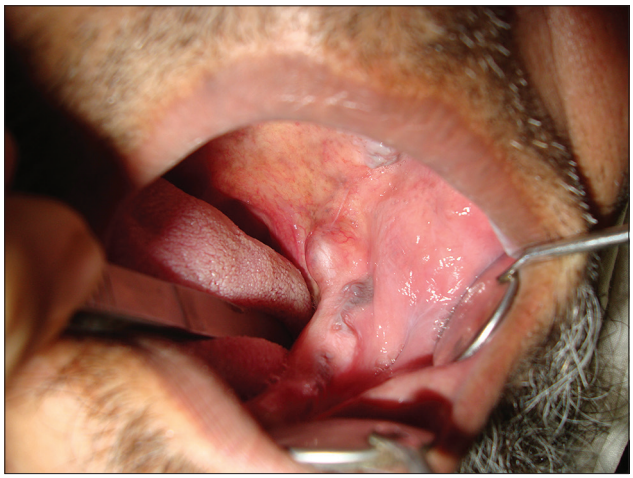

Figure 1: Intraoral photograph showing well-circumscribed nodular mass in the left retromolar trigone measuring 2 cm × 2 cm in diameter

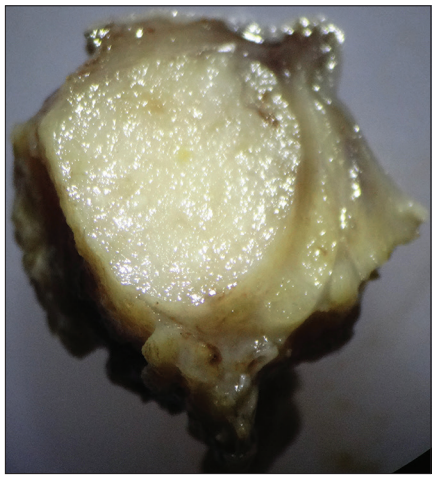

Figure 2: Cut surface of well-encapsulated grayish-white tumor mass with no evidence of cystic areas, hemorrhage or necrosis

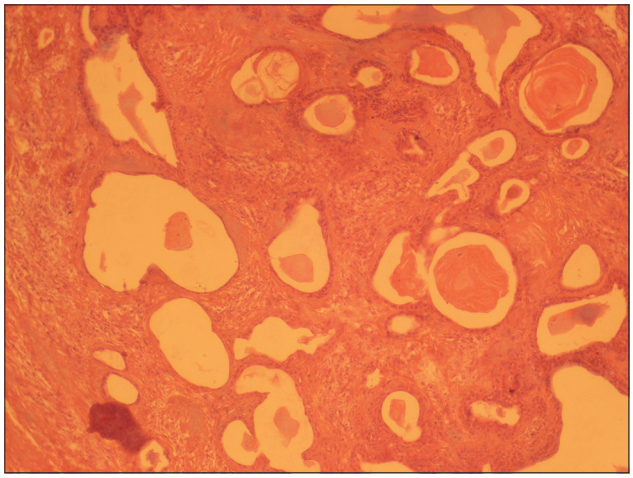

Figure 3: Benign mixed tumor composed of both epithelial and myoepithelial cells in a myxoid mesenchymal background (×4)

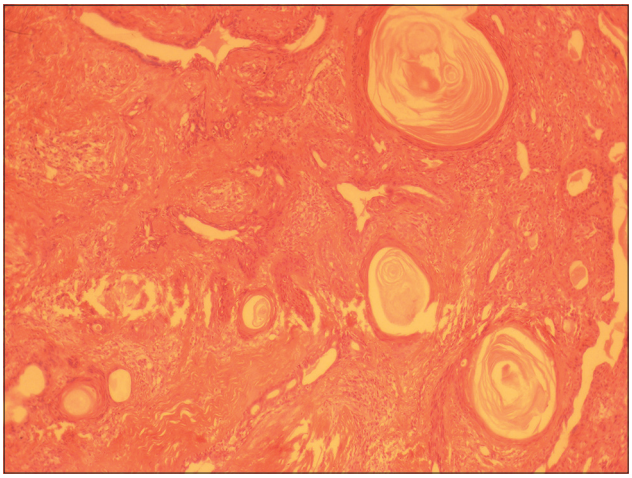

Figure 4: Multiple keratin cysts of variable size lined by stratified squamous epithelium (×10)

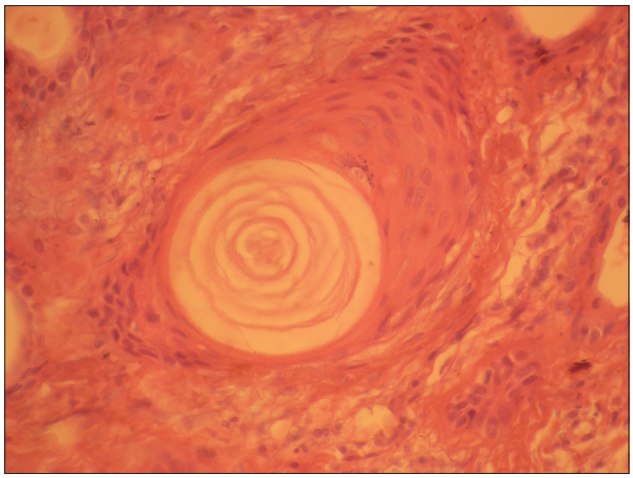

Figure 5: Keratin-filled multicystic spaces are lined by metaplastic squamous cells (×40)

cysts containing keratotic lamellae and some solid squamous cell islands presenting keratin pearls. Extensive squamous metaplasia with cystic changes in PA, especially in the absence of chondromyxoid stroma, can mistakenly lead to a diagnosis of benignity, such as choristoma or keratocystoma, and malignancy including mucoepidermoid carcinoma and squamous cell carcinoma on microscopy due to limited and selective samplings.

Keratocystoma, previously known as choristoma, is a benign salivary gland tumor resembling a trichoadenoma. It also exhibits solid squamous cell islands surrounded by the basement membrane within the collagenous stroma.[6] Goulart *et al*. believe that the PA and keratocystoma may constitute related lesions, representing different stages in the evolution of a specific type of salivary gland tumor.[7,8] However, keratocystoma lacks myxochondromatous, myoepithelial or glandular components that are demonstrated in our case.

Regarding the differential diagnosis with squamous cell carcinoma, the absence of cytological atypia, metastasis, necrosis, invasion as well as minimal cellular proliferative activity and the presence of a fibrous capsule in the case presented here weigh against the diagnosis of malignancy.[9,10] Compagno and Wong reported that microscopically PA of the nasal cavity resembles mixed tumor of the major salivary glands but due to high epithelial cellularity and little stromal component, this benign tumor can be mistaken for malignant epithelial neoplasm.[11]

Microscopically, mucoepidermoid carcinoma (MEC) presents mucous, intermediate and squamoid (epidermoid cells) and is usually multicystic. Unlike our case, the cystic spaces of MEC are usually lined by mucous cells and prominent keratinization is rare, with scarce epidermoid cells associated with keratin production including keratin pearl formation.[12,13] There are reported cases regarding limitations of cytological procedure in the diagnosis of such salivary gland neoplasms. This is because of lack of the architectural features and the tumor-stroma interface, which are both of critical importance in the diagnosis of this salivary gland neoplasm.[6,7] There has been recent interest in the application of antibodies to cytokeratin 7 and cytokeratin 20 for determining the site of origin of epithelial tumors. Draeger *et al*. have reported the expression of cytokeratin 7 in the tubules and acini of the epithelial component of PAs. Strong expression of cytokeratin 7 and focal cytokeratin 20 expression in the squamous islands of the tumor.[4,14]

Wide local excision is the treatment of choice in these lesions. Higher proliferative index was noticed in the epithelial lining of such keratin-filled cysts compared to the conventional PA. It may signify that the squamous metaplasia resulting in the large keratin-filled cyst in PA may be clinically significant, probably relate to an important growth potential.[6]

Conclusion

To prevent the misdiagnosis of PA with exuberant squamous metaplasia as a malignancy, cautious and systematic approach in the histopathologic interpretation of the epithelial and connective tissue component is needed. It is important to be aware of this possibility to distinguish it from malignant lesions and to avoid unnecessarily aggressive therapy.

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