Case Report

# Extensive Squamous Metaplasia in Minor Salivary Gland Neoplasm Mimicking Squamous Cell Carcinoma: Diagnostic dilemma in Aspiration Cytology


## Abstract

The surgical management of salivary gland lesions depends on cytology diagnosis, in conjunction with clinical findings and imaging studies. It is extremely important to differentiate benign and malignant salivary gland lesions preoperatively. The distinction can be challenging in aspiration cytology due to metaplastic changes, cystic changes, variable cellular components within the lesions, variants of neoplasms, and sampling issues. We are presenting the case of a 42-year-old female patient who presented with a nodular lesion in the hard palate. Fine-needle aspiration cytology of the lesion was cellular and showed sheets and singly scattered squamous cells with minimal cytological atypia. As the differential diagnosis included variety of lesions ranging from nonneoplastic lesions to benign and malignant neoplasms, surgery under frozen section control was advised. Frozen sections also showed extensive squamous areas. A minor component showing bilayered ductal pattern in a background of chondromyxoid stroma also noted. Diagnosis of a salivary gland neoplasm, possibly pleomorphic adenoma with extensive squamous metaplasia was given. Although squamous metaplasia has been reported in salivary gland neoplasms, it is extremely rare to find extensive squamous metaplasia enough to cause significant diagnostic confusion. The awareness of this extensive squamous metaplasia in benign salivary gland lesions help to distinguish it from malignant lesions and to avoid unnecessarily aggressive therapy.


**Keywords:** *Fine-needle aspiration cytology, minor salivary gland neoplasm, squamous metaplasia*


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## Introduction

Fine-needle aspiration cytology (FNAC) is a simple and cost-effective procedure and provides valuable information regarding various neoplastic and nonneoplastic lesions of salivary gland with a high degree of accuracy. Occasionally, overlaps can occur between benign and malignant conditions due to heterogeneity of the cell types, metaplastic changes, and sampling issues.[1,2] Multiple passes representing the entire mass, imaging findings, and familiarity with cytopathology of salivary gland lesions may decrease the incidence of misdiagnosis and improve accuracy.[2]

## Case Report

A 42-year-old female patient presented with swelling in the hard palate of 3-year duration. Examination revealed a 1.2 cm × 1 cm firm to hard swelling on left side of hard palate. There were no palpable lymph nodes. Computerized tomography scan showed submucosal soft-tissue lesion hard palate abutting the bone, without bony erosion.

FNAC of the lesion was cellular and showed sheets and singly scattered squamous cells. There was no overt cytological atypia, increase in mitosis, or atypical mitosis [Figure 1]. The long history, submucosal localization, scan findings pointed toward nonneoplastic lesions, or benign neoplasms. However, because of the presence of high cellularity and mild atypia, the possibility of a well-differentiated squamous cell carcinoma could not be totally excluded. Hence, surgery under frozen section control was advised.

Frozen sections revealed a well-delineated neoplasm with extensive squamous areas. The squamous cells were arranged in nests admixed with keratin filled cysts lined by squamous epithelium. Mitotic figures were sparse, and there was no evidence of cellular atypia, necrosis, capsular invasion, or aggressive growth pattern.



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Focal area showed classical bilayered ductal pattern with luminal cuboidal cells and variably shaped, abluminal, and myoepithelial cells in a background of chondromyxoid stroma [Figure 2].

Diagnosis of a salivary gland neoplasm, possibly pleomorphic adenoma with extensive squamous metaplasia was given.

## Discussion

Cytodiagnosis of salivary gland neoplasms can be challenging due to diverse range of diseases that affect the salivary glands and may lead to problems and pitfalls in diagnosis. Nonneoplastic and neoplastic conditions of the salivary gland can exhibit squamoid or frank squamous epithelial differentiation. Common nonneoplastic conditions associated with squamous metaplasia include chronic sialadenitis, radiation-induced change of salivary glands, and necrotizing sialometaplasia. Benign salivary gland neoplasms such as pleomorphic adenoma, basal cell adenoma, and Warthin's tumor can exhibit squamous cell metaplasia. Extensive squamous metaplasia can lead to false-positive diagnosis including mucoepidermoid carcinoma (MEC) and squamous cell carcinoma.[1-3]

Metaplasia is a change, in which one terminally differentiated cell type is replaced by another cell type. Metaplasia is considered an adaptive change occurring in response to repeated epithelial damage. If the cause is removed, metaplasia may be reversible. As squamous epithelium is more resistant to damage than other forms of epithelia, squamous metaplasia is a common form of metaplasia. Squamous metaplasia of salivary duct epithelium can occur in response to viral infections, obstruction of ducts by calculi, chemicals, ionizing radiation, and Vitamin A deficiency. The metaplasia may be a preneoplastic lesion progressing to carcinoma.[1,4]

In their experiment, Dardick *et al.* induced squamous metaplasia in rat salivary glands by arterial ligation. Squamous metaplasia was formed through the gradual dedifferentiation and hyperplasia of the acinar-intercalated duct system.[4,5] They observed formation of tonofilaments and desmosomes in the luminal and abluminal myoepithelial cells. Studies have shown that the varying degree of squamous metaplasia could be a consequence of the switch in the genetic programming of cytokeratin filaments induced by ischemia in the salivary glands. Thus, the most probable etiology for squamous metaplasia was found to be ischemia.[5]

Minor salivary gland neoplasms with squamous metaplasia occurring in the oral cavity can be mistaken for squamous cell carcinoma, especially in aspiration cytology, which can lead to overtreatment of the patient with associated morbidity.[4]

Pleomorphic adenoma can exhibit great histologic diversity including mucous, sebaceous, oncocytic, and squamous metaplasia – sometimes with the formation of keratin pearls.[3] About 25% cases of pleomorphic adenoma can show focal squamous metaplasia, probably related to ischemia.[6] However, pleomorphic adenoma with exuberant squamous metaplasia is uncommon and can be diagnostically challenging. The formation of extensive keratin-filled cysts lined by squamous epithelium is extremely rare.[3,4] The diagnostic difficulty is more in FNAC and incision biopsy, due to limited and selective sampling. A slow growing circumscribed, submucosal growth, without any radiological features of aggressive behavior should alert the pathologist regarding benign nature of the lesion.

The most important differential diagnosis is squamous cell carcinoma. The absence of worrisome features on microscopic examination-cytological atypia, increased mitotic activity, necrosis or invasion will help to determine the benign nature of these lesions.[4]

Microscopically, MEC presents mucous, intermediate, and squamoid (epidermoid) cells and is usually multicystic. The cystic spaces of MEC are usually lined by mucous cells and prominent keratinization is rare.[1]

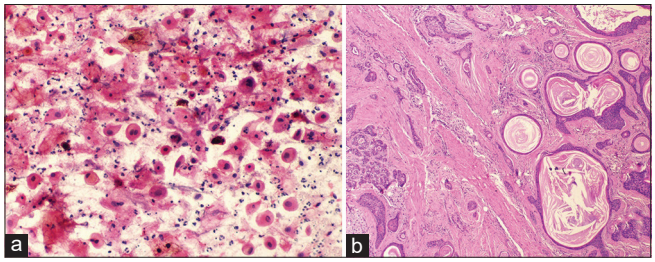


**Figure 1: (a) Aspiration cytology showing singly dispersed squamous cells with minimal atypia (Pap, ×200), (b) Excision of mass showing areas of squamous differentiation (H and E, ×50)**

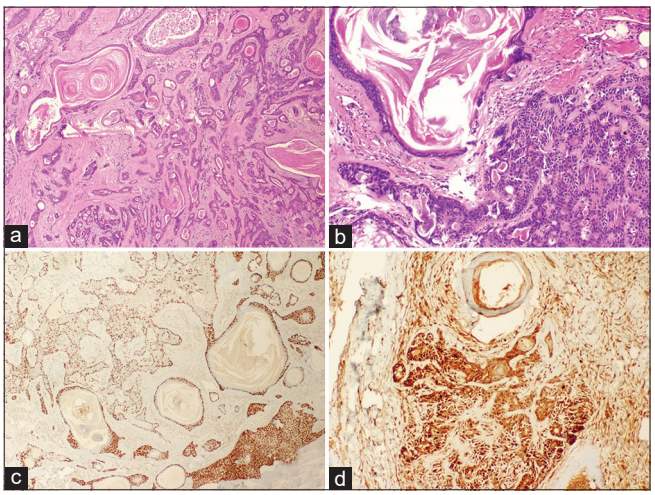


**Figure 2: (a) Section showing focus of bilayered epithelial cells in a chondromyxoid matrix and areas of squamous differentiation (H and E, ×50), (b) Higher power view showing two components (H and E, ×100), (c) p63 highlights myoepithelial cell layer and squamous component (IHC, ×50), (d) S100 highlights myoepithelial cells (IHC, ×100)**

## Conclusion

Distinction between nonneoplastic processes, benign lesions, and/or malignancies of salivary gland can be challenging due to the heterogeneity of the cell types, metaplastic changes, and sampling issues. Cytomorphology of benign and malignant lesions may overlap. Exuberant squamous metaplasia in nonneoplastic lesions and benign neoplasms can lead to false-positive diagnosis, resulting in overtreatment of the patient. Familiarity with cytopathology of salivary gland lesions and their overlapping conditions, along with the correlation of cytology findings with clinical and radiological findings may play an integral role in the management of patients with salivary gland lesions.

### Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient has given her consent for her images and other clinical information to be reported in the journal. The patient understands that name and initials will not be published and due efforts will be made to conceal identity, but anonymity cannot be guaranteed.

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### Conflicts of interest

There are no conflicts of interest.

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