

Adenosquamous carcinoma of the tongue: A case report and an overview of histogenetic concepts

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Abstract

Adenosquamous carcinoma (ASC), a rare variant of squamous cell carcinoma, is an aggressive and highly infiltrating epithelial neoplasm, which has a distinct histomorphological features comprising simultaneous areas of squamous cell carcinoma and adenocarcinoma. Some researchers consider it as a controversial neoplasm, as it may arise from the ducts of the minor salivary gland or from the overlying surface epithelium. In the head-and-neck region, commonly affected sites include paranasal sinuses, larynx and oral cavity. Areas of occurrence in the oral cavity include palate, tonsillar pillar areas, tongue and floor of the mouth. The prognosis of the neoplasm is considered poor due to its early recurrence, local and distant metastasis and low survival rate. This article reports a case of ASC affecting the posterior part of the tongue in a 50-year-old male patient and an overview of its histogenetic concepts.

Keywords: Adenosquamous carcinoma, oral cavity, squamous cell carcinoma, tongue

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Received: 21.01.2020, **Accepted:** 29.01.2020, **Published:** 28.02.2020

INTRODUCTION

Oral squamous cell carcinoma comprises the most common and significant proportion of malignant neoplasm in the oral cavity. Histologically, it manifests as several variants, such as conventional, basaloid, spindle/sarcomatoid, verrucous, papillary, adenosquamous and adenoid/acantholytic squamous cell carcinoma (ASCC), out of which adenosquamous carcinoma (ASC) is an uncommon and a rare variant.^[1] The WHO classification of head-and-neck tumors in 2017 defined ASC as “a malignant tumor that arises from the surface epithelium and shows both squamous and glandular differentiation.”^[2] It is a high-grade, aggressive, highly infiltrating and an extremely

rare variant of malignant epithelial neoplasm with a high metastatic rate (80%) exhibiting poor prognosis.^[3,4] It shows a male predisposition, with a tendency to develop in the sixth and seventh decades. Tobacco, both in its smoking and chewing form, and alcohol consumption have been implicated as the etiological factors. The origin of this tumor might be from the ducts of the minor salivary glands or from the overlying surface epithelium containing basal cells with divergent differentiation. In most of the cases, the squamous cell carcinoma component may be *in situ* or invasive, and the adenocarcinomatous component comprises glandular structures.^[5] Several investigators had thought ASC as a controversial tumor resembling mucoepidermoid carcinoma (MEC), but its increased

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How to cite this article: Prabhakar M, Sabarinath B, Sivapathasundharam B, Vasanthakumar V. Adenosquamous carcinoma of the tongue: A case report and an overview of histogenetic concepts. J Oral Maxillofac Pathol 2020;24:S110-4.

Access this article online

Quick Response Code:



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DOI:

10.4103/jomfp.JOMFP_25_20

aggressiveness, worse prognosis and high metastatic rate in comparison with high-grade MEC caused it to be considered as a separate and distinctive entity.^[6] Conceptual knowledge about the histogenesis of the tumor would eradicate any such controversies. The purpose of this article is to report a case of ASC in the posterior part of the tongue with a note on histogenetic concepts, possible theories of origin and differential diagnoses.

CASE REPORT

A 50-year-old male patient was referred to a private dental clinic with the complaint of a nonhealing ulcer on his right posterior ventrolateral portion of the tongue in relation to 30 and 31 tooth region (universal system) for the past 3 months. The patient revealed a habit of cigarette smoking for the past 30 years. There was no gross facial asymmetry noticed on extraoral examination. On intraoral examination, an ulceroproliferative lesion, measuring approximately 2 cm × 2 cm with indurated margins, was seen on the right posterior ventrolateral portion of the tongue extending from 30 to 31 tooth region. The surface of the ulcer appeared erythematous with irregular borders and was tender on palpation. Lymph nodes on the right cervical region were palpable, nontender and firm in consistency. Based on the above findings, a clinical impression of carcinoma of the tongue was made. Incisional biopsy was performed, and the specimen was sent for histopathological examination.

Grossing showed two grayish white soft-tissue specimens, firm in consistency with irregular surface. On histopathological examination, the surface epithelium was dysplastic, infiltrating into the underlying connective tissue stroma [Figure 1]. Two distinct components were noticed in the connective tissue, which were in close proximity

with each other: the superficial squamous component and the deeper glandular component [Figure 2]. Squamous component revealed malignant squamous epithelial cells arranged in solid nests and islands, resembling typical well-differentiated squamous cell carcinoma with few areas of the island showing keratin pearl formation and individual cell keratinization [Figure 3]. The glandular component revealed squamous cells arranged in ductal pattern with few areas of the ducts showing amorphous eosinophilic intraluminal content [Figure 4]. Special staining with periodic acid–Schiff (PAS) and mucicarmine showed positivity for the intraluminal content and confirmed the secretory nature of the glandular component [Figures 5 and 6]. With the above characteristic histological findings, a final diagnosis of ASC was made. Immunohistochemistry was done as an adjunct on the tissue specimen for markers such as pancytokeratin and Ki-67. The tumor cells revealed strong positivity for pancytokeratin in both squamous and glandular component and a low Ki-67 index [Figures 7 and 8].

DISCUSSION

ASC is a high-grade, aggressive, highly infiltrating and extremely rare variant of malignant epithelial neoplasm with a distinct histomorphological features comprising simultaneous areas of squamous cell carcinoma and adenocarcinoma exhibiting high metastatic rate and poor prognosis.^[3,4] Literature report of ASC started with the series of cases published by Gerughty in 1968, and thereafter, a countable number of case reports had been published with different sites of occurrence including lung, esophagus, stomach and pancreas, to name a few. In the head-and-neck region, the common sites of occurrence include larynx, followed by oral cavity with male-to-female ratio of 6:1.^[7] ASC has been

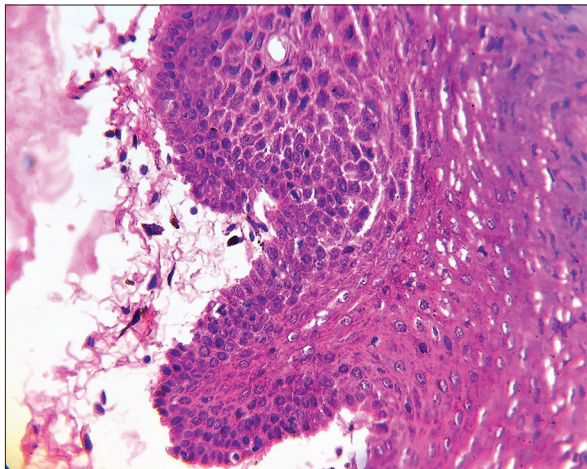


Figure 1: Dysplastic surface epithelium

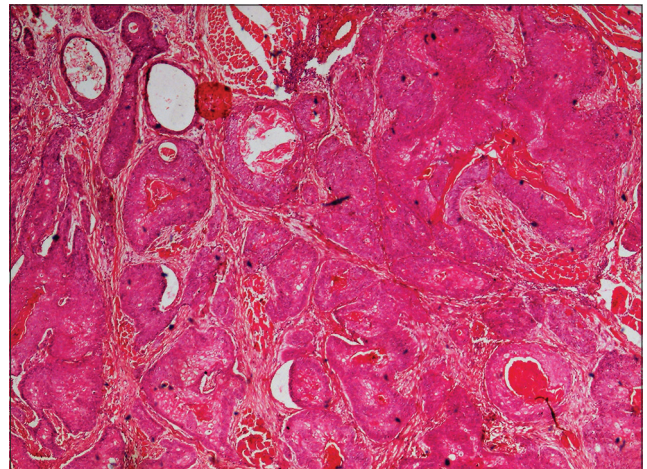


Figure 2: Squamous and glandular components

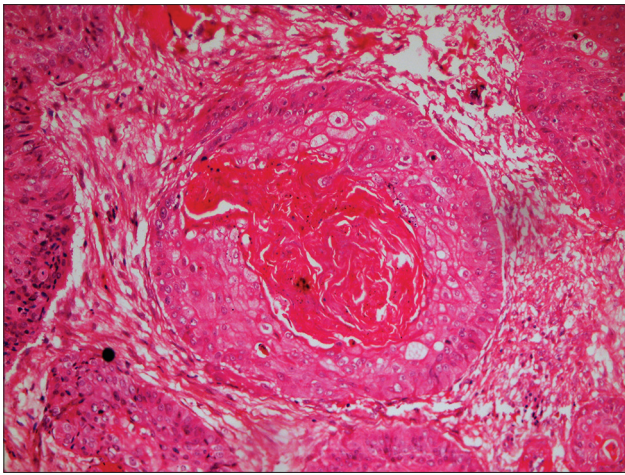


Figure 3: Squamous island with keratin pearl formation

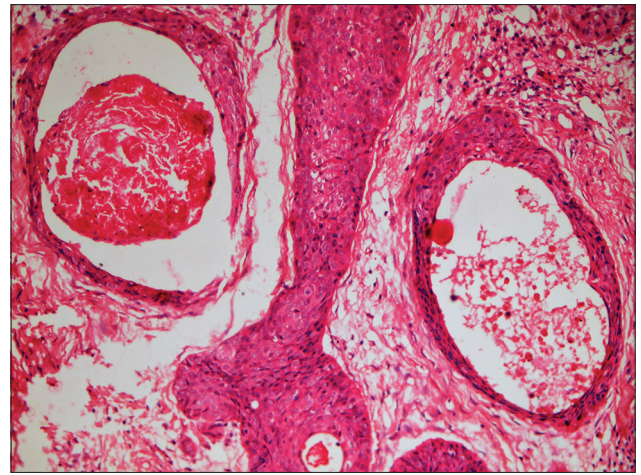


Figure 4: Glandular areas with intra-luminal content

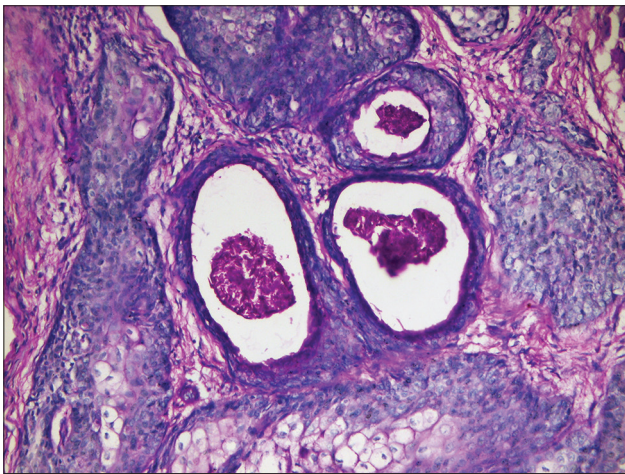


Figure 5: Periodic acid-Schiff positivity for intraluminal content

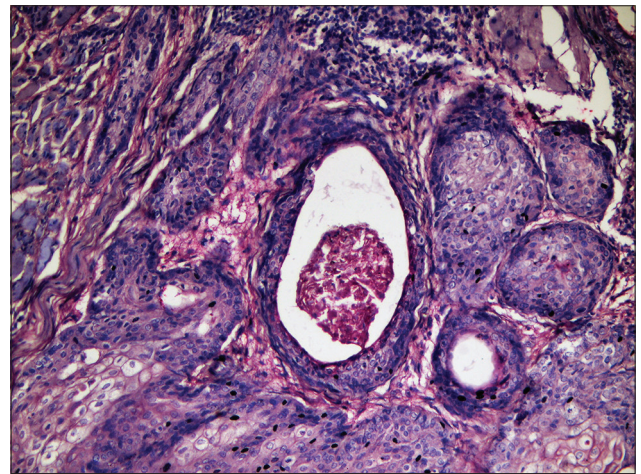


Figure 6: Mucicarmine positivity for intraluminal content

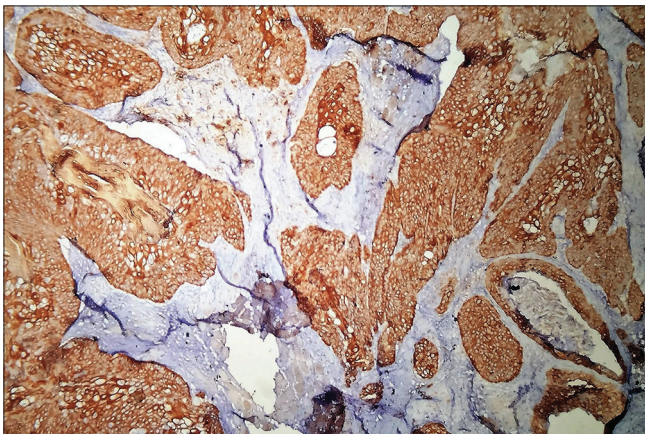


Figure 7: Pancytokeratin positivity of the tumor islands

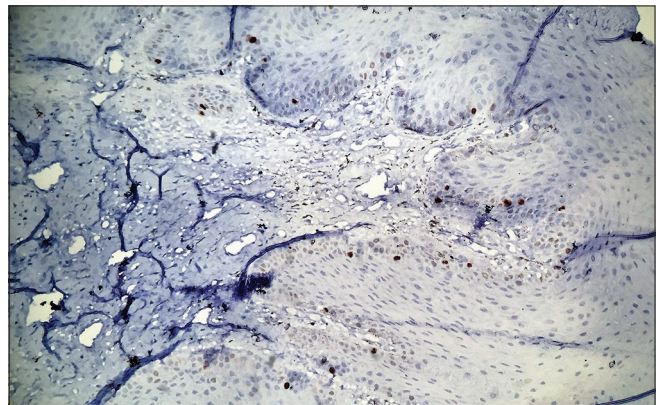


Figure 8: Low Ki-67 expression in the surface epithelium

reported in a broad incidence of age group that ranges from 22 to 80 years.^[3] A thorough literature search reveals varying number of ASC cases occurring in the tongue, with recent literature review stating only 17 cases reported thus far.^[8]

Different theories have been postulated regarding the origin of this tumor that it arises either from the cells of the salivary gland or from the reserve/basal cells of the surface epithelium that are capable of divergent differentiation to a glandular component.^[9] Divergent differentiation, which is otherwise termed as a metaplastic change, is certainly a

rare phenomenon and when it occurs, can lead to diagnostic uncertainty. In an attempt to resolve the controversies pertaining to the theories of the origin of ASC, the following hypotheses for the origin of the squamous and glandular components are suggested.

- (i) The basal or reserve cell in the surface epithelium differentiates to squamous component, which in turn differentiates into prosoplastic glandular components
- (ii) The bipotential undifferentiated basal or reserve cells differentiate simultaneously into squamous and glandular components
- (iii) The ductal epithelial cells dedifferentiate into squamous components
- (iv) Separate individual and distinct foci of squamous component from basal cells and glandular components from minor salivary glands.

ASC exhibits dual histomorphology with the squamous component in superficial areas and adenocarcinoma component in deeper areas. Usually, the squamous component will be arranged in the form of solid nests or islands of malignant epithelial cells arising from the dysplastic surface epithelium. The adenocarcinoma component consists of duct such as punched out spaces lined by epithelium with amorphous eosinophilic intraluminal content.^[3,4] A significant diagnostic criteria for ASC had been postulated by Alos *et al.*, which includes (i) the most common keratinizing SCC, (ii) adenocarcinoma component in the deeper portion and (iii) severe dysplasia or carcinoma *in situ* in the surface epithelium.^[6] The present case also revealed similar findings such as dysplastic surface epithelium with squamous component exhibiting focal areas of keratinization and typical glandular component with intraluminal mucinous content.

Special staining of the intraluminal content with PAS and mucicarmine often reveals positive evidence for mucin production but is not fundamental criteria for diagnosis. Some tumors, despite the true neoplastic glanduloductal formation, may not contain mucin.^[10] Various authors in the literature have used a wide range of immunohistochemical (IHC) markers. Some of the commonly used markers include pancytokeratin for epithelial cells, carcinoembryonic antigen for tumor progression, Ki 67 for proliferation rate, p53 for tumor suppression and p63 for squamous differentiation.^[11] As the present case had significant histopathological features suggestive of ASC, IHC was used only as an adjunct and was restricted to pancytokeratin, which showed strong positivity in both squamous and glandular components. Literature reveals high proliferative index for most malignant neoplasms; however, in the present case, Ki-67

positivity was restricted only to the basal cells of the squamous component. This represents a low proliferative index (approximately 10%), which in turn prompts a possibility for a low-grade entity in oral ASC, as is also reported in the breast.^[12]

Differential diagnosis of ASC is to be taken as an essential consideration as its histopathological findings mimic the most common malignant salivary gland neoplasm, MEC as well as ASCC. Although several authors include basaloid squamous cell carcinoma, conventional squamous cell carcinoma and necrotizing sialometaplasia in the differential diagnoses, differentiating ASC from MEC and ASCC seems to be appropriate for the discussion due to their overlapping histological features.^[3]

MEC, which also has biphasic morphology, consists of glandular, intermediate and epidermoid components. The absence of dysplasia in the surface epithelium and lack of keratin pearl formation in MEC distinguishes it from ASC; however, high-grade MEC is rarely associated with keratin pearl formation. In addition, the presence of intermediate cells and widespread glands with retained lobular arrangement found in MEC, is usually absent in ASC.^[5] Recent molecular techniques involving CRTC1/3– MAML2 gene fusion, which is commonly associated with MEC, is not seen in ASC and therefore helps in their differentiation.^[13] The present case did not demand such diagnostic molecular studies as the histopathological findings were sufficient for distinguishing ASC from MEC.

ASCC, which is also a variant of conventional SCC, consists of pseudoglandular spaces with acantholytic cells. The absence of mucin in the duct-like spaces represents that these spaces are formed by the acantholysis of the cells and are not true ducts. Differences between ASC, MEC and ASCC are highlighted in Table 1.

ASC, being highly infiltrative and metastatic, needs to be treated with surgical intervention in association with radiation therapy and chemotherapy. Poor prognosis with high metastatic rate (80%) and low survival rate (20%–25%) with frequent local recurrences account for the aggressiveness of the neoplasm.^[14] Sufficient and proper biopsy specimen with complete examination of the same, along with supportive knowledge of its origin, helps the pathologist to overcome the diagnostic challenges in such lesions.

Financial support and sponsorship

Nil.

Table 1: Differentiating features between adenosquamous carcinoma, mucoepidermoid carcinoma and acantholytic squamous cell carcinoma

Features	ASC	MEC	ASCC
Epithelial dysplasia	+	-	+
Keratinization	+	+/-	+
Lobular arrangement	-	+	-
Intermediate cells	-	+	-
Glandular spaces	True glandular spaces located in deeper part	Widespread	Pseudo glandular spaces due to cellular acantholysis
Mucin secretion	+	+	-
Acantholysis	-	-	+

+: Present, -: Absent, +/-: Rarely seen, ASCC: Acantholytic squamous cell carcinoma, ASC: Adenosquamous carcinoma, MEC: Mucoepidermoid carcinoma

Conflicts of interest

There are no conflicts of interest.

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