Case Report

Oral adenosquamous carcinoma: Report of a rare entity with a special insight on its histochemistry

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Abstract

Adenosquamous carcinoma (ASC) of the head and neck (H and N) is an aggressive variant of squamous cell carcinoma (SCC). They are described as SCC subtype with high infiltrative capacity and also presents with dual histomorphology, having both squamous and glandular cell components. ASC of the H and N region is considered as a controversial tumor, as it is similar to salivary gland mucoepidermoid carcinoma. It has been described in a variety of body sites, including uterine cervix, lung and pancreas. ASC rarely develops in the upper aerodigestive tract, particularly in the oral cavity. The affected sites in oral cavity include palate, tonsillar pillar areas and floor of the mouth. To the best of our knowledge in the literature, only 17 cases of ASC in the floor of the mouth have been reported. Hereby, we report an additional case of ASC occurring in the floor of the mouth in a 70-year-old male patient.

Key Words: Adenosquamous cell carcinoma, glandular cell component, mucoepidermoid carcinoma, squamous cell component

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INTRODUCTION

Oral squamous cell carcinoma (OSCC) is the most common malignant neoplasm of epithelial cells, and the cell origin is oral keratinocyte.[1] Histologically, OSCC is of different types which include conventional SCC, basaloid SCC, spindle cell/sarcomatoid SCC, verrucous carcinoma, papillary SCC, adenoid/acantholytic/pseudoglandular SCC and adenosquamous carcinoma (ASC).[2] Each variant has its unique histological appearance. Among all these variants of OSCC, ASC is rare, aggressive malignant neoplasm in head and neck (H and N) region and has distinct squamous and glandular component as described by World Health Organization (WHO).[3]

According to the WHO 1995 classification of tumors of the upper respiratory tract and ear, ASC of H and N region was defined as "A malignant tumor with histological features of both adenocarcinoma and SCC."[4] It is also considered as a controversial tumor, as it is similar to salivary gland mucoepidermoid carcinoma (MEC), but Evans in 1984 highlighted the worse prognosis of ASC of H and N over high-grade MEC and proposed that ASC should be considered as a distinctive neoplasm.[5]

ASC of H and N was described by Gerughty *et al.*, in 1968 in a series of 10 patients, where it has been shown to be extremely aggressive with 80% of patients developing metastasis.[6] ASC rarely develops in upper aerodigestive tract affecting the supraglottic region of larynx and oral cavity.[7] The most common site in oral cavity is tongue followed by palate, tonsillar pillar areas and floor of mouth.[3] To our knowledge in the

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literature, only 17 cases of ASC in the floor of the mouth have been reported. Hereby, we report an additional case of ASC occurring in the floor of the mouth in 70-year-old male patient [Table 1].

CASE REPORT

A 70-year-old male reported with pain in the left lower region of mouth since 2 months. The patient was a smoker and had a habit of alcohol since 50 years with unremarkable medical history. Extraoral examination revealed no facial asymmetry [Figure 1a]. Bilateral submental and submandibular lymph nodes were palpable which were tender and firm in consistency measuring approximately 1 cm × 1 cm in size. Intraoral examination revealed a small solitary ulcerated lesion with everted margins extending from lateral side of ventral portion of tongue to floor of mouth on the left side measuring approximately 7 cm × 3 cm in size [Figure 1b]. The lesion is erythematous and irregular in shape. On palpation, all the inspectory findings were confirmed and the swelling was firm in consistency. Based on these findings, a provisional diagnosis of carcinoma of the floor of the mouth was given.

Histopathological examination of incisional biopsy revealed infiltration of stratified squamous epithelium into underlying connective tissue stroma [Figure 2a]. The tumor was composed of two distinct components: Superficial squamous component and deeper glandular component [Figure 2b]. Squamous component revealed typical well differentiated SCC adjacent to dysplastic areas in the epithelium. Numerous areas of keratin pearls along with single cell keratinization were also noticed [Figure 3a]. Glandular component revealed ductal structures with varying degrees of cellular and nuclear pleomorphism [Figure 3b]. Areas of mucous cells were dispersed within the stroma. Areas of intracellular and intraluminal mucinous material and some acantholytic cells were also seen in lumen of ducts. The amorphous mucinous material within the lumen of ducts was highlighted with periodic acid-Schiff (PAS) [Figure 4a] and mucicarmine stain [Figure 4b]. Immunohistochemistry revealed strong positivity for both squamous and glandular components with respect to pancytokeratin AE1/3 and finally the case was diagnosed as adenosquamous cell carcinoma [Figure 5]. The patient was referred to cancer institute for proper treatment and follow-up.

Table 1: Review of previous cases of oral adenosquamous carcinoma reported in the floor of the mouth

Author	Age	Sex	Number of cases
Gerughty *et al*.[6]	47	Male	2
	57	Male	
Siar and Ng[8]	71	Male	1
Yoshimura *et al*.[9]	Mean age - 63	-	8
Alos *et al*.[5]	42	Male	3
	54	Male	
	43	Male	
Carvalho *et al*.[7]	74	Male	1
Schick *et al*.[10]	71	Male	1
Shyamala *et al*.[11]	54	Male	1
Present case	70	Male	1

DISCUSSION

ASC is an extremely rare tumor with <100 cases having been reported in English literature. They constitute about 0.6% and 0.1% of lung and colon cancers respectively and 1.1% of all malignant epithelial salivary gland tumors.[10] The histogenesis of ASC is not completely understood, but it was thought that the origin is from both glandular and surface epithelial origin.[3] Ellis suggested that dysplasia of the surface mucosal epithelium is an important diagnostic criteria and considered the tumor to arise synchronously from mucosal and salivary gland epithelium.[12] According to Fonseca *et al*., ASC originates from surface mucosal epithelium on the basis of surface mucosal dysplasia giving rise to invasive tumor with normal minor salivary glands in proximity.[13] The origin of ASC in the present case was in accordance with Ellis.

Recently, it was also proven that human papillomavirus (HPV) is an important etiological agent in H and N carcinomas particularly in the oropharynx and nasal cavity. High-risk HPV (HPV-16) has been detected in about 80% of SCC cases. The virus contributes to carcinogenesis by expressing E6 and E7 oncoproteins which bind to p53 and retinoblastoma (Rb). These are critical regulators of cell cycle and apoptosis which on disruption causes the cells to proliferate and fail to undergo apoptosis appropriately. Inactivation of Rb leads to overexpression of p16 which is a good surrogate marker of HPV. The presence of HPV, overexpression of p16 and significant expression of E6 and E7 transcripts indicates the biological and significant role of HPV in the tumor.[14]

In the H and N region, ASC is predominantly seen in tongue, palate, floor of the mouth and larynx with a peak incidence

Figure 1: (a) Extra- and (b) intra-oral picture

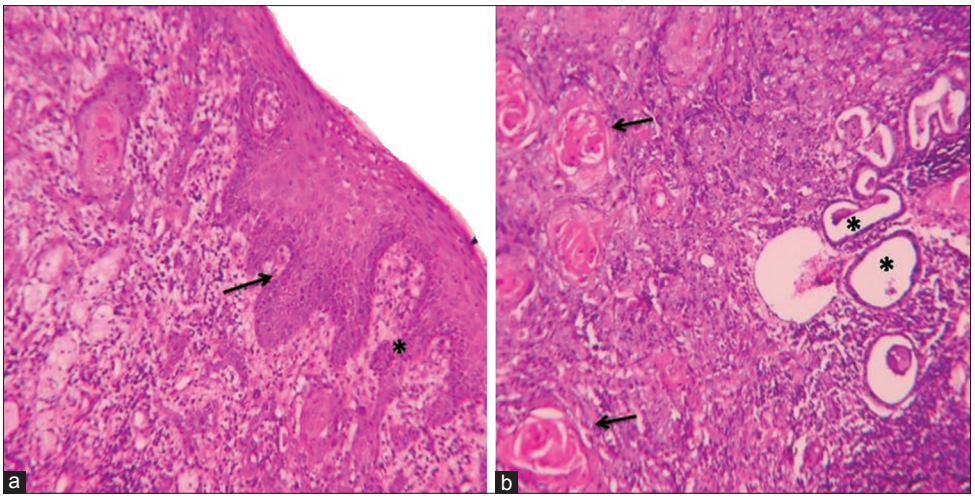

Figure 2: (a) Stratified squamous epithelium (indicated by arrow mark) infiltrating into underlying connective tissue stroma (indicated by an asterisk) (H&E stain, ×40). (b) Squamous component (indicated by arrow mark) and glandular component (indicated by asterisk) (H&E stain, ×100)

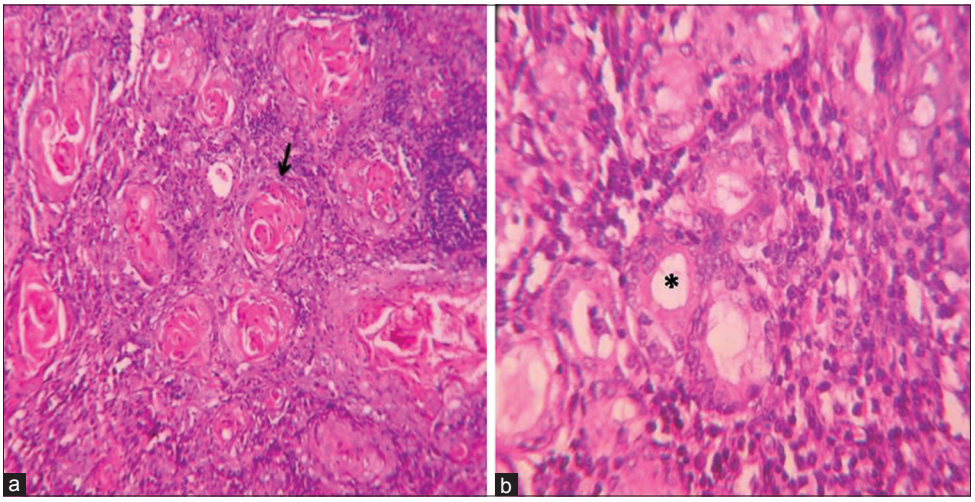

Figure 3: (a) Squamous component with numerous areas of keratin pearls (H&E stain, ×40) and (b) glandular component with ductal structures with smooth edges (H&E stain, ×100)

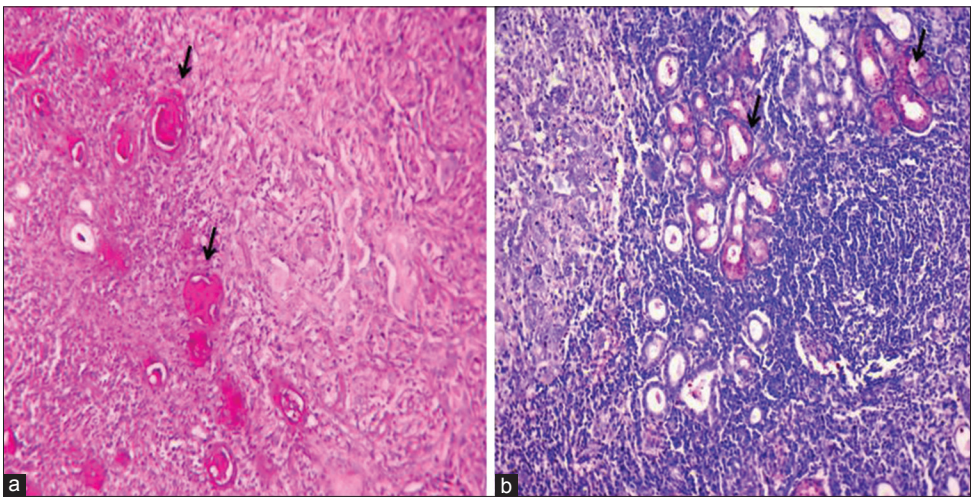

Figure 4: The adenoid component showing positivity for mucins (a) Periodic acid-Schiff stain, ×40, and (b) mucicarmine, ×40

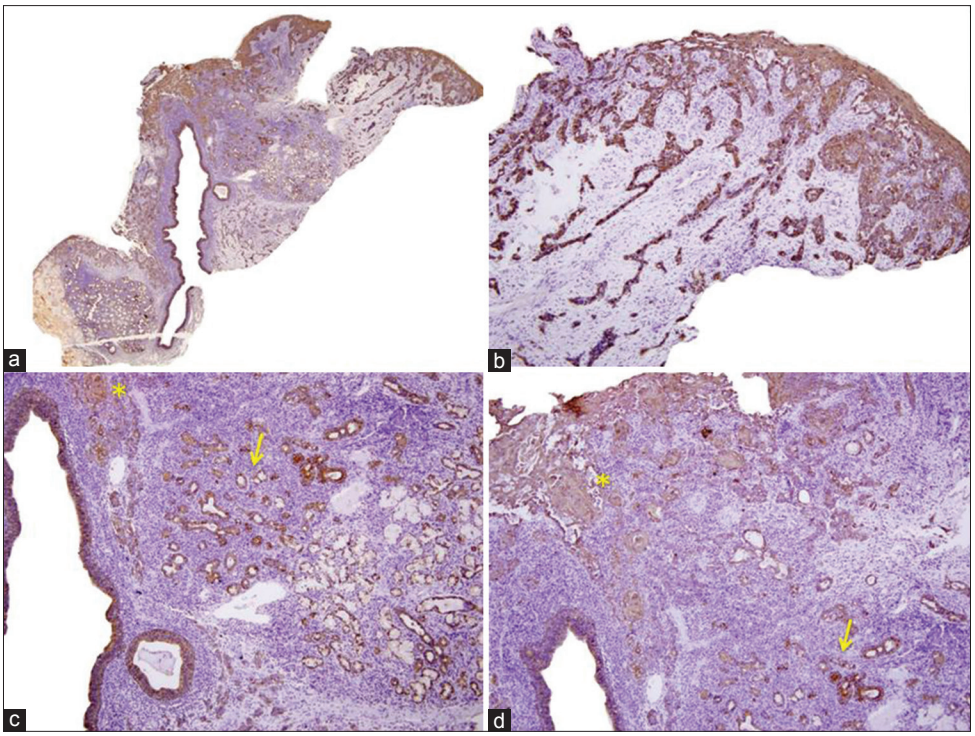

Figure 5: Pancytokeratin AE1/3 positivity for both squamous (indicated by asterisk) and glandular component (indicated by arrow mark) of adenosquamous cell carcinoma [IHC stain, (a) ×20, (b) ×20, (c) ×40, (d) ×40]

in the fifth decade (male:female ratio is 3:1).[15] Clinically, approximately 40% of patients complain of pain on the initial appointment which is mainly because of the tendency of tumor to spread by perineural invasion. Other tumor-related symptoms include odynophagia, otalgia, tongue numbness, bleeding and weight loss.[7] Till now, very few cases have been reported in the floor of the mouth. The present case was an additional case of ASC occurring in the floor of the mouth which was reported in 70-year-old male and was associated with pain.

As defined by WHO, ASC exhibits dual histomorphology, with both squamous and true adenocarcinoma component.[6] The squamous cell component usually predominates and appears in superficial areas arising from surface epithelium. The mucosal epithelium presents with severe dysplasia or carcinoma *in situ*. The presence of variable extent of foci of keratinization was also noticed.[5] The adenocarcinoma component is usually found in deeper areas which are composed of ductular structures with variable number of mucous cells. Typically, the glandular formation should consist of punched out spaces with smooth edges rather than ragged edges.[6] The present case also revealed similar findings, i.e. the mucosal epithelium in squamous cell component presented with severe dysplasia with focal areas of keratinization and the glandular component revealed ductular structures with smooth edges and variable mucin production.

Alos *et al*. suggested the following diagnostic criteria for ASC which includes: (i) The most common component is keratinizing SCC; (ii) adenocarcinoma component in the deeper portion and (iii) severe dysplasia or carcinoma *in situ* in the surface epithelium.[5] The present case was also in accordance with the above-mentioned criteria.

Histochemical examination was performed to differentiate ASC from adenoid/acantholytic SCC which revealed PAS and mucicarmine positivity for the amorphous material present within the lumen of ducts indicating true glandular formation. Immunohistochemically, the glandular component of ASC is positive for pancytokeratin, epithelial membrane antigen, CK7/8, CAM 5.2, CEA and negative for CK20 whereas squamous cell component is positive for pancytokeratin, CEA and negative for CK7/8, CK20 and CAM 5.2.[3,7] As pancytokeratin is positive for both the components, the present case was performed with the same and revealed positivity for both squamous and glandular components.

Differential diagnosis of ASC is of major importance because of its behavior [Table 2]. ASC is an aggressive tumor, with spread to cervical lymph nodes, locoregional and distant recurrence after treatment.[16] The treatment includes surgery alone, as well as association with radiation therapy and/or chemotherapy. A high metastatic rate about 80% and low 5 years survival rate which is about 20–25% was expected.[7]

Table 2: Differential diagnosis of adenosquamous carcinoma

Adenosquamous carcinoma	Mucoepidermoid carcinoma	Basaloid squamous cell carcinoma	Acantholytic/adenoid squamous cell carcinoma
Severe dysplasia or carcinoma *in situ* Origin mainly from squamous epithelium Keratinization of squamous cells Glands in deeper invasive parts Secondary invasion of seromucous glands No lobular arrangement No intermediate cells True glandular spaces with variable mucin production	No dysplasia From salivary gland striated duct No keratinization of squamous cells Widespread glands Secondary invasion of squamous epithelium Lobular arrangement Intermediate cells present	Tumor cells – predominantly basaloid Duct like structures – due to squamous cell proliferation Lacks true adenocarcinoma differentiation	Pseudoglandular spaces – due to cellular acantholysis No mucin production Acantholytic, dyskeratotic epithelial cells – present

CONCLUSION

ASC is a rare malignant neoplasm which is aggressive and associated with poor outcome when compared to conventional SCC and also presents with high rate of lymph node metastasis. ASC should be ruled out from MEC, basaloid SCC and adenoid SCC. The precise histopathological diagnosis helps the clinician to plan the accurate treatment.

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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