CASE REPORT

Adenosquamous carcinoma: Histogenetic and molecular insight with a report of a case

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Abstract

Adenosquamous carcinoma showing distinct squamous and glandular components histologically is a highly aggressive, malignant tumor with rare occurrence in the oral cavity. Few studies have suggested that the cases have shown aggressive course with a high tendency toward metastasis compared to squamous cell carcinoma or even high grade mucoepidermoid carcinoma. It is a controversial tumor with respect to its histogenetic origin. In this review, we have addressed the debate on histogenesis of this malignancy, the molecular events that are responsible for the glandular differentiation, diagnostic criteria along with a case report.

Keywords:
Adenosquamous carcinoma, glandular, histogenesis, mucoepidermoid

Introduction

Adenosquamous carcinoma (ASC), a controversial variant of squamous cell carcinoma (SCC), as the name implies, possesses histomorphologic features of an adenocarcinoma and SCC.[1] It has been described in a variety of body sites, including the uterine cervix, lung, and pancreas, but its existence in the head and neck region as a distinct entity was somewhat controversial for many years. Some investigators considered ASC to be a high grade mucoepidermoid carcinoma (MEC).[2] Gerughty et al. in 1968 demonstrated ASC in the upper respiratory tract in a series of 10 patients. Their investigation suggested the neoplasm to be extremely aggressive, with 80% of the patients showing metastasis.[3] ASC shows worse prognosis compared to even high grade MEC. The clinical and histopathologic differences in ASC presentation has promoted it to be considered as a separate entity.[4] Its rare occurrence in the oral cavity has prompted us to report this case of ASC in the floor of the mouth along with a discussion on histogenesis and molecular pathogenesis of ASC in this article.

Case Report

A 54-year-old male patient visited out-patient department of Bidar Institute of Medical Sciences, Bidar with a complaint of an ulcer with a duration of 4 months on the floor of the mouth on the right side extending up to the right lateral border of tongue covering the right ventral surface. Ulcerative mass was approximately 4 cm × 5 cm in dimension, with indurated margins. No lymph node involvement was noticed on examination. A provisional diagnosis of carcinoma floor of the mouth was made. Incisional biopsy investigation revealed areas of SCC presenting with cellular pleomorphism, keratin pearl formation, individual cell keratinization, and numerous mitotic figures [Figure 1] along with areas showing glandular pattern of proliferation with ductal differentiation of malignant neoplastic cells [Figure 2]. Mucin production by the adenocarcinoma component was confirmed by periodic acid Schiff [Figure 3] and mucicarmine stain [Figure 4]. With these features, a final histopathologic diagnosis of ASC was made.

Discussion

Yoshimura et al. reviewed 19 cases of ASC in Japan from 1986 to 2001. In their study, they observed that ASCs occurred at an average age of 63 years, with 74% of the ASCs occurring in the floor of the mouth and the tongue, the other sites of occurrence were the palate and mandibular alveolus. Chief complaints were painless mass formation (28%), pain and/or sensory abnormality (28%), painful ulcer or swelling (22%), simple ulcer (11%), and miscellaneous others (11%). The clinical presentations of ASC were tumor with ulceration (58%), tumor mass (26%), and ulcer (16%).[5]

Concurrent with this observation, the site of ASC in this case is floor of the mouth and presented as a painless ulcer. Generally,
Adenosquamous carcinoma has been considered to be a very aggressive malignancy with a poor prognosis.\(^\text{[3-6,10]}\)

However, the Japanese cases examined herein did not reflect such poor prognoses.\(^\text{[5]}\) More such analytical studies should shed light on the behavior and prognosis of ASC.

Though etiopathogenesis of ASC is not clear, there is unanimous agreement among authors about its aggressive behavior and propensity for loco-regional and distant metastases. In a study by Ramya \textit{et al.}, a strong male predilection (Male: Female = 6:1) was observed, and the tumors occurred over a broad age range (21-87 years). The larynx was the most common site (48.4%), followed by the oral cavity (30%). Most tumors were the high stage at the time of presentation. The 18 cases that were observed in their study showed local recurrence or nodal metastases in 55.6% cases and distant metastases in 22.2% cases.\(^\text{[4]}\) Keelawat \textit{et al.} in a review of 58 cases of head and neck ASC, reported 65% regional metastases, 23% distant metastases, and 43% of patients dying of the disease.\(^\text{[11]}\) The lung is the most common site for distant metastases. The literature available supports that ASC is more clinically aggressive with 22-23% distant metastasis than typical head and neck SCC, with only 10-15% distant metastases,\(^\text{[12,13]}\) and SCC also has 5 years survival of approximately 50%.\(^\text{[14]}\)

**Histogenesis**

ASC is a rare variant of head and neck SCC that is characterized by mixed differentiation, with both SCC and true adenocarcinoma, as defined by the World Health Organization.\(^\text{[15,16]}\)

ASC tumor mass is composed of SCC components intermixed with glandular patterns suggesting glandular differentiation of the neoplastic cells. The diagnosis of ASC will be made on the histogenetic criteria defined by Gerughty \textit{et al.} Four basic components will be observed, those are ductal carcinoma in situ, adenocarcinoma, SCC, and a mixed carcinoma. The SCC part must show two or more of the following features: (1) Intercellular bridging, (2) keratin pearl formation, (3) parakeratotic differentiation, (4) individual cell keratinization, and (5) cellular arrangements showing...
pavement or mosaic patterns. The production of mucin was once a prerequisite for diagnosis, but now mucin presence is not diagnostic criteria in the presence of true gland formation.

The histogenesis of ASC is debatable as there is not much literature on the histogenetic aspect of ASC. Mostly, due to the rarity of this malignancy or lack of controlled studies. Gerughty et al. have suggested totipotential cells from the excretory duct of minor salivary glands. Hyams et al. have considered mucosal lining of the upper respiratory tract as a source. Gerughty et al. also suggested glandular origin with ductal carcinoma in situ preceding the fully developed ASC.

Cytokeratin (CK) 10/13 was expressed in all the cells except basal cells of squamous components of ASC and SCC, whereas basal cells expressed CK 14. CK 18 was only positive in luminal cells of the adenosquamous part and negative in SCC components. Overall this study suggested the oral mucosal origin of ASC with markers for discriminating ASC and SCC. In another study, all glandular components were positive for carcinomaembryonic antigen and low molecular weight CK (19KD), and the squamous component was negative for both.

Ramya et al. have studied the probable role of human papilloma virus (HPV 16 and 17) in ASC of the head and neck. They suggested that ASC are relatively heterogeneous with regard to localization and HPV status. Most of the cases show p53 protein overexpression/mutation, as demonstrated by immunostaining. Their study also revealed that only small minority of cases are HPV-related, and mostly occur in the oropharynx and nasal cavity, which are the sites known for high prevalence of HPV-related tumors. The HPV-related oro-pharyngeal cases, in particular, appear to do very well clinically, akin to other SCC variants in the oropharynx that are HPV-related.

Conclusion

ASC is an aggressive malignancy with a diverse source for its histogenesis. There are also cases with less aggressive behavior especially those associated with HPV. This behavioral contrast needs to be understood better with more clinical, histopathological and molecular studies.

References