SHORT COMMUNICATION

Meticulous diagnosis of adenoid squamous cell carcinoma: A sine qua non

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Abstract

Adenoid squamous cell carcinoma, representing a rare histologic subtype of oral squamous cell carcinoma shares a considerable histopathological and immunohistochemical overlap with a few aggressive lesions. It is important for the pathologist to be aware of the possibilities of potentially misdiagnosing this entity. Hence, an attempt is made in this commentary, to acquaint the pathologist to the same.

Keywords

Adenoid squamous cell carcinoma, adenosquamous carcinoma, oral squamous cell carcinoma

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Introduction

The most common malignancy in the upper aerodigestive tract, oral squamous cell carcinoma (OSCC), comprising 50% of all head and neck carcinomas,[1] is now being increasingly acknowledged to manifest in the form of different histological variants [Table 1].[2,3] The classification of OSCC into various subtypes has significant implications with regards to its treatment and prognosis apart from just being an academic interest. Among the different variants of OSCC, adenoid squamous cell carcinoma (ASCC), first described by Lever in 1947[4] is a rare entity. ASCC (synonyms being, acantholytic SCC, pseudoglandular SCC, angiosarcoma-like SCC, pseudo-angiosarcomatous carcinoma) histologically presents as a SCC with pseudoglandular spaces in the stroma with dys-cohesive acantholytic cells within these spaces.[5] Our intention, in this short commentary, is to reiterate the importance of diagnosing this entity, as there is a repeated tendency by the pathologist to misdiagnose the same as mucoepidermoid carcinoma, vascular neoplasms, specially angiosarcoma and adeno squamous carcinoma (ASC).[6,7]

Pitfalls in Diagnosis of ASCC

ASCC, arising due to sun damage, most commonly manifests near the lips at the vermilion border[8] and less frequently in the mucosal sites of the upper aerodigestive tract including, oral cavity, tongue and nasopharynx,[9] as ulcerations or exophytic

Table 1: Histological variants of OSCC

Verrucous carcinoma
Carcinoma cuniculatum
Papillary squamous cell carcinoma
Adenoid (acantholytic) squamous cell carcinoma
ASC
Basaloid squamous cell carcinoma
Spindle cell carcinoma
Giant cell (pleomorphic) carcinoma
Undifferentiated carcinoma

ASC: Adeno squamous carcinoma, OSCC: Oral squamous cell carcinoma
Patil, et al. Adenoid squamous cell carcinoma

The tumor microscopically shows numerous pseudolumens/pseudoglandular spaces lined by a basal layer of polygonal cells with the central lumina accommodating dys-cohesive acantholytic cells with some necrotic debris and blood. The pseudolumens are believed to be formed due to central acantholysis of the advancing epithelial nests and islands in the stroma. A moderate to high degree of dysplasia and prominent keratin pearls are noted in the epithelial cells.

Pitfall 1

There have been observations by pathologists, wherein the ‘basal’ layer of the pseudolumens may show acantholysis and pose as individual cells or units in the advancing front. In such cases Woolgar et al. recommend the reporting of these cases as conventional SCCs with a dyscohesive advancing front as opposed to a diagnosis of ASCC. There are also rare possibilities of acantholysis affecting most of the tumor and the histology becoming mostly dyscohesive individual cells. Such lesions are characterized as “non-cohesive OSCCs,” but the prognostic significance is not known.

Pitfall 2

Massive acantholysis of the tumor may sometimes cause the tumor to mimic vascular proliferations. Apart from giving the appearance of pseudovascular spaces, the epithelial cells lining the pseudolumens may have a hobnail pattern and hence the synonyms angiosarcoma-like SCC, pseudo-angiosarcomatous carcinoma or pseudovascular ASCC. Nappi et al. in their case series, noted that six acantholytic cutaneous squamous cell carcinomas, closely resembled angiosarcomas on conventional histologic examination. However, none of them were immunoreactive for factor VIII antigen, and two out of three cases studied were CD 34 negative. They also found that the control group of six angiosarcomas were all negative for epithelial membrane antigen and cytokeratin. Driemel et al. however, caution that one has to consider two possibilities as far as the immunoreactivity of these two lesions are concerned. On one side angiosarcomas may contain cytokeratin positive cells and the numerous vessels, if present in ASCC, may show positivity for the endothelial markers. According to these authors, angiosarcoma and ASCC share some clinical, histopathological and immunohistochemical overlap. The expression of Fli-1 in angiosarcoma and In-5 in ASCC are specific distinguishing features.

Pitfall 3

The most common diagnostic dilemma we come across is the misdiagnosis of ASCC as ASC. ASC is a subtype of SCC/OSCC that possess histological features of both adenocarcinoma and SCC. Occurring most commonly in men in their sixth-seventh decade, it is known to manifest orally in the tongue, maxillary alveolus and floor of the mouth.

Microscopically, the squamous component is usually predominant, moderately to poorly differentiated and shows prominent dyskeratosis. ASC has a glandular component that is noted in the deepest areas of the tumor and should not be incorrectly interpreted as arising due to acantholysis. The glandular differentiation of ASC is differentiated from the pseudoglandular pattern of ASCC, by the glandular mucins staining positive for PAS, mucicarmine and alcin blue and the glands immunohistochemically reacting with carcinoembryonic antigen, CAM5.2 and cytokeratin 7. Mucoepidermoid carcinoma may be included in the differential diagnosis of ASC. However, this can be easily eliminated by the presence of keratin pearls in ASC and the lack of mucocytes. Figures 1 and 2 summarize how to differentiate ASCC from other lesions.

We reported a case of ASCC in our department recently, which, like our comments above, was almost misdiagnosed as ASC. PAS and mucicarmine were negative, but the mandatory requirement for mucin is not a requisites according to few examiners for a diagnosis of ASC. In a state of dilemma, we observed that the pseudolumens apart from mimicking true ducts also resembled vascular spaces. Furthermore, the presence of acantholytic cells in these spaces tipped our diagnosis in favor of ASCC.

Sometimes the acantholytic cells present in the pseudolumen undergoes disintegration. This mainly happens due to lack of perfusion of nutrition to the acantholytic cells from adjacent connective tissue stroma. On histopathological examination, this degeneration appears as faint eosinophilic or amphophilic granular material in the pseudolumen. In contrast, the lumen of the ASC contains secretions of glandular cells that histopathologically appears as faint eosinophilic or amphophilic homogeneous material. Thus, we believe that in the absence of acantholytic cells in the lumen, the histopathological appearance of the non-cellular material can guide us to the diagnosis.

One additional feature we observe in the ASCC is presence of the cellular cannibalism in the acantholytic cells. This again is attributed to the lack of nutritional supply to the acantholytic cells in the lumen. To survive in the low nutritional environment the cancer cells start engulfing the adjacent weaker cells.

Conclusion

We, in this commentary, have tried to put across the significance and the necessity for a correct diagnosis of ASCC, as it can mimic more aggressive lesions like angiosarcoma or ASC. Hence, diligent and prudent observation when diagnosing this lesion can help in averting a misdiagnosis.
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References


Figure 1: Flowchart helping differentiation between adenoid squamous cell carcinoma and vascular lesions (corresponding to pitfall 2)

Figure 2: Flowchart helping differentiation between adenoid squamous cell carcinoma, adeno squamous carcinoma and mucoepidermoid carcinoma (corresponding to pitfall 3)


