Case Report

HPV-Related Multiphenotypic Sinonasal Carcinoma Presenting as a Gingivobuccal Sulcus Lesion

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Abstract

Introduction: HPV-related multiphenotypic sinonasal carcinoma (HMSC), originally known as HPV-related carcinoma with adenoid cystic carcinoma-like features, is a distinct neoplasm that is seen in the sinonasal tract which exhibits features of both surface-derived neoplasm and salivary gland carcinoma (particularly adenoid cystic carcinoma), and is associated with high-risk human papillomavirus (HPV).
Case Presentation: A 52-year-old man was evaluated for an ulcer over the left upper alveolus and retromolar triangle. It was diagnosed initially as conventional squamous cell carcinoma and treated accordingly for over 2 years. Over time, there was an increase in the size of the lesion up to 5x4x4cms, epicentered in the left maxilla. However, there was no evidence of lymph node involvement or distant metastasis. Re-biopsy of the lesion in the left gingivo-buccal sulcus was done and evaluated. The histomorphology showed an overlap between a surface-derived neoplasm (squamous cell carcinoma) and a salivary gland neoplasm (adenoid cystic carcinoma). Ancillary methods also detected multiphenotypic differentiation (p16 block positivity along with ductal epithelial component expressing PAN-CK, CK7, CD117, and myoepithelial component expressing S-100, p63 and SMA) which lead to the identification of the lesion as HMSC.
Conclusion: As the HMSC entity is distinct from conventional squamous cell carcinoma and salivary gland carcinoma, it is important to identify its histological characteristics and differentiate it from its mimickers.

Keywords: HPV-related multiphenotypic sinonasal carcinoma; Human papillomavirus; Adenoid cystic carcinoma; sinonasal tract.

Introduction

HPV-related multiphenotypic sinonasal carcinoma (HMSC), originally known as HPV-related carcinoma with adenoid cystic carcinoma-like features, is identified as a distinct neoplasm of the sinonasal tract. It resembles a surface-derived neoplasm as well as has features of salivary gland carcinoma (particularly adenoid cystic carcinoma) [1, 2].

HMSC is associated with high-risk human papillomavirus (HPV). HPV has a strong association with approximately 20-25% of head and neck cancers, mostly in the region of the oropharynx. However, the sinonasal tract has also been identified as a site for HPV-associated lesions/neoplasms. HPV-related neoplasms usually have a better prognosis [1, 3, 4, 5].

Although HMSC presents as a large mass, the behavior is more indolent, underscoring the importance of recognizing this entity to establish a suitable treatment protocol.

Case Report

A 52-year-old male presented with a lesion in the left upper gingivo-buccal sulcus which was diagnosed as conventional squamous cell carcinoma initially and was treated accordingly for 2 years. There was a gradual increase in the size of

the lesion as compared to previous Contrast-Enhanced Computed Tomography scans and attained a size of 5x4x4cms epicentered in the left sinonasal region. Consequently, a re-biopsy of the sinonasal lesion was done for further evaluation. On examination of the re-biopsy specimen, the tumor cells were seen involving/arising from the overlying epithelium but did not have classical characteristics of squamous cell carcinoma. The tumor was biphasic with ductal and myoepithelial differentiation, with basaloid tumor cells predominantly in solid and cribriform pattern, separated by hyalinised stroma. Foci of abrupt keratinization were seen amidst the tumor cells. The tumor cells expressed p16 (block positivity) indicating HPV association. The ductal epithelial component expressed PAN-CK, CK7 and CD117. S-100 and SMA were expressed by the myoepithelial component in the tumor.

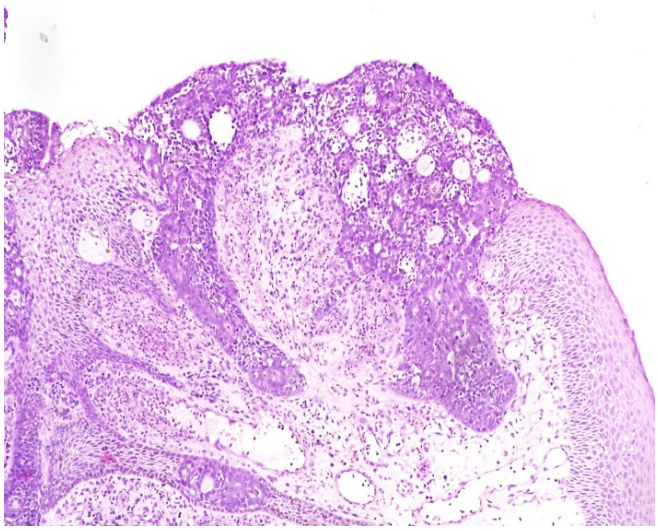

Figure 1: Tumor cells seen involving the surface epithelium.

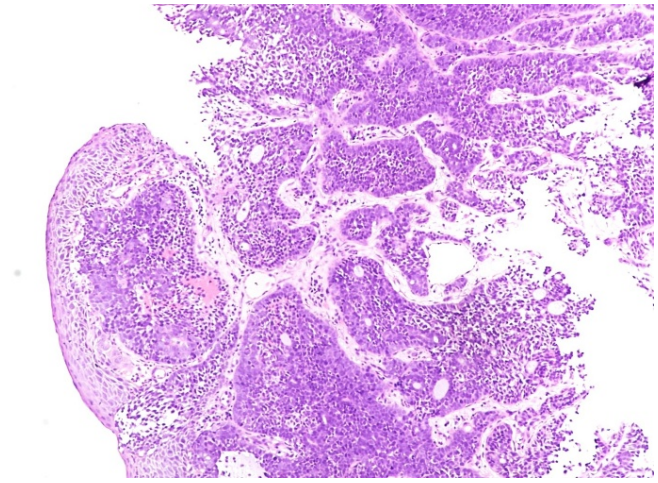

Figure 2: Basaloid cells seen in both solid and cribriform patterns, separated by hyalinised stroma.

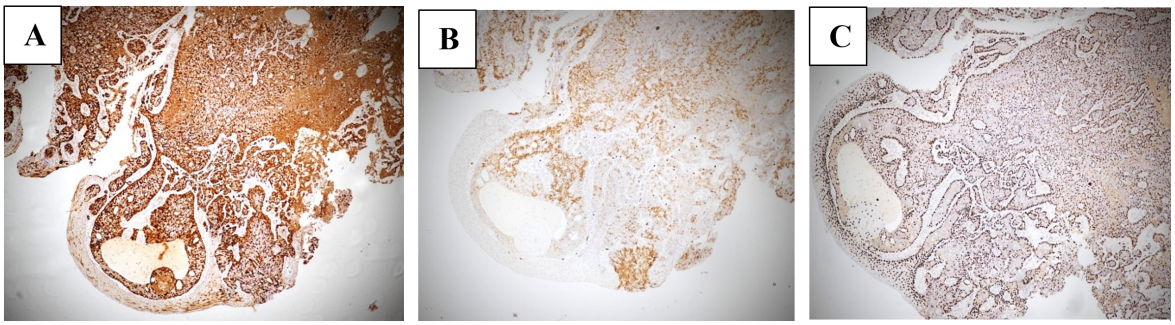

Figure 3: (A) p16 block positivity in the tumor cells, (B) CD117 expression in the epithelial component of the tumor, (C) p63 expressed by the myoepithelial cell layer in the tumor.

Discussion

The case under study had been previously diagnosed and treated as conventional squamous cell carcinoma based on the biopsy of the gingiva-buccal sulcus lesion. However, due to the gradual progression of the size of the tumor (which by then occupied the sinonasal region) and absence of metastasis, a re-biopsy from the sinonasal region was considered. It was this biopsy from the sinonasal region which showed the precise histomorphology consistent with HMSC.

The studies of Bishop JA et al [6], Hwang SJ et al [7] and Andreasen S et al [8] have characterized HMSC with the following common features: Origin from the sinonasal tract, involvement of the mucosal epithelium with atypical squamous cells and morphological appearance of a salivary gland neoplasm (adenoid cystic carcinoma) having ductal/epithelial and myoepithelial components. The tumors harbored transcriptionally active HPV but fusions related to salivary gland neoplasms (particularly fusion of the MYB gene which characterizes adenoid cystic carcinoma) are not detected. The case under study represents all these features. However, fusions related to salivary gland neoplasms have not been evaluated for due to lack of resources.

The term "Multiphenotypic" has been used for this entity as there is histomorphologic variation including squamous, ductal and myoepithelial lines of differentiation [1, 2]. The case under study also has demonstrated multiphenotypic differentiation (ductal and myoepithelial) as evidenced by the expression pattern of the immunohistochemistry markers (Figure 3).

HMSC has been called a distinct entity due to several factors. It is considered different from other HPV-related oropharyngeal lesions in view of clinical and behavioral factors. HPV-related carcinomas of the oropharyngeal region affect primarily the 5th-7th decade while HMSC affects a wider age group (28-90 years). HPV16 has been implicated in most of the oropharyngeal malignancies, while HPV33 has been found to be associated with HMSC. Oropharyngeal HPV-related malignancies are known to frequently metastasize to the lymph nodes while lymph node metastasis has not been recorded in the HMSC cases studied so far [1, 2, 3]. Even the present case under study does not show lymph node metastasis even after 2 years of initial presentation. It showed an increase in size over time and appeared to be locally aggressive.

HMSC involves the nasal cavity and paranasal sinuses, often with extension into adjacent structures. In the sinonasal tract, HPV is associated mostly with non-keratinising squamous cell carcinoma. A novel form of HPV-associated carcinoma having a morphological overlap of squamous cell carcinoma and salivary gland neoplasm (Adenoid cystic carcinoma) was described by Bishop et al [4]. The previous term ''HPV-related carcinoma with adenoid cystic carcinoma-like features" was put as a provisional entity (as a form of non-keratinising squamous cell carcinoma) in the WHO classification of tumors of the head and neck region.

Conclusion

The knowledge of HMSC is important to isolate such cases from its mimickers. Since these cases behave in a more indolent way, they can be followed up closely to study the prognostic characters in due course of time.

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