

**Original contribution**

# Human papillomavirus–associated adenocarcinoma of the base of the tongue

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**Summary** Human papillomavirus (HPV) is a major cause of oropharyngeal squamous cell carcinoma with characteristic clinical and pathologic features relative to their non-HPV-associated counterparts. Here we describe 2 cases of HPV-associated adenocarcinoma of the oropharynx. Both cases arose at the base of the tongue, and neither had the histologic or immunohistochemical features of a primary salivary gland tumor or metastasis from another location. One patient had metastases to neck lymph nodes and the lungs and died of disease 37 months after diagnosis. Evidence for an HPV association consisted of strong diffuse expression of p16, polymerase chain reaction–based detection of HPV16 DNA sequences, and localization of HPV by in situ hybridization within tumor cells of both primary and metastatic lesions. These results further expand the spectrum of HPV-associated head and neck malignancy. This rare entity should be distinguished from primary salivary gland adenocarcinoma and may be a candidate for HPV-specific targeted therapies.

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**1. Introduction**

Human papillomavirus (HPV) is a major cause of human cancer. Although best characterized in carcinomas of the cervix and anogenital region, HPV is now well recognized as a major cause of squamous cell carcinomas occurring in the head and neck (HNSCC). HPV-associated HNSCC is distinguished both clinically and histologically from non-HPV-associated HNSCC, for which the primary risk factor is tobacco use. HPV-associated HNSCCs predominantly arise in the oropharynx, particularly in the base of the tongue and

palatine tonsil. These tumors more often arise in individuals who have never smoked, and they occur at a modestly younger age on average than their smoking-associated counterparts [1]. The distinction between HPV- and non-HPV-associated HNSCC has become of increasing clinical relevance because it is now generally accepted that HPV-associated HNSCC has a significantly better prognosis, reflected in both disease-free and overall survival [2,3].

Smoking-related HNSCC typically shows a well-differentiated appearance, often with prominent keratinization. By contrast, HPV-associated HNSCC commonly shows a more immature basaloid appearance with a higher nuclear-to-cytoplasmic ratio and a denser chromatin pattern. HPV-associated HNSCC often presents with low T stage disease and prominent metastatic disease to neck

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