

# Diagnostic role of detecting HPV in a FNAC of metastatic laterocervical lymph node in a case of occult HPV-related head and neck squamous cell carcinoma

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## Key words

Fine-needle aspiration cytology • Human papillomavirus • Occult primary tumor • Basaloid squamous cell carcinoma

## Summary

Human papillomavirus (HPV)-related head and neck squamous cell carcinomas (HNSCC) are radiosensitive tumors and have a better prognosis than the conventional keratinizing HNSCC. Despite extensive radiographic and clinical evaluation in approximately 3% to 5% of patients who present with cervical lymph node metastases, the primary tumor remains

occult. The lack of a clinically identifiable primary tumor usually leads to more aggressive therapy, which can result in higher morbidity. Herein, we report a case of a patient with an occult HPV-related HNSCC, diagnosed detecting HPV in a fine needle aspiration cytology (FNAC) of metastatic laterocervical lymph nodes.

## Introduction

Human papillomavirus (HPV)-associated head and neck squamous cell carcinoma (HNSCC) accounts for up to 25 % of all HNSCCs<sup>1</sup>. These tumors largely arise from the oropharynx, particularly the tonsil and base of tongue. The first manifestation of HPV-associated HNSCC is frequently as metastasis to cervical lymph nodes. These metastases are often cystic with a predominantly non-keratinizing, basaloid morphology<sup>1</sup>. Patients who present with these metastases usually have a clinically identifiable primary tumor<sup>2,3</sup>. However, in approximately 3 % to 5 % of patients, the origin of the tumor is not clinically evident<sup>4</sup>. When the primary tumor remains unknown, wide-field irradiation is applied, resulting in increased morbidity. Because fine-needle aspiration cytology (FNAC) often is the first diagnostic procedure performed in patients with head and neck masses, some studies have explored the value of identifying HPV in FNAC of neck metastases to determine the origin of occult primary HNSCC<sup>5</sup>. Herein, we report a case of a patient with an occult HPV-related HNSCC, diagnosed detecting HPV in a FNAC of metastatic laterocervical lymph nodes.

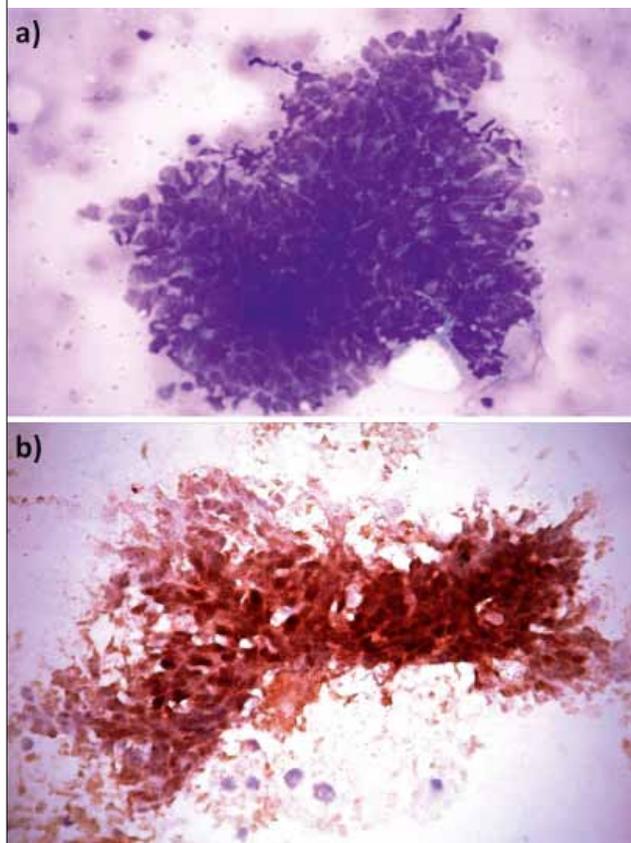
## Case report

A 54-year-old man presented to our hospital for a right laterocervical lymphadenopathy, not associated with pain or compressive symptoms and centrally hypoechoic at the ultrasonography. A FNAC of the lymph nodes was performed; wet fixed and air dried smears were made and stained with May-Grunwald Giemsa (MGG). FNAC revealed a few small lymphocytes and a monomorphic population of basaloid cells, forming clusters with peripheral palisading. The nuclear-cytoplasmic ratio was high, with dense hyperchromatic nuclei (Fig. 1A). Immunohistochemically, the cells showed a strong positivity for cytokeratins, p63, and p16 (Fig. 1B), and were negative for synaptophysin. Therefore, a diagnosis of metastatic basaloid SCC, probably of the head and neck region, was made. Pyrosequencing was performed to detect and genotype HPV DNA on the MGG smears; HPV type 16 DNA was detected, so the diagnosis was confirmed, and the patient was properly treated.

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**Fig. 1. a)** cluster of basaloid cells with peripheral palisading, high nuclear-cytoplasmic ratio and dense hyperchromatic nuclei (MGG; 400x). **b)** Immunohistochemically, the cells showed a strong positivity for p16 (400x).



## Discussion

Conventional HNSCC differs from HPV-related SCC epidemiologically, clinically, histologically, cytologically, and molecularly. It is more common in patients aged < 40 years and usually presents as a small or occult primary with advanced neck disease. Tobacco use and alcohol abuse are not prevalent risk factors, and sexual habits are important in the transmission of the virus<sup>6,7</sup>. Most HPV-related SCC, as discussed above, arise in the oropharynx, particularly in the tonsils and the base of the tongue. They are radiosensitive tumors and have a better prognosis than the conventional keratinizing HNSCC. Despite extensive radiographic and clinical evaluation, including magnetic resonance imaging, computed tomography scans, positron emission tomography scans, and multiple endoscopic biopsies, in approximately 3% to 5% of patients who present with cervical lymph node

metastases, the primary tumor remains occult. Even after extensive diagnostic workup with targeted biopsies, only 1 in 3 primary tumors is identified<sup>8</sup>. The lack of a clinically identifiable primary tumor usually leads to more aggressive therapy, which can result in higher morbidity. Therefore, it is important to identify the primary tumor and to make a correct diagnosis of HPV-related HNSCC in order to provide a targeted therapy<sup>9</sup>. FNA biopsies often are the first diagnostic procedure performed in patients who present with a neck mass, so that has led to study the possibility that, by identifying HPV-related SCC in FNA biopsies of cervical lymph nodes, it may be possible to determine the site of an occult primary. In our case, the morphological features of the metastasis, the positivity for p16 of the neoplastic cells and the detection of HPV 16 in the FNAC allowed to make a correct diagnosis of HPV-related HNSCC and to carry out proper treatment for the patient. So, our case highlights the diagnostic utility of FNAC of neck masses in patients with an occult primary head and neck cancer and the diagnostic value of detecting HPV in these specimens.

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