# Cytopathology in focus: Direct HPV testing in FNAs from cervical lymph node metastases

## Swikrity U. Baskota, MD

May 2020—According to a Centers for Disease Control and Prevention study from 2008 to 2012, there are about 16,000 cases of HPV-positive oropharyngeal squamous cell carcinoma per year in the United States. These carcinomas tend to present with small primary lesion and early nodal metastases as an initial manifestation of the disease. Furthermore, carcinoma of unknown primary presenting as a cystic metastasis in the head and neck has been linked frequently to oropharyngeal squamous cell carcinomas, mainly of palatine tonsils and base of the tongue. Because it is easy to access these clinically evident neck masses, fine-needle aspiration cytology has been the cornerstone of the diagnoses of these lesions.

It is recommended that HPV-DNA testing be done in these FNA samples to identify the site of unknown primary and determine the HPV status of a metastatic node from a known oropharyngeal squamous cell carcinoma. Determining that an oropharyngeal squamous cell carcinoma is positive for high-risk HPV has significant implications for patient prognosis, and it is now integrated into the recently updated AJCC Cancer Staging Manual, eighth edition. HPV status also determines patient eligibility for clinical trials of new treatment regimens and modalities.

In recent years, several studies have been done to confirm high-risk HPV, using DNA/RNA-based in situ hybridization, polymerase chain reaction-based methods, or HPV L1 immunohistochemistry along with p16 immunohistochemistry. Recently there has been a paradigm shift to molecular testing of high-risk HPV DNA in liquid-based cytology fine-needle aspiration cytology specimens from the head and neck region using various platforms like Aptima, Cervista, Cobas, Hybrid Capture 2, and BD Onclarity. However, there are rare to no published studies that used the same HPV-testing platform in both the cytological and follow-up surgical specimens.

In the study by Rollo F, et al., at Regina Elena National Cancer Institute of Rome, Italy, 63 liquid-based cervical FNA cytology samples and the corresponding formalin-fixed, paraffin-embedded tissues for 39 cases were tested for HPV DNA using the PCR-based INNO-LiPA HPV Genotyping Extra II (Fujirebio). Excellent agreement was observed between cytology and histology specimens (raw agreement: 97.5 percent; Cohen κ: 0.94). Furthermore, they had success with yield of HPV-DNA material in predominantly necrotic cytology samples. In addition, there was excellent correlation between p16 and HPV-DNA results in the histology specimens (Rollo F, Doná MG, Pellini R, et al. Cytology and direct human papillomavirus testing on fine needle aspirates from cervical lymph node metastases of patients with oropharyngeal squamous cell carcinoma or occult primary. *Cytopathology.* 2018;29[5]:449–454).

Rollo F, et al., demonstrate in their study that INNO-LiPA is a valid HPV-DNA testing platform for liquid-based cytology samples, even in cases with extensive necrosis. While this testing platform is not currently approved for use in the United States, the study is recommended reading because it provides further evidence of the value of HPV testing of predominately necrotic cervical lymph node FNAs and serves as a framework for laboratories aiming to validate HPV testing methods for liquid-based cytological specimens. 

*Dr. Baskota is a PGY-3 AP resident at the University of Pittsburgh Medical Center and a member of the CAP Cytopathology Committee.*