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ORIGINAL ARTICLE

Ultrasonography-guided fine-needle aspiration with concurrent small core biopsy of neck masses and lymph nodes yields adequate material for HPV testing in head and neck squamous cell carcinomas

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Squamous cell carcinoma;
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Introduction Human papillomavirus (HPV)-associated head and neck squamous cell carcinoma (HNSCC) is a distinct epidemiologic and pathologic disease that is increasing in frequency. Currently, there is no clinical standard for obtaining diagnostic material or determining HPV status in the workup of these patients. The purpose of this study was to the determine the specimen adequacy for HPV testing on material obtained by ultrasonography-guided fine-needle aspiration and small core biopsy of neck masses and lymph nodes in patients with HNSCC.

Materials and methods Cases were reviewed for patients who (1) underwent ultrasonography-guided fine-needle aspiration with or without small core biopsy of neck masses and lymph nodes, (2) were diagnosed with HNSCC, and (3) were tested for HPV. Several HPV detection methods were used, including p16, HPV 16 and 18, and high-risk and wide spectrum HPV in situ hybridization.

Results Of the 63 patients studied, 48 (76.2%) were male and 15 (23.8%) were female. The overall adequacy rate of cell block and small core biopsy material was 88%. Forty-five of 63 patients (73%) tested positive for HPV. Overall agreement was achieved in 92.9% of cases in which both p16 and HPV in situ hybridization were performed. On available surgical follow-up, histocytologic correlation for HPV-related testing was 100%.

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Conclusions Ultrasonography-guided fine-needle aspiration with concurrent small core biopsy of neck masses and lymph nodes, along with on-site evaluation by a pathologist, yields adequate material for reliable HPV-related testing in HNSCC and should be incorporated into the routine pathologic evaluation for these patients.

Introduction

Human papillomavirus (HPV)-related head and neck squamous cell carcinoma (HNSCC) has become a well-established entity that represents a subset of biologically and clinically distinct SCCs. HPV-related HNSCC increased by 225% from the late 1980s to the early 2000s[1] and may surpass the annual number of cervical cancers by the year 2020.[2] This escalation of cases is due to high-risk HPV, particularly type 16, which has been recognized as a causative agent in up to 70% of oropharyngeal cancers.[2]

These cancers often present at an advanced clinical stage with metastatic cervical nodal involvement, despite being characterized by small primary tumor size. Furthermore, the primary tumor site cannot be identified in up 5% of these cases.[3] Interestingly, metastatic lesions resemble primary tumor lesions, maintaining p16 and HPV expression.[4,5] HPV studies can, therefore, be performed on tissue obtained from more accessible sites, such as neck lymph nodes and masses. Despite higher staged disease, these patients have a lower risk of tumor progression and have a significantly improved overall survival than do patients with conventional HPV-negative HNSCC.[6-8] Therefore, some have suggested that this subset of patients should be treated differently and less aggressively. In fact, the College of American Pathologists and the National Comprehensive Cancer Network have recommended routine HPV testing as part of the pathologic evaluation of oropharyngeal SCCs for prognostic purposes.

Fine-needle aspiration (FNA) is a safe and cost-efficient, minimally invasive technique routinely used to evaluate head and neck masses. Using ultrasonography (US)-guided FNA along with immediate on-site interpretation by a cytologist enhances sensitivity of FNA to obtain adequate material for HPV testing. Furthermore, obtaining a small core biopsy after the diagnostic site has been identified by FNA provides additional material to be used for diagnostic purposes and ancillary testing. This practice could provide early and valuable diagnostic, prognostic, and therapeutic information. Because of these reasons, the purpose of this study was to the determine the specimen adequacy for HPV testing on material obtained by US-guided FNA and small core biopsy of neck masses and lymph nodes in patients with HNSCC.

Materials and methods

This study was approved by the Johns Hopkins Medicine Institutional Review Board. The Johns Hopkins Hospital Cytopathology database was retrospectively searched for US-guided FNA and concurrent small core biopsy cases of mass lesions and lymph nodes yielding a diagnosis of SCC with a head and neck primary. From November 21, 2005, through August 22, 2014, a total of 63 cases were identified for review. Medical records including the cytopathology reports and prior surgical pathology reports were reviewed, and clinical information including the patients' age, sex, race, tumor site, and diagnosis was recorded.

All 63 specimens were collected under US guidance and a pathologist or a cytotechnologist was on-site to evaluate the specimen for adequacy. All patients were scanned by a radiologist to find the most suspicious mass or lymph node prior to the FNA procedure. The FNAs were performed using a 25-gauge spinal needle, and the small core biopsies were performed with a 20-gauge core biopsy device after administration of 1% buffered lidocaine for local anesthesia. Multiple aspirations were performed for each case and small core biopsies were taken when the size and the anatomical site of the lesions allowed. None of the patients reported any complications due to the FNA procedure.

The aspirated material was prepared using both air-dried and alcohol-fixed methods. The aspirates were immediately smeared on glass slides and either air-dried, or fixed in 95% ethanol. The air-dried slides were stained with Mercedes Medical Platinum Line Quik-Dip fixative and stain during on-site evaluation (Fig. 1A, B). The alcohol-fixed slides were stained by the Papanicolaou methodin the cytology laboratory (Fig. 1C, D). The remaining material in the needle was rinsed with Hank balanced salt solution and was processed to create formalin-fixed paraffin-embedded cell blocks. When clinically appropriate, small core biopsies were obtained and immediately stored in formalin to be processed and paraffin-embedded. Paraffin-embedded cell blocks and small core biopsies were processed in the histology laboratory and were cut into 5-μm sections and subsequently stained with hematoxylin and eosin(Fig. 2A). HPV studies and immunohistochemical (IHC) stains were performed on cell block or core biopsy material depending on specimen adequacy.

For each case, adequacy for HPV testing and the cytological integrity and cellularity were determined by reviewing the cell block and small core biopsy when it was available. Two authors (D.A. and Z.M.) reviewed all the cytologic specimens, core biopsies, HPV studies, and other ICH stains. The results were recorded and differences were resolved by consensus. HPV status was determined using several detection methods, including the p16 immunostain and HPV 16, HPV 18, high-risk HPV, and wide spectrum (WS) HPV by in situ hybridization (ISH). Different