Peterson's Press

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INSIDE THIS ISSUE:

Throat Cancer & HPV Infection 1

Welcome Scott Woborny, Systems Manager 2

New Cervical Cytology Screening Guidelines 2

"Grandfather" TC Clause to Expire June 30 2

"Dual Review" Imager Up and Running 2

UP FRONT

Throat Cancer and Human Papillomavirus (HPV) Infection

Feriyl Bhaijee, MD

The term *throat cancer* refers to malignancies of the pharynx and larynx. The vast majority of these are squamous cell carcinomas (SCC). Traditional risk factors for throat cancer include tobacco use and alcohol consumption. However, in the oropharynx, particularly the tonsil, human papillomavirus (HPV) infection has emerged as a prominent risk factor. HPV is found in 45% to 95% of oropharyngeal SCC. Unlike tobacco-related throat cancer, which is decreasing in incidence with declining rates of tobacco use, HPV-related oropharyngeal SCC shows increasing incidence in several Western countries.

The association between oropharyngeal SCC and HPV infection is now well established. HPV subtypes are classified as high- or low-risk based on their malignant potential. Only high-risk HPV subtypes (including 16, 18, 31, 33, and 35) have been associated with oropharyngeal SCC of which HPV 16 is the most common subtype identified in HPV-positive cancers. High-risk HPVs produce two oncoproteins, E6 and E7, which facilitate viral replication and malignant transformation. HPV E7 protein binds to and degrades the retinoblastoma protein (pRb), which results in upregulation of the p16 protein. HPV-positive tumors frequently show high expression of p16, thus detection of the p16 protein by immunohistochemistry is considered a useful surrogate marker for HPV-positivity. HPV-positive oropharyngeal SCC represents a distinct subset of head and neck SCC. HPV-positive cancers, especially tonsillar cancers, usually present at a younger age, and often without a prior history of tobacco and alcohol use. It appears, however, that HPV-associated oropharyngeal SCC is, in some ways, a sexually transmitted disease: factors such as number of sexual partners (including oral sex partners), prior history of genital warts, and HIV infection confer a higher risk of tonsillar and base-of-tongue cancers.

Despite smaller primary tumor sizes at presentation, HPV-positive cancers often present with large, cystic, nodal involvement. These lateral cervical metastatic masses may mimic branchial cleft cysts, especially in younger patients. Histologically, HPV-positive tumors are typically nonkeratinizing, and 'basaloid' in appearance, in contrast to the keratinizing appearance of HPV-negative SCC.

Overall, however, HPV-positive oropharyngeal SCC has a better prognosis than HPV-negative cancers, regardless of lymph node involvement, age, gender, clinical stage, tumor differentiation, or treatment strategy. Studies show an 80% to 95% two- to three-year overall survival rate for patients with HPV-positive SCC, compared to a 57% to 62% rate for those with HPV-negative cancers. The pathogenetic mechanisms underlying the association between HPV positivity and improved outcome are not clearly understood and may involve a combination of patient- and tumor-related factors. HPV-positive tumors have significantly fewer chromosomal abnormalities than HPV-negative cancers.

Oropharyngeal SCC is usually treated by surgical resection and adjuvant chemoradiotherapy. Transoral robotic surgery (TORS), an emerging robotic-assisted technology, offers disease control in both HPV-negative and HPV-positive patients with oropharyngeal SCC when followed by appropriate adjuvant therapy. The clinical benefits of TORS include avoidance or dose reduction of adjuvant chemoradiotherapy and improved swallow function and cosmetic outcome. Randomized controlled trials are needed to determine the appropriate role of TORS in clinical management.

The clinical significance of HPV infection in laryngeal SCC is unclear. Meta-analysis suggests that up to 25% of laryngeal SCC contains HPV infection and, as in oropharyngeal SCC, HPV 16 is the most commonly identified subtype.

In summary, HPV-related oropharyngeal SCC represents a distinct clinicopathologic subtype of head and neck SCC. HPV positivity in oropharyngeal SCC confers a better prognosis than HPV negativity, and HPV status is a robust prognostic indicator for overall survival, treatment response, and tumor control. HPV infection also occurs in laryngeal SCC, but the clinical relevance thereof requires further investigation.

NEWS AND NOTES

WELCOME SCOTT A. WOBORNY

Please make welcome Scott Woborny, Systems Manager. Extraordinary patient care is more dependent upon information technology than ever, and Scott is here to ensure you benefit from all services available. Peterson Laboratory offers you Online Test Ordering, Online Results Viewing, Online Supply Ordering, Auto faxed Results and result interfaces as appropriate. No doubt you will personally experience his highly-developed information technology skills soon.

A native of Waterville, Scott brings previous experience in information technology with Landmark National Bank, NCR/ AT&T and Farm Bureau. You may contact Scott at swoborny@petersonlab.com, (desk) 785-539-5363, ext 151, (cell) 785-587-5708.

NEW PAP SCREENING GUIDELINES

The American Cancer Society, the American Society for Colposcopy and Cervical Pathology, and the American Society for Clinical Pathology recently released new guidelines for the prevention and early detection of cervical cancer. The finalized updated guidelines recommend:

- Women should not be screened before age 21. Women 21 to 29 should be screened with the Pap test alone (conventional or liquid-based) every three years. HPV testing should NOT be used for screening in this age group.
- For women 30 and over, the preferred approach is the Pap test plus HPV testing ("co-testing") every five years. Continued screening with the Pap test alone (without HPV testing) every three years is an acceptable alternative. While screening with HPV testing alone is promising, at this time it is not recommended for most clinical settings.
- Screening is not recommended for women over age 65 who have had at least three consecutive negative Pap tests or at least two negative HPV tests in the last 10 years, with the most recent test in the last 5 years. Women in this age group who have a history of pre-cancer (CIN2 or a more severe diagnosis) should continue routine screening for at least 20 years.
- Women who have undergone a hysterectomy (with removal of the cervix) for reasons not related to cervical cancer or pre-cancer should not be screened.
- Women who have been vaccinated against HPV should follow the age-specific recommendations in these guidelines (for unvaccinated women).
- Women with a slightly abnormal Pap test result (called "ASC-US") and a negative HPV test can be screened again with co-testing in 5 years or with the Pap test alone in 3 years.
- Women with a negative Pap result but a positive HPV test can either be re-screened with co-testing in one year, or tested with a test for specific types of HPV (HPV16 and HPV 18).

The new guidelines are not intended for women with a history of cervical cancer, exposure to DES in utero, or women who are immunosuppressed (e.g. HIV positive). Costs and other financial issues were not considered in creating the guidelines.

TC GRANDFATHER PROVISION TO EXPIRE JUNE 30TH

The TC Grandfather Provision allows independent laboratories to bill Medicare for the technical component (TC) of services provided to hospital patients. Any hospital that had an existing arrangement with an independent lab prior to 1999 was covered, or 'grandfathered." The TC of laboratory services could be billed directly to Medicare by the independent laboratory. Elimination of the Grandfather Provision has been proposed consistently since its passage. On February 22, 2012, Congress eliminated the Provision, with a four-month extension expiring June 30.

After June 30, independent laboratories such as Peterson Laboratory Services will be required to invoice hospitals for the TC of the pathology services they provide to Medicare patients. In the coming weeks, we will be taking extra care to educate our clients on this issue and prepare you for the resulting changes, should the provision not get extended.

"DUAL REVIEW" IMAGER UP AND RUNNING

With the new guidelines for cervical cancer screening calling for a 5-year testing interval, accuracy is more important than ever. As our client, you have the assurance of "dual review" computer-assisted pap screening process. Eighty-seven percent of all physicians choose the ThinPrep pap test, and more than 70% of those are imaged.

Interfering Substances: CLSI, ACOG and ASCCP all recommend that no lubricant be used during pap testing. Warm water may be used. If you are using a plastic speculum, or in instances when a lubricant must be used, take care not to contaminate the cervix or collection devices with lubricant. A tiny amount of lubricant may be used, just enough to sparingly coat the speculum with a gloved finger, avoiding the tip of the speculum. These organizations also recommend not taking a pap during menses.

ThinPrep imaging measures DNA content to identify areas of interest for cytology review. The result is increased disease detection including pre-cancerous (CIN 2 and 3) High Grade Intraepithelial. We welcome your visit to see the imager in action—very impressive!

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