



Florida/Caribbean AIDS Education and Training Center

HIV CareLink

A Newsletter for HIV/AIDS Primary Care Providers

ABOUT US

The Florida/Caribbean AIDS Education and Training Center provides state-of-the-art HIV education, consultation, and resource materials to health care providers in Florida, Puerto Rico and the US Virgin Islands.

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Journal Watch: Oral Cancer and Human Papillomavirus (HPV)

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Human papillomavirus (HPV) has been established as a major etiological factor of anogenital cancer. In addition, HPV has been implicated in oral carcinogenesis, but its detection rates appear to be highly variable, depending on the patient population tested, the molecular methodology used, as well as the type of oral specimen investigated. HPV infection and disease, including that of the oral cavity, has not dramatically declined since the introduction of potent combination therapy to control HIV. Two manifestations of HPV in the oral cavity that may be on the rise are HPV-32-associated oral warts and HPV-16-associated oral cancers.¹

While tobacco and alcohol are the primary risk factors for development of head and neck squamous cell carcinoma (HNSCC), epidemiological studies report a strong association with HPV in a subset of HNSCC.²

Risk of Head and Neck Squamous Cell Carcinoma

- For pharyngeal cancer, risk increased with increasing alcohol consumption (OR 5.1 for ≥ 25 vs < 3 drinks/week) and smoking (OR 6.9 for ≥ 45 pack year vs never smoked) among HPV-16 seronegative subjects but not among HPV-16 seropositive subjects.³
- However, among light drinkers or never smokers, HPV-16 seropositivity was associated with a 30-fold increased risk of pharyngeal cancer. These authors concluded that alcohol or tobacco use does not further increase risk of HPV-16-associated pharyngeal cancer.³
- There is additional evidence that supports considering HPV-16-positive HNSCCs and HPV-16-negative HNSCCs as distinct cancers because the risk factor profiles differ.

HPV-Associated Head and Neck Cancer

- HPV-associated cancers represent a distinct clinico-pathological entity, which is generally characterized by a younger age at onset, basaloid or warty histopathology, association with sexual behavior, and better prognosis, when compared with their HPV-negative counterparts.⁴
- The incidence of oropharyngeal cancers, has been increasing in the US. As a substantial proportion of noncervical cancers are caused by HPV-16 and 18. Current HPV vaccines, targeting those types, may hold promise in reducing burden of HPV-associated noncervical cancers (oral and anal), in addition to cervical cancers.⁵

Anal Cancer Preceding Oral Cancer

Two recent case reports described HIV-infected patients who first developed HPV-related anal squamous cell carcinoma (SCCA) and later developed oral SCCA. Both patients were responding to antiretroviral therapy with undetectable viral loads when they developed oral cancer. This further supports the need for careful oral and anal screening for HIV-infected patients.⁶

HPV-Associated Oral Cancer⁷

Sites

- A study from the Centers for Disease Control and Prevention identified and reviewed 44,160 (US, 1998-2003) cases of potentially HPV-associated cancers of the oropharynx and oral cavity.
 - Tonsil was the most common site (43.6%)
 - Base of tongue was second (38.4%)
 - Other sites (18.0%)

Incidence

- Highest among blacks
- Higher among non-Hispanics and men than Hispanics and women
- Annual incidence rates of potentially HPV-associated cancers of the tonsil and base of tongue both increased significantly from 1998-2003, whereas the incidence rates of cancer at the comparison sites (i.e. those not shown prior to be associated with HPV) generally decreased.

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- With widespread implementation of HPV vaccination, the incidence of HPV-associated cancers should be monitored.

Oropharyngeal Cancer and Risk Assessment

A high lifetime number of vaginal-sex partners (≥ 26) was (OR, 3.1; 95% confidence interval [CI], 1.5 to 6.5), and a high lifetime number of oral-sex partners (≥ 6) (OR, 3.4; 95% CI, 1.3 to 8.8) were associated with oropharyngeal cancer. Oropharyngeal cancer was significantly associated with oral HPV (any of 37 types) infection (OR, 12.3; 95% CI, 5.4 to 26.4), oral HPV-16 infection (OR, 14.6; 95% CI, 6.3 to 36.6), and HPV-16 L1 capsid protein seropositivity (OR, 32.2; 95% CI, 14.6 to 71.3). HPV-16 DNA was detected in 72% (95% CI, 62 to 81) of 100 paraffin-embedded tumor specimens, and 64% of patients with cancer were seropositive for the HPV-16 oncoprotein E6, E7, or both.⁸

These authors concluded that oral HPV infection is strongly associated with oropharyngeal cancer among subjects with or without the established risk factors of tobacco and alcohol use.⁸

HPV Transmission and Saliva⁹

Saliva is an oral fluid that may play a role in HPV transmission, although the detection rates of the virus are lower than found in tissue. HPV-related pathology is increased in the oral cavity of HIV-infected individuals.

In this study, saliva samples were collected from 68 patients with SCCA and 34 HIV-infected individuals. HPV DNA sequences were detected by L1 consensus PCR, followed by restriction fragment length polymorphism (RFLP) analysis and DNA sequencing to type HPV. Results demonstrated HPV DNA detected in 7/68 (10.3%) of oral cancer patients and 12/34 (35.3%) of HIV infected individuals, a significant difference. The prevalence in HPV positive samples of oncogenic types of HPV was similar in oral cancer and HPV infected cases (71.4% and 66.7%) respectively. HPV type 16 was the most common type in both groups.

The quantitative detection of HPV in saliva significantly depended on immune system efficiency, and the increased detection rates of HPV in saliva of HIV-infected individuals may be associated with development of HPV-related oral lesions, including malignancy.

Prognostic Value for HPV Associated Oral Cancers¹⁰

HPV is a risk factor for head and neck cancers, yet HPV-associated tumors have better prognosis than HPV-negative tumors. Presence of antibodies to HPV-16 E6 and E7 oncoproteins are associated with better clinical outcomes.

Summary

- These findings underscore the importance of oral (and anal) examinations for all subjects to assess for HPV lesions, as well as squamous cell carcinoma, regardless of CD4 count or viral load.
- These findings also support the importance of protected sex regardless of HIV viral load.
- Protection is recommended even if the patients have low or non-detectable HIV viral loads, as HPV is reportedly more likely to be in saliva in these cases.

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