Lower Genital Tract Neoplasia in Women With HIV Infection

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Although overall death rates from the acquired immune deficiency syndrome (AIDS) are declining rapidly, the incidence of human immunodeficiency virus (HIV) in women continues to climb, and HIV-associated gynecologic disease is also likely to increase over the next decade. In this paper on lower genital tract neoplasia in women with HIV infection, Abercrombie and Korn review some of the many studies documenting the increased incidence of cervical human papillomavirus (HPV) and HPV-associated disease in this population. The clinical importance of these studies is underscored by recent data from New York City, where the incidence of invasive cervical cancer increased significantly from 1990 to 1995 in HIV-positive women, compared to the general population of 25- to 49-year-old women.[1]

Anogenital HPV Infection in Women
As noted by Abercrombie and Korn, anogenital HPV infection in women is often multifocal, and women with cervical infection or lesions are at increased risk for vaginal, vulvar, and anal lesions. Anal HPV infection deserves additional comment because, although relatively rare, the incidence of anal cancer is increasing. From 1973 to 1989, the incidence of this infection in US women rose by over 35%, and it continues to rise at a rate of almost 2% per year.[2] Current estimates of the incidence of anal cancer are 7/1,000,000 in men and 9/1,000,000 in women.[2] In Denmark, women with a history of cervical intraepithelial neoplasia or invasive cervical cancer had an odds ratio of 5.2 for the subsequent development of anal cancer compared with colon cancer, and the association between cervical and anal cancer was at least as strong as that between cervical and vulvar cancer.[3] In the United States, women with cervical cancer had a relative risk of 4.6 for subsequent anal cancer, as compared with the general population, and women with primary anal cancer had a relative risk of 3.4 for a subsequent case of high-grade cervical intraepithelial neoplasia.[4]

Association Between Anal Cancer and HPV
A number of investigators have demonstrated an association between anal cancer and HPV.[5,6] In contrast to cervical cancer, the biology of anal cancer is not well described. Nevertheless, despite their origin at different anatomical sites, cervical and anal cancers appear to have much in common. Infection with HPV frequently occurs in areas of squamous metaplasia. In the cervix this is the transformation zone; in the anus, it is the transitional epithelium of the anorectal junction. Both cervical and anal cancers frequently arise in these junctional regions from cervical squamous intraepithelial lesions (CSILs) or anal squamous intraepithelial lesions (ASILs), respectively. A model for the natural history of anal HPV infection and ASILs has been described for men who have sex with men, and prospective studies confirm the increased incidence and progression of ASIL in HIV-positive homosexual men. In one cohort, 15% of homosexual men developed high-grade ASIL over a mean follow-up period of 20 months.[7] In another, the incidence of high-grade ASIL within 2 years was 20% in HIV-positive homosexual men with normal cytology and no lesions seen at baseline anoscopy.[8] Overall, the experience with men suggests that immunosuppression is associated with high-level HPV infection and potentially precancerous anal disease. Studies of the natural history of anal disease in men have also shown that anal lesions may progress...
to a higher level in a short period, and that regression of these lesions is rare. Together with recent studies documenting an increase in anal cancer among men with AIDS, these data suggest that a high proportion of HIV-positive men may be at risk for anal cancer. Two cross-sectional studies have documented an increased prevalence of anal HPV infection and disease in HIV-infected women as well. In one early study, HIV-infected women were at increased risk for both cervical and anal HPV infection and epithelial abnormalities, as compared with HIV-negative women, and those HPV-associated abnormalities were linked with immunosuppression. In this cohort, anal HPV infection and disease were at least as common as cervical infection and disease.[9]

Subsequently, a similar study involving a larger cohort of women with and without HIV infection described comparable rates of anal cytologic abnormalities and HPV infection.[10] Although prospective data for women are not available, these cross-sectional data suggest that women with HIV infection are also at increased risk of developing anal cancer. As with cervical disease, anal cancer is probably preventable with appropriate screening and treatment.

**Would Screening for ASIL in HPV-Infected Women Be Beneficial?**

The hypothesis that screening for ASIL may offer benefit is predicated on the assumption that these lesions, particularly when high grade, have the potential to progress to invasive anal cancer. This assumption relies largely on knowledge of the natural history of similar lesions in the cervix. No studies of the natural history of ASIL in women or the efficacy of therapy for ASIL in preventing cancer have yet been conducted. However, evidence to date suggests that the sensitivity of anal cytology is similar to the sensitivity of cervical cytology.[3,11]

In a study aimed at assessing anal cytology as a screening tool for anal disease, Palefsky and colleagues performed 2,958 anal examinations of 407 HIV-positive and 251 HIV-negative homosexual or bisexual men who were participating in a prospective study of ASIL. They compared these cytologic results with those obtained through biopsy of visible lesions on anoscopy. Abnormal cytology was defined to include atypical squamous cells of undetermined significance (ASCUS) and ASIL. The sensitivity of anal cytology for the detection of biopsy-proven ASIL was 69% in HIV-positive men at their first visit and 81% for all subsequent visits combined. The absence of columnar cells did not affect the sensitivity, specificity, or predictive value of anal cytology.[12]

The incidence of cervical cancer has declined dramatically in the United States, largely as a result of cytologic screening. A similar preventive approach for anal cancer may be worthwhile and, indeed, is recommended for HIV-infected homosexual men.[2] The extent to which women known to be at increased risk for anal cancer (eg, women with high-grade cervical intraepithelial neoplasia or immunosuppression) would also benefit from anal cytologic screening is currently unknown. With the advent of highly active antiretroviral therapy, women with HIV infection will certainly live longer. If the incidence of anal disease increases in women as it has in men, strategies for the prevention or early detection of anal cancer in women with HIV will be needed.

**References:**


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