Editorial Comment: Screening for Anal Dysplasia—Are We All on the Same Page?

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By AIDS Reader [1]

Anal cancer has become one of the most common non–AIDS-defining tumors in HIV-infected persons.1,2 The incidence of anal intraepithelial neoplasia (AIN) is also markedly increased in HIV-positive men,3 particularly those who have sex with men (MSM), despite the introduction of highly active antiretroviral therapy.4

Current evidence indicates that premalignant high-grade anal squamous lesions can progress to invasive anal carcinoma over time. Using cervical cancer prevention as a paradigm, anal cytology has thus been recommended as a primary screening tool for anal dysplasia in at-risk HIV-positive men.5,6 Men whose anal Papanicolaou (Pap) test yields abnormal results should undergo high-resolution anoscopy (HRA) to identify dysplastic lesions, to obtain biopsy specimens, and if feasible, to treat the lesions.7

HRA is analogous to colposcopy of the cervix. We commend Siekas and Aboulafia8 for establishing an anal dysplasia clinic for HIV-infected men in Seattle. To further advance this field and facilitate patient care, all health care providers (HIV clinicians, surgeons, and pathologists) dealing with anal lesions should endeavor to effectively communicate the correct location of the lesion (eg, anal canal, anal margin, perianal region) and its diagnosis in an agreed-on manner.

There is an anatomical, a histological, and a surgical anal canal.9,10 The anatomical anal canal extends from the dentate (pectinate) line to the anal verge. The dentate line is an important macroscopic landmark of the anal mucosa. Tumors above this line drain to the perirectal and paravertebral lymph nodes, whereas those below the dentate line drain to the inguinal and femoral nodes. The histological anal canal extends from the anal valves and sinus to the anal verge. The histology of the anal canal mucosa (from the rectum to the anal margin) consists of glandular, transitional, and then squamous epithelium. The boundary of the anal margin with perianal skin (epidermis) is indistinct on macroscopic examination. The surgical anal canal begins where the rectum enters the palpable puborectalis sling (anorectal ring) and ends at the anus (anal verge). The perianal skin (anal margin) is defined by the appearance of skin appendages. The anatomical location of anal cancer is important for cancer staging purposes. Staging (using the TNM classification) of anal carcinoma should be performed in accordance with the criteria described by the American Joint Committee on Cancer.11 Unlike mucosal carcinomas of the anal canal, those arising from the anal margin and perianal region should be staged using skin cancer criteria.11

The term “condyloma acuminatum” is used to refer to a common anogenital wart, the most common manifestation of human papillomavirus (HPV) infection of the anal and perianal region. In HIV-infected persons, anal condylomata have a low propensity for progression to malignancy. Since clinically banal condylomata may harbor areas of high-grade anal dysplasia, it is recommended that they be removed and if feasible submitted for histopathological evaluation. Advanced presentation of warts may reflect more aggressive disease rather than a failure of early diagnosis.

Squamous dysplasia of the anal canal diagnosed on histopathological grounds is termed “AIN.” AIN is divided into 3 grades based on progressively severe cytological atypia and the level of involvement of the squamous mucosa by dysplastic cells: AIN I (mild dysplasia), AIN II (moderate dysplasia), and AIN III (severe dysplasia or carcinoma in situ).12,13 AIN of the anal canal usually occurs in the transitional epithelium and squamous epithelium below the dentate line. AIN I is considered a low-grade squamous lesion (LGAIN), whereas AIN II and AIN III are considered high-grade squamous lesions (HGAIN). Like the Bethesda system used for reporting anal cytology, a 2-tiered system (LGAIN and HGAIN) offers better interobserver reproducibility. Bowen disease refers to squamous dysplasia...
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(usually carcinoma in situ) of the anal margin and adjacent perianal skin. Anal Pap tests need to be done on specimens from the entire anal canal; that is, epithelial cells from the glandular mucosa, anal transformation zone, and squamous portion should be represented. Adequacy of an anal-rectal exfoliative cytology sample is defined by sufficient cellularity (of nucleated squamous cells), evidence of sampling above the keratinized portion of the anal canal (ie, by the presence of rectal glandular cells and/or squamous metaplastic cells), and absence of obscuring material (eg, fecal material). A 2-tiered (Bethesda) system has been advocated to report dysplastic anal cytology findings: identified as a low-grade squamous intraepithelial lesion or high-grade squamous intraepithelial lesion (HSIL). While the sensitivity of abnormal cytology to detect HSIL in HIV-positive men is higher than in HIV-negative MSM, overall, the anal Pap test in the HIV-positive population is an inaccurate predictor of high-grade anal dysplasia on biopsy. The optimum use of HPV testing on an anal cytology sample in this setting has yet to be defined, given that multiple high-risk HPV types are highly prevalent in anal samples obtained from men infected with HIV.

The goal of screening is to detect anal dysplasia early and eradicate AIN, thereby preventing the progression of such lesions to invasive squamous cell carcinoma (SCC). SCCs make up the majority of all primary anal cancers. Varied histopathological patterns of anal carcinomas reflect the diverse histology of this anatomical area. Fortunately, treatment options for anal dysplasia and anal cancer in HIV-infected persons are expanding, which may lead to decreased morbidity and mortality. Expertise in treating such patients is important. More studies, particularly in the area of anogenital HPV infection in men, are needed. Soon, the impact of the HPV vaccine, which is currently approved for use in women and is in clinical trials in men, on anogenital HPV infection will need to be assessed. Providing good-quality anal dysplasia clinics is necessary to help accomplish this feat. We are appreciative of authors such as Siekas and Aboulafia for sharing their experience with us. As clinics and procedures expand and proliferate, we call for standardization in anatomical, cytological, and surgical pathology reporting.

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