

Cytopathology and more: Interrater agreement of anal cytology

Benjamin L. Witt, MD

May 2013—Anal-rectal cytology has been used to evaluate HPV-related lesions of the anal canal, particularly in high-risk populations. Because anal cancer is uncommon in the general population, there is no utility in surveillance cytologic assessment on a population-wide scale (as with the Pap test for cervical disease). However, in certain populations, such as men who have sex with men (MSM) and HIV-positive men and women, the risk for anal cancer is higher and approaches the risk of cervical cancer reported in unscreened populations of women. Thus, given that anal cancer shares an HPV-related etiology with cervical cancer and involves a similar squamous mucosal site, anal cytology has been recommended as a method of screening for the prevention of anal cancer through the detection of precancerous lesions (anal intraepithelial neoplasia, AIN). Although the Bethesda terminology, criteria, and guidelines for anal cytology specimens parallel those for cervical cytology, degenerative cellular changes, extensive keratinization, and contaminating fecal material frequently make it more difficult to evaluate these specimens than to evaluate cervical specimens. Because there are limited data on the interobserver agreement of anal cytology (as compared with cervical cytology), Teresa M. Darragh, MD, et al., investigate interrater agreement of anal cytology as well as the relationship between biomarkers and anal cytologic interpretations (*Cancer Cytopathol.* 2013;121[2]:72-78).

To study these issues, their study enrolled 363 men age 18 and older who were identified as HIV-positive through the Kaiser HIV registry and not previously diagnosed with anal cancer. These men had anal swabs collected into two PreservCyt vials, routine testing for *Chlamydia trachomatis/Neisseria gonorrhoeae*, a digital rectal exam, and high-resolution anoscopy (HRA). Lesions that were suspicious on HRA were biopsied and evaluated for AIN. ThinPrep slides were prepared from the swab collections and independently interpreted by two pathologists using standard Bethesda classification. Biomarker testing for p16^{INK4a}/Ki67 dual immunostaining (using a CINtec Plus cytology kit) was performed on the residual PreservCyt cytology specimens. The second PreservCyt vial was tested for HR-HPV, including separate detection of HPV-16 and HPV-18 DNA using a Cobas 4800 HPV test. Additional HPV testing (using PreTect HPV-Proofer assay) for HPV-16, -18, -31, -33, and -45 was also performed on the second vial.

From their findings, Darragh, et al., concluded that there was moderate to good agreement between two cytopathologists who were evaluating anal cytology using samples from HIV-infected MSM. Additionally, their results demonstrated that the frequency of detection for several biomarkers and the diagnosis of AIN2+ increased with the increasing severity of the anal cytology interpretation.

The interobserver agreement was similar to a previous study by Lytwyn, et al. (*Cancer.* 2005; 103[7]:1447-1456) that used four pathologists to independently assess anal cytology specimens. The Lytwyn study also made interesting observations as the authors found anal cytology interobserver agreement compares similarly to overall kappa agreement for anal biopsy specimens (0.54 and 0.59, respectively). Additionally, they found that reliability for the Bethesda classification system was moderate, except for the ASC-US category, which had a kappa of 0.12.

This study by Darragh, et al., along with its comparison to the previous study by Lytwyn, et al., is recommended reading for cytopathologists and their respective laboratories that interpret and/or process anal cytology specimens. In addition to addressing the important issue of interobserver reproducibility regarding anal cytologies, they provide good insight into the subject of using biomarkers as objective standards that may help maintain the performance standard for anal cytology interpretations.□

Dr. Witt, a member of the CAP Cytopathology Committee, is an assistant professor of anatomic pathology at the University of Utah where he works in general surgical pathology and cytopathology. He is the director of the cytopathology rotation for residents and supervises the medical student rotation on the anatomic pathology



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