Cervical and Anal Cancer Screening in HIV-infected patients

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Educational Objectives:

1. Describe the risk factors of cervical cancer and anal cancer.
2. Appreciate guidelines for cervical and anal cancer screening in HIV-infected patients.
3. Know who to refer for colposcopy and anoscopy.
4. Describe the preventative measures for cervical and anal cancer.

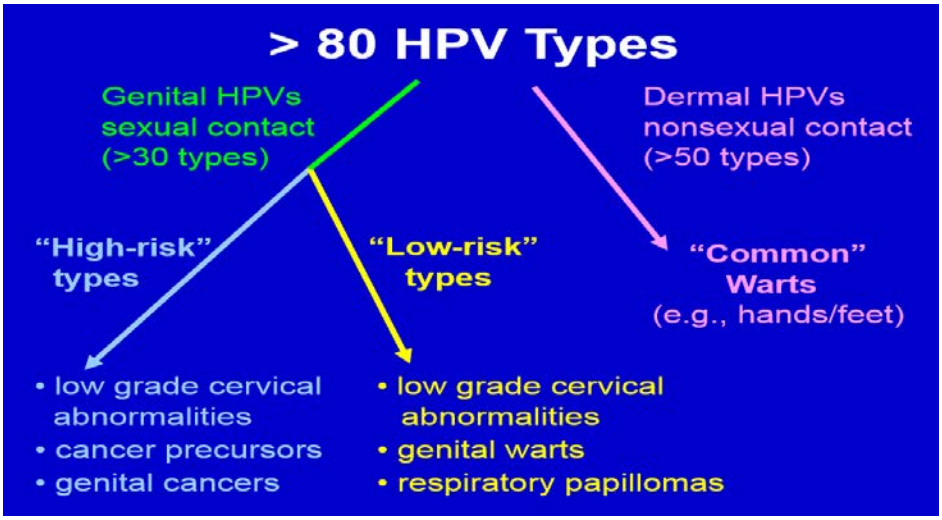
CASE ONE:

Ms H is a 27 year old woman with history of HIV (diagnosed 3 years ago, Last VL undetectable, CD4 count 561, with good adherence on dolutegravir/abacavir/lamivudine) presents to clinic for routine follow up. On exam, she has normal vital signs, with unremarkable exam. Her last PAP smear was 2 years ago.

Questions:

1. What are the risk factors associated with cervical cancer?

There are about 30 to 40 HPV gentoypes that infect the genital mucosa. High risk types are those that possess the genetic signal to incorporate into host DNA and are associated with genital cancers and include serotypes **16, 18, 31, 33, 35, 39, 45, 51, 52, 56, etc. S**eventy percent of cervical cancer is associated with HPV 16 and 18. Risk factors of cervical cancer include early onset of sexual activity, multiple or high-risk sexual partners or impaired ability to clear HPV infection (immunosuppression), cigarette smoking, and oral contraceptive use.



2. How often should HIV-infected women be screened for cervical cancer?

HIV-infected women have higher incidence, prevalence, and persistence of HPV compared to general population. Among HIV infected women, rates of HPV associated cancer increase as CD4 decrease and viral load increases (1). Guidelines from the American College of Obstetricians and Gynecologists and the USPSTF recommend that HIV infected women should have a Pap smear twice a year in the first year after diagnosis of HIV, then annually if their prior Pap smears are normal (1,2).

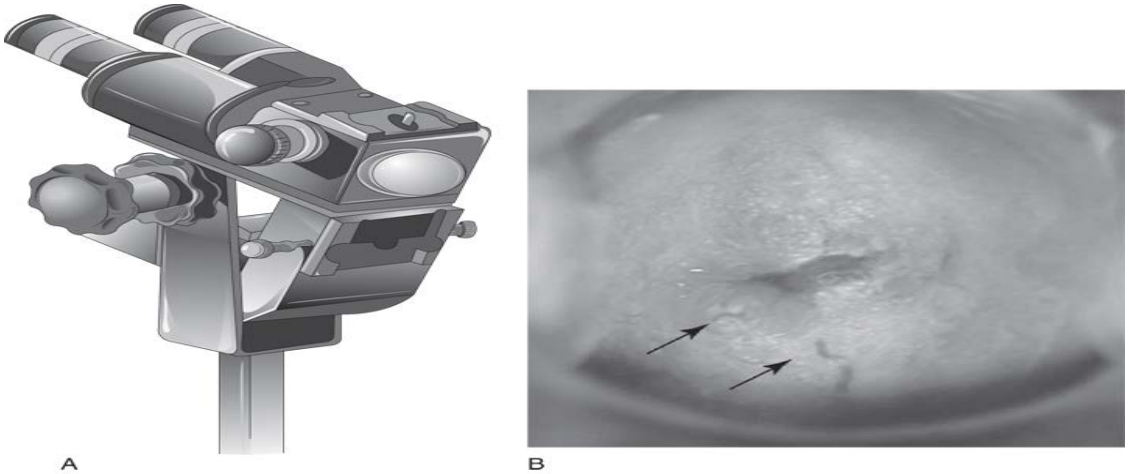
CASE ONE CONTINUED:

Pap smear is obtained in clinic. You obtain the cytological results and it reads atypical squamous cells of undetermined significance (ASC-US) with reflex HPV positive for high risk

3. What is your next step in management?

HIV-infected women found to have ASC-US or LGSIL without histologic evidence of high-grade CIN, have low risk of progressing to CN 2 or higher (about 12%) (1). Thus, the American Society for Colposcopy and Cervical Pathology 2006 consensus guidelines state HIV-infected women with ASC-US be managed the same way as women without HIV.

Patients with ASC-US with reflex positive for high risk HPV subtype should undergo colposcopy. Colposcopy allows magnifying views of cervix, vagina, and vulva. When atypical legions are found, samples are taken to determine the pathology.



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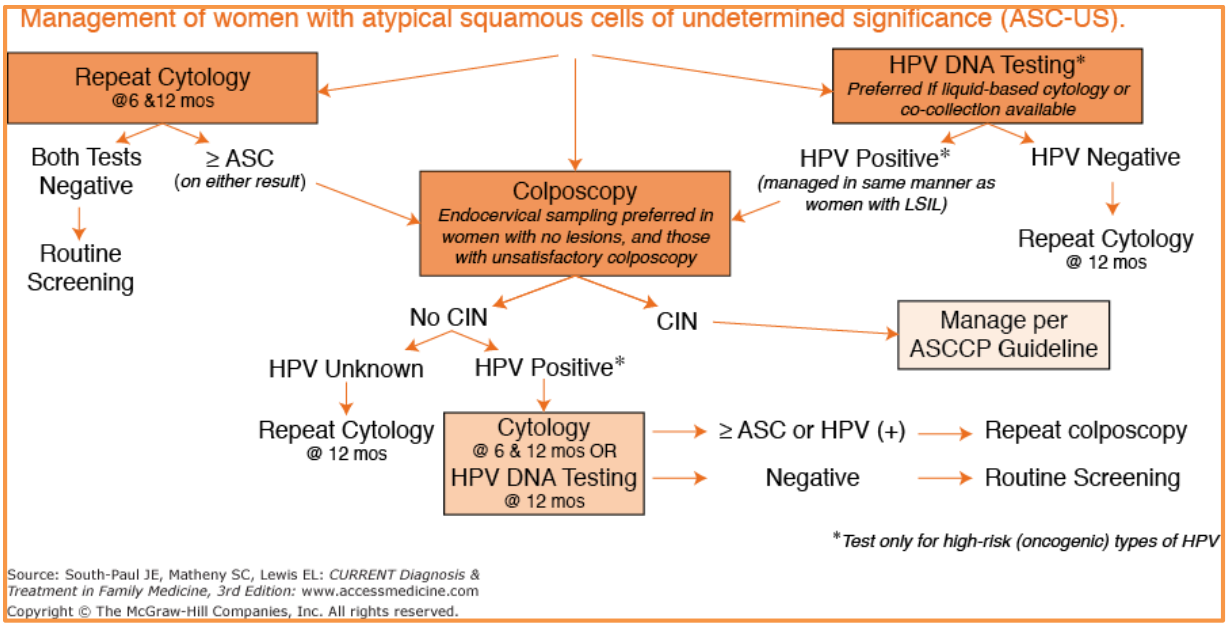
CASE ONE CONTINUED:

Colpscopy results show no CIN.

4. What is your next step in management?

As long as colposcopic exam was adequate, and the patient has no biopsy-confirmed CIN, repeat follow-up with cervical cytology in 12 months is recommended (1,3). If follow up cervical cytology show ASC-US, colposcopy should be repeated.



CASE TWO:

Mr A is a 26 year old man with history of HIV (last VL 13,000, CD4 140, non-adherent to ARVs), presents to clinic for routine follow up. He acquired HIV through unprotected anal intercourse. He is one of your new patients, and he has deferred the exam of the anal area on prior visits. Patient notes he has had recent anal itching and spots of blood on his tissue when he wipes.

5. How are precursors of anal squamous cell cancer classified? What are the risk factors of developing such lesions?

Anal cytology is classified in the same way as cervical cytology by the Bethesda System of cervical cytology classification: normal, atypical, squamous cells of uncertain significance, low-grade squamous intraepithelial lesions, or high-grade squamous intraepithelial lesion.

Risk factors for anal SIL include high risk sexual behavior, men who have sex with men, HIV infection, injection drug use, current smoker, history of cervical cancer, vulvar cancer, high grade cervical intraepithelial neoplasia. For example, the incidence of anal cancer in general population is about 0.8 cases per 100,000, whereas in the HIV-infected MSM population it is about 70 per 100,000 population.

6. Who should be screened for anal cancer and how often?

There are currently no randomized clinical trials or cohort studies to know the value and best frequency of screening of anal SIL in at-risk patients. In addition, a systemic review by Chiao et al in Clinical Infectious Disease 2006 concluded that due to the absence studies, it is unknown whether screening with anal pap smears for anal cancer is effective in preventing anal cancer. However, the rationale for screening HIV-infected patient relies on 1) the similarities of cervical and anal cancer and 2) success of cervical cancer screening in reducing cervical cancer.

There are no formal guidelines given by United States Public Health Services. The New York State Department of Health Guidelines recommend obtaining anal cytology at baseline and annually in HIV-infected patients who 1) are men who have sex with men, 2) have history of anogenital condylomas, 3) women with abnormal cervical and/or vulvar histology (5).

CASE TWO CONTINUED:

Mr A undergoes an anal exam. On physical exam, he has anal warts. You perform an anal pap. Anal cytology results show low grade anal squamous intraepithelial neoplasa.

7. How do you perform an anal pap smear?

A Dacron cotton swab should be used. The swab can be moistened with tap water. Avoid using a cotton swab on a wooden stick, because these often break and will splinter. The patient may be placed in the lateral recumbent position. In women, the dorsal lithotomy position may be used as when completing a cervical Pap smear. The Dacron swab is inserted 5 to 6 cm without direct visualization. Firm lateral pressure is applied to the swab handle. It is rotated and slowly withdrawn from the anal canal.1 Make sure to sample the transition zone during removal, as this area, which separates the columnar epithelium of the rectum from the keratinizing anal squamous mucosa, is the site where most anal intraepithelial neoplasms arise.

If digital rectal exam is to be performed with the addition of a lubricant, the cytology should be obtained prior to the introduction of any lubricant.

8. What is your next step in management? What referral(s) will you make?

Mr A should be referred for high-resolution anoscopy (HRA). HRA is similar to colposcopy, as it allows visualization of perianal skin, anal canal, and distal rectal tissue. HRA allows magnification for abnormal lesions. HRA is typically performed by colorectal, obstetrics/gynecology or Gastroenterology specialists. Patients should be referred to HRA if anal pap smear results show atypical cells of undetermined significance, atypical cells of undetermined significance high grade, low grade squamous intraepithelial lesion, high grade squamous intraepithelial lesion (5).

CASE TWO CONTINUED:

Your patient undergoes HRA. His biopsy shows anal intraepithelial neoplasia (AIN), grade 1.

9. What is your next step?

Low-grade lesions (AIN 1) has low risk of progressing to anal cancer and do not need to be treated. However, if patients find the symptoms such as burning or itching unbearable this should be treated. For follow up of Mr A, there are no guidelines. Annual digital rectal exam, anal cytology and HRA to detect progression into high risk lesions are recommended by an article in OncoTargets and Therapy.

10. How could cervical and anal cancer been prevented in the above two cases? What is the dosing schedule?

The United States Advisory Committee on Immunization Practices (ACIP) recommends the use of 9-valent HPV vaccine for female patients from the age of 13 through 26 years of age. The vaccine series can be started at the age of 9 years. Male patients should be vaccinated from age 22 to 26 years. The 9-valent vaccine protects against HPV 16 and 18, as well as give additional cancer types. The HPV vaccine is administered in a 3-dose schedule. The doses are given at 0 months, 1-2 months, then 6 months after first dose (8).

Required Reading:

1. Panel on Opportunistic Infections in HIV-Infected Adults and Adolescents. Guidelines for the prevention and treatment of opportunistic infections in HIV-infected adults and adolescents: recommendations from the Centers for Disease Control and Prevention, the National Institutes of Health, and the HIV Medicine Association of the Infectious Diseases Society of America. Available at http://aidsinfo.nih.gov/contentfiles/lvguidelines/adult_oi.pdf.
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