Abnormal Pap Test Results

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Clinical Challenges

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Case Study

Ms. M is a 22-year-old female with her first atypical squamous cells–unspecified (ASC-US) Pap test result. She has been on oral contraceptives for three years, and her annual Pap tests all have been normal to date. The patient is a nonsmoker in a monogamous sexual relationship. She has no history or current presentation of genital condyloboma. A reflex human papillomavirus (HPV) hybrid capture II test revealed she was positive for high-risk types of HPV DNA.

Ms. M was advised to undergo a colposcopy to evaluate her cervix for evidence of pathology and possible biopsies as indicated, but she declined this procedure as something to which she was not willing to consent. She was vague about the reasons for her hesitation but appeared apprehensive when the procedure was discussed and was unwilling to listen to details.

The patient’s decision was noted in the chart, and a follow-up Pap test was scheduled in three months. This second Pap test also was evaluated as ASC-US, and Ms. M once again was encouraged strongly to consent to a colposcopy for cervical evaluation.

Clinical Problem Solving

Responding to this clinical challenge are Susanne Phillips, RN, MSN, NP, a certified family nurse practitioner in private practice at the Pacific Family Wellness Center in Irvine, CA, and Diana Lithgow, RN-CS, MSN, FNP, a certified family nurse practitioner at the Laguna Beach Community Clinic in California.

How does your institution handle the ASC-US Pap test follow-up?

S. Phillips: My partner and I follow the American Society for Colposcopy and Cervical Pathology guidelines. With ASC-US Pap test results, we order reflex HPV DNA testing. Because our Pap testing is performed with a liquid cytology method, this is conducted without a second patient visit to the office. If the test comes back with high-risk DNA types, patients are referred for colposcopy. If the test is negative, we repeat the Pap test in six months. Patients with Pap test results of atypical squamous cells that cannot rule out high-grade disease are sent directly for a colposcopy.

D. Lithgow: The providers at the Laguna Beach Community Clinic have a similar algorithm. In addition, we also take into account patients’ age and cervical cytology history. Even with a negative HPV DNA profile, women older than 30 or with a history of abnormal cytology in the past have been sent immediately to colposcopy for cervical evaluation. Because persistence of HPV infection is associated with increased cervical pathology, women older than 30 (who may have persisted with the HPV infection over time) are at greater risk for cervical cancer. Most HPV infection is transient; therefore, women younger than 30 years of age are more likely to clear the virus from their systems within several months.

What are the clinical challenges associated with the follow-up ASC-US Pap test?

S. Phillips: First and foremost, the adequacy of the Pap test has to be considered. To aid in a sufficient collection of cells with the initial or follow-up Pap test, we instruct patients to avoid the use of any vaginal preparations (i.e., douches, vaginal medications, creams, contraceptives, lubricants) for 48 hours prior to the appointment date and avoid intercourse the night before their appointment. Additionally, the Pap test should not be collected when patients are menstruating. We use the liquid cytology method because more cells are collected in the liquid-based sample than with conventional slide cytology. In fact, 80% of the cellular sample in conventional slide cytology is left on the cytobrush and discarded. Liquid cytology increases the representative sample of cells obtained for laboratory evaluation.

D. Lithgow: If an ASC-US Pap test result is obtained, performing an adjunctive test, such as the HPV DNA typing test, assists in the management decision process. With such poor sensitivity, the Pap test is unable to provide the entire cervical picture. We do not have any method of culturing for HPV; therefore, this molecular detection technique of DNA typing is a good tool in patient assessment. Adding HPV adjunctive testing to the Pap test increases the sensitivity of detecting pathology to approximately 90%. The ASC-US and low-grade squamous intraepithelial lesion (LSIL) triage study compared the sensitivity and specificity of three management approaches to detect high-grade squamous intraepithelial lesions (HSILs) in women with ASC-US or LSIL: direct colposcopy referral, triage to colposcopy based on HPV results, and triage based on cytology alone. The ASC-US and LSIL study validated the use of HPV DNA testing as a sensitive method to detect HSIL in lower level cytology (i.e., ASC-US and LSIL) (Solomon et al., 2001).

How would you approach Ms. M when trying to persuade her to seek further assessment?

S. Phillips: I would try to determine what her concerns were regarding the colposcopy procedure. I often find that patients have a misunderstanding based on a friend’s or family member’s personal experience or an unfounded fear of the procedure. Clear, nontechnical communication with patients and written support literature to take home in dispelling these fears.

D. Lithgow: The biggest challenge in managing patients with low-grade cervical cytology results is helping them to understand this very complicated picture. We are dealing with a virally mediated cancer with erratic clearance from the body because of high-risk behavioral
(e.g., cigarette smoking) and biologic (e.g., age, medical history) cofactors. Screening for this cancer has a complicated management algorithm, and national experts differ in their opinions. How can we help Ms. M to understand all of this?

Ultimately, if Ms. M does not follow up with the colposcopy, we need to document her declination in the chart. We need to be clear regarding the potential consequences, including progression to cervical cancer. If she still refuses the recommended care, she must sign a chart note that recommends colposcopy as soon as possible.

Clinical Highlights:
Atypical Squamous Cells–Unspecified Pap Test and Human Papillomavirus Testing Dilemma

**Definition:** Atypical squamous cells–unspecified (ASC-US) is part of the Bethesda System of reporting Pap test results. In 2001, some nomenclature changed and ASC-US replaced the previous descriptor, “atypical squamous cells of undetermined significance.” The previous descriptor was overused and deemed too subjective. The Bethesda System created two new categories to replace its previous one: ASC-US and atypical squamous cells–high-grade. This change was made in the hope of improving follow-up triage strategies. Cervical squamous cells with definite abnormalities fit into one of two categories: low-grade or high-grade squamous intraepithelial lesions (SILs) (Solomon et al., 2001).

**Incidence:** Worldwide, 20,000 women die every year from cervical cancer. However, the death rate from this cancer is declining because of improved screening techniques and effective intervention therapy. In the United States, 4,100 deaths per year are attributed to cervical cancer (American Cancer Society, 2003).

**Pathophysiology:** Human papillomavirus (HPV) is a known precursor to the development of cervical pathology, known as SILs in cytology and cervical intraepithelial neoplasia (CIN) in histopathology. The persistence of the virus and a high viral load at the cervical site produce cervical pathology. This virus has many DNA types, and some are known to cause CIN more often than others. Women who are infected with these high-risk DNA virus types are at risk for developing cervical pathology and are identified as “at risk.” Infection with this virus is transient in most women; however, patients who do not seek treatment for the infection develop cervical pathology.

**Findings:** An HPV infection, resulting in an abnormal Pap test, is typically subclinical. Visible alterations, such as erosions, lesions, or acetowhite changes, may occur on the cervical surface with the application of 3% trichloracetic acid (i.e., vinegar). Cervical friability and postcoital bleeding may be seen in advanced pathologic changes.

**Differential diagnosis:** Most high-grade cervical disease is detected via colposcopy in women with ASC-US and low-grade, SIL Pap test results. Therefore, high-grade disease must be considered a possibility in all ASC-US results.

**Screening:** The Pap test, or cervical cytology, is a screening test with poor sensitivity and false-negative rates of 50% (Solomon et al., 2001). HPV detection testing may be used to determine ASC-US management. Many clinicians are utilizing the HPV reflex testing in this way, but others do not have confidence in this approach. In 2001, the American Society for Colposcopy and Cervical Pathology sponsored a consensus committee to develop guidelines for management of atypical squamous cell Pap results. Wright, Cox, Massad, Twigg, and Wilkinson (2002) prepared the final guidelines. The complete guidelines are available online at www.asccp.org. To summarize, the guidelines state that repeat cervical cytology testing, colposcopy, or HPV DNA testing for high-risk virus types are all acceptable alternatives for management (see Figure 1).

**Reference**