How should you evaluate a patient who has a cytologic diagnosis of atypical glandular cells (AGC)?

Consider comprehensive assessment that includes pelvic examination, colposcopy, endocervical curettage, cervical biopsy, ultrasonography (US), and endometrial biopsy—especially if the woman is older than 60 years, hasn't had a Pap test within the past 2 years, has never had a Pap test, or has a low educational status. That's the conclusion of this prospective study of a screened population of 8,281 women.

FAST TRACK

Adhere to 2006 ASCCP guidelines for the management of women who have a cytologic finding of atypical glandular cells

Cheng WF, Chen YL, You SL, et al. Risk of gynaecological malignancies in cytologically atypical glandular cells: follow-up study of a nationwide screening population. BJOG. 2011;118(1):34–41.

EXPERT COMMENTARY
Charles J. Dunton, MD, Director, Division of Gynecologic Oncology, Lankenau Medical Center, Wynnewood, Pa, and **Norman A. Brest, MD,** Department of Obstetrics and Gynecology, Lankenau Medical Center, Wynnewood, Pa.

AGC is a relatively uncommon cytologic finding, with a mean reporting rate in 2003 of just 0.4% in the United States, according to guidelines from the ASCCP, the society for lower genital tract disease.[1]

"Although AGC is frequently caused by benign conditions, such as reactive changes and polyps, clinicians should be aware that it is not uncommon for AGC to be associated with a significant underlying neoplastic condition, including adenocarcinomas of the cervix, endometrium, ovary, and fallopian tube. Recent series have reported that 9%–38% of women with AGC have significant neoplasia…and 3%–17% have invasive cancer," the guidelines state.[1]

In recent years, evidence-based guidelines such as this one have helped clinicians improve the care that they offer to their patients. Nevertheless, the cytologic diagnosis of AGC presents a dilemma. The significant rate of neoplasia associated with this finding, combined with the lack of sensitivity of methods of evaluation, is responsible for this quandary. Although clinicians try to avoid over-testing, there is a real concern about missing a critical diagnosis.

As ASCCP guidelines point out, all of the diagnostic testing done to investigate this cytologic finding lack sensitivity.[1] This observation led to the recommendation that multiple modalities be combined in the evaluation of these patients.[1] **Previously published data suggest that women with AGC cytology are under-managed in both their initial and secondary evaluations.**[2]

Authors explore management in women found to have cancer

Cheng and colleagues report on a large series of women who had a first-time diagnosis of AGC. These patients were drawn from an extensive, heterogeneous screening population in Taiwan. The report focuses only on patients who were ultimately found to have a diagnosis of invasive cancer—not those who had premalignant conditions such as cervical intraepithelial neoplasia (CIN) 2, CIN 3, adenocarcinoma in situ, or endometrial hyperplasia. The study confirms a high relative risk (RR) of gynecologic malignancy among women with a cytologic finding of

AGC. The greatest risk is cervical cancer (RR, 17.85), followed by uterine cancer (RR, 5.68) and ovarian cancer (RR, 2.04).

Should we include US imaging in our assessment?

Current guidelines recommend colposcopy, endocervical curettage, cervical biopsy, and human papillomavirus (HPV) DNA testing (for high-risk types only) in women who have AGC. They also call for endometrial assessment among women at risk of uterine malignancy, including all women older than 35 years and those younger than 35 who have risk factors, such as unexplained vaginal bleeding, or a condition that suggests chronic anovulation.

Cheng and colleagues also include a recommendation for US imaging in women who have AGC, because of the risk of ovarian cancer. However, although the relative risk of ovarian cancer is roughly doubled among women who have AGC, compared with women with normal cytology, the absolute risk remains quite low. In this sample of 8,281 patients, for example, there were only 12 cases (0.14%).

Nor do the data presented by Cheng and colleagues make a compelling case for the addition of routine US in these patients. However, based on the results of this study, it may be prudent to consider US in certain risk groups when evaluation of the cervix and uterus is negative, such as women who have a family history of ovarian cancer, women who have breast cancer, or women who have a cytologic finding of adenocarcinoma.

HPV DNA testing was not included in this study

The authors suggest, instead, that this modality could be used for triage. However, both of the studies they cite to back this recommendation precede the 2006 ASCCP guidelines, which recommend testing for high-risk HPV types as part of the initial evaluation of women who have AGC but advise against using HPV DNA testing for triage.

WHAT THIS EVIDENCE MEANS FOR PRACTICE

We should adhere to ASCCP guidelines for the management of women who have AGC cytology, by performing:

- colposcopy with endocervical sampling in all women with this designation
- endometrial sampling in women 35 years and older and in women younger than 35 who have unexplained vaginal bleeding, chronic anovulation, or other clinical indications suggesting that they have a heightened risk of neoplastic endometrial lesions
- HPV DNA testing at the time of colposcopy.

As we mentioned, pelvic ultrasonography may be advisable if the patient has certain risk factors for ovarian cancer, such as a family history of ovarian malignancy, age older than 60 years, persistent AGC, or a cytologic finding of adenocarcinoma without uterine or cervical origin.

Compliance with these guidelines will reduce the risk of a missed diagnosis of neoplasia or cancer without excessive testing.

Women who have persistent AGC despite a negative comprehensive evaluation may be at increased risk of clinically significant disease. Clinicians should be aware of the guidelines for these women, which include the need for excisional biopsies and endometrial evaluation.[4]

››CHARLES J. DUNTON, MD, AND NORMAN A. BREST, MD

More recent studies have confirmed that the sensitivity of HPV DNA testing is only approximately 80%, which is not sufficient for triage in this population.[3] Such testing may reassure clinicians—but only after complete evaluation of the cervix and uterus. It can be used to guide subsequent surveillance after diagnostic studies, however.

References

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