



Hysteroscopic removal of adenocarcinoma (concomitant with a benign polyp) in a postmenopausal woman with abnormal uterine bleeding.

ILLUSTRATION: KIMBERLY MARTENS FOR OBG MANAGEMENT

Office hysteroscopic evaluation of postmenopausal bleeding

Postmenopausal bleeding can indicate endometrial carcinoma. When and how can hysteroscopy make the difference in diagnosis (and operative intervention)?

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Postmenopausal bleeding (PMB) is the presenting sign in most cases of endometrial carcinoma. Prompt evaluation of PMB can exclude, or diagnose, endometrial carcinoma.¹ Although no general consensus exists for PMB evaluation, it involves endometrial assessment with transvaginal ultrasonography (TVUS) and subsequent endometrial biopsy when a thickened endometrium is found. When biopsy results reveal insufficient or scant tissue, further investigation into the etiology of PMB should include office hysteroscopy with possible directed biopsy. In this article I discuss the prevalence of PMB and steps for evaluation, providing clinical takeaways.

Postmenopausal bleeding: Its risk for cancer

Abnormal uterine bleeding (AUB) in a postmenopausal woman is of particular concern to the gynecologist and the patient because



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of the increased possibility of endometrial carcinoma in this age group. AUB is present in more than 90% of postmenopausal women with endometrial carcinoma, which leads to diagnosis in the early stages of the disease. Approximately 3% to 7% of postmenopausal women with PMB will have endometrial carcinoma.² Most women with PMB, however, experience bleeding secondary to atrophic changes of the vagina or endometrium and not to endometrial carcinoma. (FIGURE 1, page 38; VIDEO 1) In addition, women who take gonadal steroids for hormone replacement therapy (HRT) may experience breakthrough bleeding that leads to initial investigation with TVUS.

The risk of malignancy in polyps in postmenopausal women over the age of 59 who present with PMB is approximately 12%, and hysteroscopic resection should routinely be performed. For asymptomatic patients, the risk of a malignant lesion is low—approximately 3%—and for these women intervention should be assessed individually for the risks of carcinoma and benefits of hysteroscopic removal.³

Clinical takeaway. The high possibility of endometrial carcinoma in postmenopausal women warrants that any patient who is symptomatic with PMB should be presumed to have endometrial cancer until the diagnostic evaluation process proves she does not.

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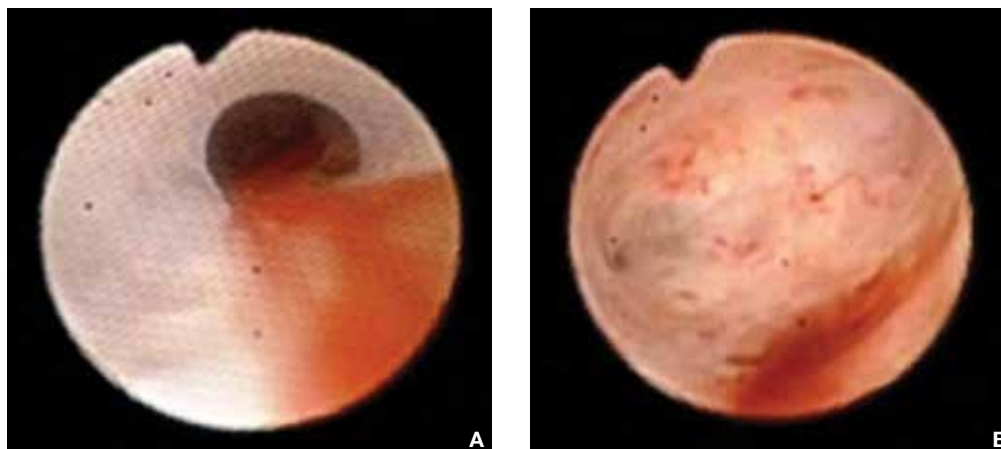
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FIGURE 1 Endometrial atrophy



Flexible hysteroscope images (A and B) in a postmenopausal woman showing endometrial atrophy. Atrophy and endometrial breakdown are seen as subendometrial petechial hemorrhage and frank blood within the cavity. Images courtesy of Amy Garcia.

Evaluation of postmenopausal bleeding
Transvaginal ultrasound

As mentioned, no general consensus exists for the evaluation of PMB; however, initial evaluation by TVUS is recommended. The American College of Obstetricians and Gynecologists (ACOG) concluded that when the endometrium measures ≤ 4 mm with TVUS, the likelihood that bleeding is secondary to endometrial carcinoma is less than 1% (negative predictive value 99%), and endometrial biopsy is not recommended.³ Endometrial sampling in this clinical scenario likely will result in insufficient tissue for evaluation,

and it is reasonable to consider initial management for atrophy. A thickened endometrium on TVUS (>4 mm in a postmenopausal woman with PMB) warrants additional evaluation with endometrial sampling (FIGURE 2).

Clinical takeaway. A thickened endometrium on TVUS ≥ 4 mm in a postmenopausal woman with PMB warrants additional evaluation with endometrial sampling.

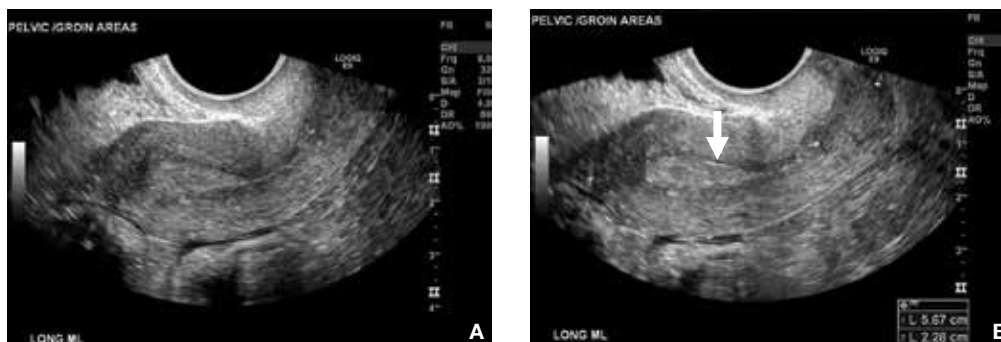
Endometrial biopsy

An endometrial biopsy is performed to determine whether endometrial cancer or pre-cancer is present in women with AUB. ACOG recommends that endometrial biopsy be

FAST TRACK

Endometrial biopsy is indicated when TVUS detects an endometrium >4 mm in a postmenopausal woman with AUB

FIGURE 2 Anteverted uterus



(A) Transvaginal ultrasound of an anteverted uterus in a symptomatic postmenopausal patient with postmenopausal bleeding showing a thickened endometrium. (B) The same image as A with an arrow (white) indicating the thickened endometrium. Images courtesy of Amy Garcia.

performed for women older than age 45. It is also appropriate in women younger than 45 years if they have risk factors for developing endometrial cancer, including unopposed estrogen exposure (obesity, ovulatory dysfunction), failed medical management of AUB, or persistence of AUB.⁴

Endometrial biopsy has some diagnostic shortcomings, however. In 2016 a systematic review and meta-analysis found that, in women with PMB, the specificity of endometrial biopsy was 98% to 100% (accurate diagnosis with a positive result). The sensitivity (ability to make an accurate diagnosis) of endometrial biopsy to identify endometrial pathology (carcinoma, atypical hyperplasia, and polyps) is lower than typically thought. These investigators found an endometrial biopsy failure rate of 11% (range, 1% to 53%) and rate of insufficient samples of 31% (range, 7% to 76%). In women with insufficient or failed samples, endometrial cancer or precancer was found in 7% (range, 0% to 18%).⁵ Therefore, a negative tissue biopsy result in women with PMB is not considered to be an endpoint, and further evaluation with hysteroscopy to evaluate for focal disease is imperative.

Clinical takeaway. A negative tissue biopsy result in women with PMB is not considered to be an endpoint, and further evaluation with hysteroscopy to evaluate for focal disease is imperative.

Hysteroscopy

Hysteroscopy is the gold standard for evaluating the uterine cavity, diagnosing intrauterine pathology, and operative intervention for some causes of AUB. It also is easily performed in the office. This makes the hysteroscope an essential instrument for the gynecologist. Dr. Linda Bradley, a preeminent leader in hysteroscopic surgical education, has coined the phrase, “My hysteroscope is my stethoscope.”⁶ As gynecologists,

FIGURE 3 Diagnostic hysteroscope



Side-by-side comparison of a small flexible diagnostic hysteroscope with a pipelle biopsy curette. Both are 3.0 mm in diameter. The small size and flexible nature of the hysteroscope facilitates evaluation of postmenopausal bleeding for a woman who may have a narrow or stenotic cervix. Image courtesy of Amy Garcia.

ologists, we should be as adept at using a hysteroscope in the office as the cardiologist is at using a stethoscope.

It has been known for some time that hysteroscopy improves our diagnostic capabilities over blinded procedures such as endometrial biopsy and dilation and curettage (D&C). As far back as 1989, Dr. Frank Loffer reported the increased sensitivity (ability to make an accurate diagnosis) of hysteroscopy with directed biopsy over blinded D&C (98% vs 65%) in the evaluation of AUB.⁷ Evaluation of the endometrium with D&C is no longer recommended; yet today, few gynecologists perform hysteroscopic-directed biopsy for AUB evaluation instead of blinded tissue sampling despite the clinical superiority and in-office capabilities (FIGURE 3).

Hysteroscopy and endometrial carcinoma

The most common type of gynecologic cancer in the United States is endometrial adenocarcinoma (type 1 endometrial cancer). There is some concern about the effect of hysteroscopy on endometrial cancer prognosis and the spread of cells to the peritoneum at the time of hysteroscopy. A large meta-analysis found that hysteroscopy performed in the presence of type 1 endometrial cancer statistically significantly increased the likelihood of positive intraperitoneal cytology; however, it did not alter the

FAST TRACK

In postmenopausal women with AUB, negative endometrial biopsy results should be followed by hysteroscopic evaluation for focal disease

Three clinical scenarios

A common occurrence in the evaluation of postmenopausal bleeding (PMB) is an initial TVUS finding of an enlarged endometrium and an endometrial biopsy that is negative or reveals scant or insufficient tissue. Unfortunately, the diagnostic evaluation process often stops here, and a diagnosis for the PMB is never actually identified. Here are several clinical scenarios that highlight the need for hysteroscopy in the initial evaluation of PMB, especially when there is a discordance between transvaginal ultrasonography (TVUS) and endometrial biopsy findings.

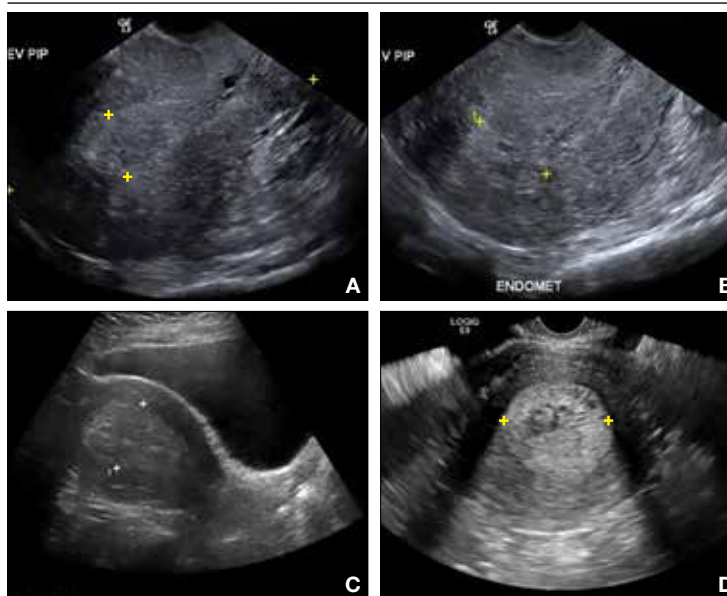
Patient 1: Discordant TVUS and biopsy, with benign findings

The patient is a 52-year-old woman who presented to her gynecologist reporting abnormal uterine bleeding (AUB). She has a history of breast cancer, and she completed tamoxifen treatment. Pelvic ultrasonography was performed; an enlarged endometrial stripe of 1.3 cm was found (**FIGURE 4A**). Endometrial biopsy was performed, showing adequate tissue but with a negative result. The patient is told that she is likely perimenopausal, which is the reason for her bleeding.

The following year, the patient has had continued AUB and is now postmenopausal by follicle-stimulating hormone level (FSH). TVUS is performed and the endometrium now measures 2.4 cm (**FIGURE 4B**). Subsequent endometrial biopsy shows scant tissue, and no additional evaluation is done. The following year, the patient still has PMB, and TVUS is performed. The endometrium now measures 4.7 cm (**FIGURES 4C, 4D**). The patient is taken to the operating room by the gynecologist for dilation and curettage (D&C). The results indicate scant, atrophic endometrium (hysteroscopy is not performed).

At the time of referral, the patient is evaluated with in-office hysteroscopy. Diagnosis of a 5 cm x 7 cm benign endometrial polyp is made. An uneventful hysteroscopic

FIGURE 4 TVUS evaluation of AUB



(**A**) Transvaginal ultrasound (TVUS) evaluation of abnormal uterine bleeding, with endometrial thickness of 1.3 cm in a patient with a history of tamoxifen therapy. (**B**) Image of second TVUS evaluation of postmenopausal bleeding (PMB), with endometrial thickness 2.4 cm. (**C**) Image of third TVUS evaluation of PMB, with endometrial thickness 4.7 cm. (**D**) Image of third TVUS evaluation of PMB, with endometrial thickness 4.7 cm. *Images courtesy of Amy Garcia.*

polypectomy is performed (**VIDEO 2**).

This scenario illustrates the shortcoming of initial evaluation by not performing a hysteroscopy, especially in a woman with a thickened endometrium with previous tamoxifen therapy. Subsequent visits failed to correlate bleeding etiology with discordant TVUS and endometrial biopsy results with hysteroscopy, and no hysteroscopy was performed in the operating room at the time of D&C.

Patient 2: Discordant TVUS and biopsy, with premalignant findings

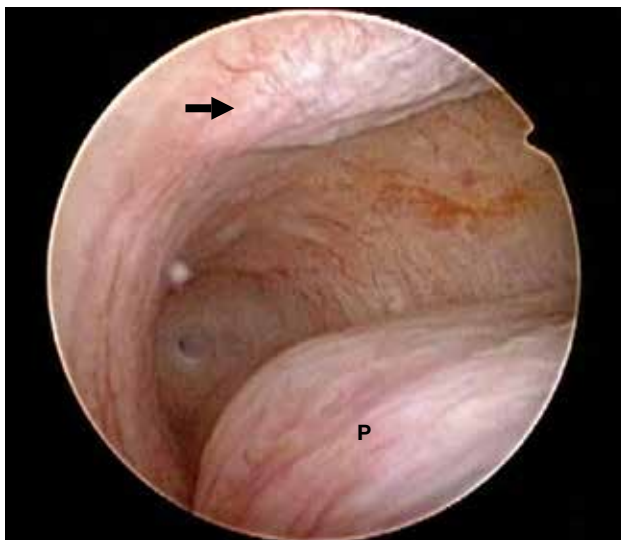
The patient is a 62-year-old woman who had incidental

clinical outcome. It was recommended that hysteroscopy not be avoided for this reason and is helpful in the diagnosis of endometrial cancer, especially in the early stages of disease.⁸

For endometrial cancer type 2 (serous

carcinoma, clear cell carcinoma, and carcinosarcoma), Chen and colleagues reported a statistically significant increase in positive peritoneal cytology for cancers evaluated by hysteroscopy versus D&C. The disease-specific survival for the hysteroscopy group

FIGURE 5 Hysteroscopy, atypical hyperplasia



Hysteroscopic image of evaluation of postmenopausal bleeding with endometrial atrophy, benign polyp (P), and focal atypical hyperplasia (arrow). *Image courtesy of Amy Garcia.*

findings of a thickened endometrium on computed tomography scan of the pelvis. TVUS confirmed a thickened endometrium measuring 17 mm, and an endometrial biopsy showed scant tissue.

At the time of referral, a diagnostic hysteroscopy was performed in the office. Endometrial atrophy, a large benign appearing polyp, and focal abnormal appearing tissue were seen (**FIGURE 5**). A decision for polypectomy and directed biopsy was made. Histology findings confirmed benign polyp and atypical hyperplasia (**VIDEO 3**). **This scenario illustrates** that while the patient was asymptomatic, there was discordance between the TVUS and endometrial biopsy. Hysteroscopy identified a benign endometrial polyp, which is common in asymptomatic postmenopausal patients with a thickened endometrium and endometrial biopsy showing scant

FIGURE 6 Hysteroscopy, adenocarcinoma



(A) Hysteroscopic image of endometrial atrophy with benign polyps (P) concomitant with adenocarcinoma (M) in a postmenopausal woman with bleeding. (B) Close-up of the adenocarcinoma (M) from image A. *Image courtesy of Amy Garcia.*

tissue. However, addition of the diagnostic hysteroscopy identified focal precancerous tissue, removed under directed biopsy.

Patient 3: Discordant TVUS and biopsy, with malignant findings

The patient is a 68-year-old woman with PMB. TVUS showed a thickened endometrium measuring 14 mm. An endometrial biopsy was negative, showing scant tissue. No additional diagnostic evaluation or management was offered.

At the time of referral, the patient was evaluated with in-office diagnostic hysteroscopy, and the patient was found to have endometrial atrophy, benign appearing polyps, and focal abnormal tissue (**FIGURE 6**). A decision for polypectomy and directed biopsy was made. Histology confirmed benign polyps and grade 1 adenocarcinoma (**VIDEOS 4A, 4B, 4C**).

This scenario illustrates the possibility of having multiple endometrial pathologies present at the time of discordant TVUS and endometrial biopsy. Hysteroscopy plays a critical role in additional evaluation and diagnosis of endometrial carcinoma with directed biopsy, especially in a symptomatic woman with PMB.

was 60 months, compared with 71 months for the D&C group. While this finding was not statistically significant, it was clinically relevant, and the effect of hysteroscopy on prognosis with type 2 endometrial cancer is unclear.⁹

Conclusion

Evaluation of PMB begins with a screening TVUS. Findings of an endometrium of ≤ 4 mm indicate a very low likelihood of the presence of endometrial cancer, and treatment for atrophy or changes to hormone

replacement therapy regimen is reasonable first-line management; endometrial biopsy is not recommended. For patients with persistent PMB or thickened endometrium ≥ 4 mm on TVUS, biopsy sampling of the endometrium should be performed. If the

endometrial biopsy does not explain the etiology of the PMB with atypical hyperplasia or endometrial cancer, then hysteroscopy should be performed to evaluate for focal endometrial disease and possible directed biopsy. ●

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