Assessment of Postmenopausal Bleeding

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SUMMARY

Postmenopausal bleeding is bleeding that occurs 12 or more months after the last menstrual period and accounts for 5% of all gynecologic office visits. While it is not always a symptom of cancer, the exclusion of endometrial hyperplasia and carcinoma is the key issue in the evaluation of patients with postmenopausal bleeding. The primary evaluation of postmenopausal women who present with abnormal uterine bleeding includes a medical history and a pelvic examination. Investigative studies, such as a uterine biopsy, ultrasound, hysteroscopy or dilation and curettage, may be required. Treatment will depend on the cause determined. The most important point is that irregular perimenopausal or postmenopausal bleeding should not be ignored or assumed to be a normal phenomenon. [International Journal of Gerontology 2008; 2(2): 55–59]

Key Words: dilatation and curettage, hysteroscopy, postmenopause, ultrasound, uterine bleeding

Introduction

Menopause, the end of ovulation and menstrual periods, naturally occurs for most women at the age of 40–55 years. The process of ending ovulation and menstruation is gradual, spanning 1 to 2 years. Postmenopausal bleeding (PMB) is bleeding that occurs 12 or more months after the last menstrual period and accounts for 5% of all gynecologic office visits. Moreover, a reported 25% of gynecologic surgeries involve abnormal uterine bleeding.

The response for the postmenopausal individual will depend on her own specific endometrial sensitivity, as well as the magnitude of the dose of the hormone supplement. Approximately one in 10 women will experience some bleeding after the menopause. Postmenopausal bleeding should always be taken seriously and be investigated, no matter how minimal or nonpersistent. Causes may be nongenital, genital extrauterine or uterine. Possible uterine conditions associated with PMB include endometrial atrophy, polyps, estrogen therapy, foreign bodies, trauma, infection, endometrial hyperplasia, and carcinoma (Table).

Uterine myoma should never be accepted as a cause of PMB. Endometrial atrophy is the most common endometrial finding in women with PMB, accounting for 60–80% of such bleeding. Women with endometrial atrophy have usually been menopausal for 10 years.

Hormonal replacement therapy accounts for 15–25% of PMB. The uterine lining responds to supplemental hormone stimulation just as it did earlier in the woman’s

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<th>Etiology of postmenopausal bleeding</th>
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<td>Cause of bleeding</td>
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<td>Endometrial atrophy</td>
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<td>Exogenous estrogens</td>
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<td>Endometrial or cervical polyps</td>
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<td>Endometrial hyperplasia</td>
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<td>Endometrial cancer</td>
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<td>Miscellaneous (e.g., cervical cancer, uterine sarcoma, trauma)</td>
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reproductive life. Unopposed moderate- or high-dose estrogen therapy when compared with placebo is associated with a significant increase in rates of endometrial hyperplasia with increasing rates at longer duration of treatment and follow-up\(^6\). Irregular bleeding and non-adherence to treatment are also significantly more likely under these unopposed estrogen regimens that increase bleeding with higher-dose therapy. The addition of oral progestogens administered either sequentially or continuously is associated with reduced rates of hyperplasia and improved adherence to therapy. Irregular bleeding is less likely under sequential rather than continuous therapy during the first year of therapy; but there is a suggestion that continuous therapy of a long duration is more protective than sequential therapy in the prevention of endometrial hyperplasia\(^6\).

Determining the underlying cause of PMB requires a thorough evaluation by a gynecologist. Treatment will obviously depend on the cause of PMB. The primary evaluation includes the history and a pelvic examination, as well as a Pap smear if appropriate, to look for vulvar or vaginal lesions, signs of trauma, and cervical polyps or dysplasia. Cervical dysplasia seldom causes abnormal uterine bleeding, but it may be associated with postcoital bleeding\(^7\). Cervical cultures may be indicated if the patient is at risk for infection or if symptoms of infection are present. While the majority of causes of PMB are benign, up to 10% of women with PMB will be diagnosed with uterine cancer\(^8\). Malignancy must be excluded as a cause of bleeding in postmenopausal patients. Postmenopausal bleeding is the most important presenting symptom of endometrial cancer. Investigative studies, such as an endometrial biopsy, ultrasound, dilatation and curettage (D&C) or hysteroscopy, may be required.

**Diagnostic Tools**

Hormonal status, including results of hormone replacement therapy, has demonstrable effects on the endometrium and plays a major role in investigation of the causes of abnormal uterine bleeding. Because 90% of PMB is associated with a benign condition, the ideal diagnostic method is noninvasive. Ultrasonography is typically used in the initial evaluation of PMB and for the guidance of further diagnostic tests\(^9\). Further evaluation for subtle genital tract pathology is recommended in patients who are at high risk for endometrial cancer and in patients at low risk who continue bleeding abnormally despite medical management\(^10\). The patients’ individual risk factors for endometrial cancer may influence the procedure or combination of procedures to be chosen. Hypertension, obesity, polycystic ovarian disease, diabetes, tamoxifen therapy, and colon or breast cancer are risk factors in addition to age\(^11,12\). The risk of developing endometrial cancer increases with age\(^12\). In women aged 40–49 years, the incidence rate of endometrial cancer is 36.5 cases per 100,000 in the United States. Endometrial carcinoma is most common in the postmenopausal age group and is most prevalent in women over 50 years of age. Thus, the American College of Obstetricians and Gynecologists recommends endometrial evaluation in women with abnormal uterine bleeding and aged 35 years and older\(^10\).

**Noninvasive Diagnostic Procedures**

**Ultrasound**

Differential diagnoses for causes of abnormal vaginal bleeding in postmenopausal patients can be well evaluated with transvaginal ultrasonography. It has greatly facilitated evaluation of pelvic disease, including leiomyoma, endometrial thickening or focal masses. Although this imaging modality may miss endometrial polyps and submucous fibroids, it is highly sensitive for the detection of endometrial cancer (96%) and endometrial abnormality (92%)\(^13\). Compared with D&C, endometrial evaluation with transvaginal ultrasonography is about 4% less accurate\(^13,14\). However, it may be the most cost-effective initial test in women at low risk for endometrial cancer, and these include those who have abnormal uterine bleeding that does not respond to medical management\(^9\).

The exclusion of endometrial hyperplasia and carcinoma is the key issue in the evaluation of patients with abnormal uterine bleeding. Transvaginal ultrasound measurement of endometrial thickness has become a routine procedure and an initial investigation in patients with abnormal uterine bleeding. The peri- and postmenopausal endometrial thickness is normally less than that in the premenopausal patient (Figure 1). During menopause, the endometrium primarily consists of a thin basalis layer, and the measurement of the endometrial echo complex represents the apposition of the two basal layers\(^15\). In general, along with endometrial thickening, the sonographic characteristics of
hyperechogenicity and heterogeneous texture represent higher risks for cancer than other patterns. An enlarged uterus, fluid within the cavity, increased blood flow, and an irregular interface of the endometrium and myometrium also suggest cancer (Figure 2).

There is debate as to whether a cut-off of 5 or 4 mm for endometrial thickness should be employed. Transvaginal ultrasound examination can reliably distinguish women with PMB who are at low risk of endometrial pathology (endometrial thickness ≤ 4 mm) from those who are at high risk (endometrium ≥ 5 mm). The 5-mm cut-off is applicable irrespective of the use of hormone replacement therapy. It is justified to refrain from endometrial sampling in women with PMB and an endometrial thickness of ≤ 4 mm, because the risk of endometrial cancer in these women is low (0.1–1.0%). However, it is not known whether these women need follow-up. About 80% of women with PMB and an endometrium of ≥ 5 mm have focally growing pathologic lesions in the uterine cavity. These should be removed by operative hysteroscopy, because D&C will fail to diagnose and remove a large proportion of lesions.

Although transvaginal ultrasonographic measurement of the endometrium is a useful, highly sensitive and noninvasive procedure, it has limitations. Some investigators have determined that it has low positive predictive value for cancer. This is especially true in women taking hormone therapy and tamoxifen, or women with recurrent PMB or PMB that occurs long after the menopause.

Sonohysterography

A refinement of vaginal probe ultrasound is saline infusion sonohysterography. A saline solution is injected into the uterus with a catheter before the vaginal probe is inserted. The presence of liquid in the uterus helps make any structural abnormalities more distinct. Its sensitivity and specificity for endometrial cancer is comparable with the high sensitivity and specificity of diagnostic hysteroscopy. Saline infusion sonohysterography is more accurate than transvaginal ultrasonography in diagnosing intracavitary lesions, and is more accurate than hysteroscopy in diagnosing endometrial hyperplasia. This test is highly sensitive (95–97%) and
also has a specificity of 70–98% for the identification of endometrial abnormality when combined with directed endometrial biopsy. Recent papers support the high diagnostic accuracy and conclude that saline infusion sonography is able to replace diagnostic hysteroscopy in the evaluation of the uterine cavity. The use of gel instead of saline as distension medium and the introduction of new three-dimensional inversion rendering techniques enhance the visualization of the endometrium and may improve the diagnostic accuracy of saline infusion sonography.

Hysteroscopy
Hysteroscopy is a special test that entails the passing of a tiny telescope through the cervix, allowing the actual visualization of the uterine cavity. Fibroids or polyps can be seen and removed and the suspicious area of tissue biopsied under direct vision. The accuracy of hysteroscopy is most useful in the diagnosis of cancer when compared with other types of endometrial disease. In a case series of 181 patients, the sensitivity was 96.6% and the specificity 100% when hysteroscopy was used in conjunction with endometrial biopsy. Although efficient in the detection of pathologic intrauterine lesions, it is only moderately successful in determining physiologic changes such as proliferative endometrium or endometrial hyperplasia.

Invasive Diagnostic Procedures
Endometrial biopsy
Endometrial biopsy is a simple office procedure which allows physicians to sample small areas of the uterine lining, while cervical biopsy allows the cervix to be sampled. A flexible catheter is introduced into the uterus, and the endometrial sample is obtained by gentle suction. This procedure is less invasive than D&C. Many family practice clinicians in the United States routinely perform endometrial biopsy. It is not known whether simple endometrial biopsies are as reliable as D&C in women without focal lesions. The sensitivity of endometrial biopsy for the detection of endometrial abnormalities has been reported to be as high as 96%. However, this office-based procedure may miss up to 18% of focal lesions including polyps and fibroids, because only a small part of the endometrium may be sampled at any one time. Although endometrial biopsy has high sensitivity for endometrial carcinoma, its sensitivity for detecting atypical endometrial hyperplasia may be as low as 81%.

D&C
D&C is often necessary for definitive diagnosis. Postmenopausal women with abnormal uterine bleeding, including those who have been receiving hormone therapy for more than 12 months, should be offered D&C for evaluation of the endometrium (96% sensitivity for the detection of cancer, with a 2–6% false-negative rate). Although D&C has been the gold standard for diagnosing endometrial cancer, it is no longer considered to be therapeutic for abnormal uterine bleeding; furthermore, it is limited in its ability to access the tubal cornua of the uterus.

Conclusion
Bleeding after the menopause is not an uncommon event. While it is not always a symptom of cancer, any amount of bleeding, scant or large, needs to be evaluated. The exclusion of endometrial hyperplasia and carcinoma is the key issue in the evaluation of patients with abnormal uterine bleeding. Transvaginal ultrasound measurement of endometrial thickness has become a routine procedure and an initial investigation in patients with abnormal uterine bleeding. Hysteroscopy allows visualization of the uterine cavity and the opportunity for targeted biopsy and removal of endometrial polyps. Outpatient endometrial biopsy, as well as D&C, is considered to be the gold standard for obtaining endometrial tissue. In conclusion, postmenopausal women with abnormal uterine bleeding, including those who have been receiving hormone therapy for more than 12 months, should be offered D&C for evaluation of the endometrium. Women who are poor candidates for general anesthesia and those who decline D&C may be offered transvaginal ultrasonography or saline infusion sonohysterography with endometrial biopsy. It is important to use the correct diagnostic tools to assess each patient, according to individual needs and histories.

References


