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Chief Complaint: “I went through menopause three years ago and now I am bleeding again.”

History of Present Illness: Rhonda is a 47-year-old, married, white female. She has been experiencing vaginal bleeding, which she describes as “spotting” for the past week after not having a menstrual period since the age of 44. The spotting is red in color and light in flow, requiring thin pads to be changed once or twice per day. The flow has been consistent for the past week. There is no associated pain. Prior to menopause, she did experience metomenorrhagia. Rhonda denies dyspareunia or post-coital bleeding; however, she is experiencing a slight, white, non-odorous vaginal discharge. She denies vaginal puritis or dryness. No fever/chills.

Current medications: Dilantin 200 mg BID and Keppra 500 mg BID for seizure disorder; Atenolol 25 mg daily and Aldactazide 50/50 one tab daily for hypertension.

Allergies: NKDA

Past Medical History: Positive for hypertension, seizure disorder, and a heart murmur.

Obstetric/Gynecologic History: Gravida 3 Para 2; 1 miscarriage. Menarche at the age of 13 years; menopause at age 44.

Surgical History: Bilateral partial salpingectomy at age 31.

Social History: Rhonda is married. She does not smoke, drink alcohol or use illicit drugs. She does drink two cups of coffee per day. She is a high school graduate and a homemaker. Rhonda eats three meals a day and walks for 30 minutes four to five times per week.

Family History: 67-year-old mother has diabetes mellitus and hypertension, alive; 70-year-old father is alive and well; 45-year-old sister alive and well, perimenopausal; 23-year-old son alive and well; 19-year-old son alive and well; does not recall health history of grandparents.

Decision Point #1: Focused history, physical exam, laboratory tests**Focused History-**

Further questioning aims to identify potential etiologies of Rhonda's postmenopausal bleeding. Causes of PMB may be nongenital, genital, extrauterine, or uterine. More information about Rhonda's family and personal health history will gain insight into potential causes:

- Did your mother have any bleeding after menopause?
- Has anyone in your family ever been diagnosed with a bleeding disorder?
- When was your last Pap test? What were the results?
- Have you ever been diagnosed with a sexually transmitted infection?

It is important to ascertain if there have been any changes in Rhonda's lifestyle habits or social history that may contribute to the bleeding. The following questions will elicit that pertinent information:

- Have you had any excess stressors in your life?
- Have you had a significant weight loss?
- Have your eating habits changed significantly recently?

Some medications can cause vaginal bleeding in a postmenopausal woman. The following questions will extract that information:

- Have you used any exogenous hormones, such as estrogen or progesterone, either past or present?
- Have you recently been treated with any steroids?

Further information during the review of systems will give insight into possible physiologic causes of the abnormal bleeding. The following questions are presented:

- Have you experienced any trauma to your genitals?
- Are you experiencing any problems with your bowels, such as constipation or bleeding after having a bowel movement?
- Are you experiencing any pain, frequency, urgency, or pain when voiding?
- Do you have any vaginal burning or dryness?

Rhonda's last Pap test was two years ago with normal results. All other questions yielded no additional pertinent history.

Physical Examination-

Vital Signs:

Height is 5'3"; weight is 171 lbs, BMI 30

BP 140/82(right arm, sitting)

General: Rhonda is a 47-year-old, overweight woman, well-groomed, and in good spirits. She has no obvious physical deformities. She has a steady gait, good posture, is able to get up and down from exam table without difficulty. Her speech is clear. She is able to hear normal conversational tone without difficulty. Body and breath without odor.

Skin: Color pink. Skin warm and moist. No rash, petechiae, or ecchymoses. Hair with average texture, normal distribution.

*HEENT: Head-*The head is normocephalic/atramatic. Face is symmetric with appropriate expression. *Eyes-* Symmetric, no erythema or exudate. *Ears:* Acuity good to normal conversational tone at 3 feet. External ears symmetric without erythema, masses or edema. *Nose:*

External nose symmetric, without erythema, edema. *Mouth and throat:* Oral mucosa pink, dentition good, pharynx without exudates. Gums pink. Tongue midline and pink. Pharynx without exudates. Soft palate and uvula mobile. Uvula midline.

Neck: Trachea midline. Neck symmetric, supple, thyroid isthmus palpable, lobes not felt. No visible lumps or pulsations. No bruits. Full range of motion, strong muscle strength.

Lymph nodes: Tonsillar, submandibular, submental, anterior and posterior cervical, preauricular, posterior auricular, occipital, inguinal, axillary, and inguinal nodes without noted lymphadenopathy or tenderness.

Chest: Thorax is symmetric with good expansion. Respirations even and unlabored. Clear breath sounds bilaterally anteriorly and posteriorly.

Breasts: Breasts symmetric and without masses or dimpling. Nipples without discharge.

Cardiovascular: Apical pulse with regular rate and rhythm Good S1, S2; no S3 or S4. No murmurs appreciated. Radial and pedal pulses palpable, strong and regular bilaterally.

Peripheral Vascular System: Extremities are warm and without edema. No varicosities or stasis changes.

Gastrointestinal: Abdomen is flat, soft, non-distended and non-tender. Active bowel sounds in all 4 quadrants. No masses or hepatosplenomegaly. No costovertebral angle tenderness. No inguinal lymphadenopathy or tenderness.

Musculoskeletal: No joint deformities. Good range of motion and strong muscle strength in hands, wrists, elbows, shoulders, spine, hips, knees, ankles.

Neurologic: Mental Status: Alert and cooperative. Thought coherent. Oriented to person, place and time. *Motor:* Good muscle bulk and tone. Gait stable, fluid. Patellar reflexes 2+ bilaterally.

Reproductive: External genitalia without erythema or lesions. Vaginal mucosa pink, atrophic. Cervix atrophic. No cervical motion tenderness. Uterus with normal size, shape and contour, non-tender. Adnexa non-tender, without masses.

Preliminary Labs and Testing:

Rhonda's initial test results are found in Table 1. It is noteworthy that in this case, the endometrial biopsy was performed during the speculum exam, prior to the transvaginal ultrasound. Both tests, however, were performed on the same day.

Table 1

Test	Result	Indication
Vaginal pH	4.7	Within normal limits
Affirm	Negative for Trichomoniasis, candidiasis, Gardnerella	No vaginal infection
Endometrial Biopsy	Negative	No endometrial cell abnormalities
Papanicolaou smear	Negative	No cervical cell abnormalities
Transvaginal ultrasound	Endometrial stripe 3.5 mm, 1 mm echogenic foci within the endometrium, left ovarian cyst, simple appearing, 1.6x0.7x1.2.	Possible endometrial polyp, possible malignancy, ovarian cyst

Decision Point #2: Differential diagnoses

Postmenopausal bleeding (PMB) accounts for 5% of all gynecologic office visits (Hsu, Chen, & Wang, 2008). The list of differential diagnoses that must be considered for any postmenopausal bleeding includes:

- Emotional stress
- Exogenous hormones
- Trauma
- Diseases of adjacent organs
- Vaginal or vulvar lesions
- Atrophic vaginitis
- Endometrial atrophy
- Endometrial hyperplasia
- Endometrial or cervical polyps
- Uterine fibroids
- Cervical cancer
- Endometrial cancer

Many of these diagnoses can be ruled out from the focused history, physical exam and preliminary laboratory data. Rhonda denies any additional stressors in her life thereby ruling out stress as a cause. Exogenous hormone use accounts for 15-25% of postmenopausal bleeding (Hsu et al., 2008). Unopposed estrogen use can lead to endometrial hyperplasia and irregular bleeding. She does not take any exogenous hormones (such as estrogens). Neither does she take blood thinners, Tamoxifen, or corticosteroids so medication effects can be ruled out. She denies any bowel or bladder problems, so diseases of adjacent organs can be effectively ruled out. The physical exam does not reveal any lesions of the vagina or vulva, signs of trauma, or cervical polyps. Cervical cancer is ruled out by a normal Pap result. Atrophic vaginitis presents with dryness and burning along with vaginal bleeding. The physical exam did reveal an atrophic vagina; however with atrophic vaginitis, the vaginal pH is between 6 and 7 (Chasson, 2006). Rhonda's vaginal pH was 4.7. This finding, along with Rhonda's denial of vaginal burning, effectively rules out atrophic vaginitis as a possible diagnosis. Endometrial hypertrophy in postmenopausal women is defined as an endometrium that measures greater than 4-5 mm (Wallace & Sanford, 2006). Since the transvaginal ultrasound indicated Rhonda's endometrium measured 3.5 mm, this diagnosis is eliminated. The ultrasound also did not show any evidence of uterine fibroids, so this too, can be ruled out.

Diagnoses that are still suspect include: endometrial atrophy, endometrial polyp, and endometrial carcinoma. These are also the three most frequent diagnoses associated with postmenopausal bleeding (Mahoney & Armstrong, 2005). A discussion of these pathologies follows.

Endometrial atrophy- The most common etiology of postmenopausal bleeding, endometrial atrophy accounts for between 60 and 80 percent of cases (Hsu et al., 2008). The postmenopausal

woman is hypoestrogenic. The epithelium of the endometrium is stimulated by estrogen, so with estrogen deficiency, the endometrium thins out and becomes atrophic (Sheikh, Sawhney, Khurana, & Al-Yatama, 2000). This atrophic endometrium is at risk for ulceration which in turn causes vaginal bleeding. For the woman taking hormone replacement therapy, the endometrium continues to be stimulated by estrogen and atrophy is less likely to occur. Measurements of the endometrial stripe on ultrasound do not provide a definitive diagnosis of endometrial atrophy. Histopathology of endometrial samples is the diagnostic tool for atrophic endometrium. However, one study reported by Sheikh, et al., (2000), indicates that for atrophic endometrium, the endometrial thickness stays in a fairly narrow range of 1-5 mm as measured through ultrasound. Rhonda's endometrium was estimated to be 3.5 mm, suggesting that atrophy may be the cause of the bleeding. The only way to obtain a definitive diagnosis is through histopathology of the endometrium.

Endometrial polyp- The echogenicity revealed in the ultrasound might indicate an endometrial polyp, but further testing is warranted. An endometrial polyp is a benign growth of the endometrium with an unknown etiology. Estrogen and Tamoxifen may fuel their growth; however, Rhonda is not taking either of these medications. Between 2 and 12% of postmenopausal bleeding is due to endometrial or cervical polyps (Yildirim et al., 2007). It is important to note that transvaginal ultrasonography has a sensitivity of 92% for diagnosing endometrial abnormalities. The endometrial biopsy did not identify a polyp; however, it is believed that up to 18% of focal lesions (such as polyps) may be missed by endometrial biopsy (Hsu et al., 2008). This is due to the fact that only a small portion of the endometrium may be sampled at a time. An endometrial polyp stands to be a possible cause of the postmenopausal

bleeding that Rhonda is experiencing, however further evaluation through saline sonohysterography is warranted to better visualize the abnormality.

Endometrial Carcinoma- While the endometrial biopsy did not indicate any abnormal cell pathology within the uterine lining, the ultrasound did reveal an echogenic focus. Endometrial biopsy has a negative predictive value of 93.7% (Mahoney & Armstrong, 2005), meaning a negative biopsy result is not definitive for ruling out carcinoma. Endometrial carcinoma must always be suspected until it can be ruled out. Endometrial cancer is the cause in 10% of postmenopausal bleeding cases (Cheng, 2006), and 80% of endometrial cancers occur in postmenopausal women (Sheikh et al., 2000). Risk factors for endometrial cancer include advanced age, hypertension, obesity, high fat diet, polycystic ovarian disease, diabetes, early menarche, late menopause, nulliparity, Tamoxifen therapy, and colon or breast cancer (Hsu et al., 2008). Another risk factor, hereditary nonpolyposis rectal cancer, is caused by a genetic mutation (Wallace & Sanford, 2006). Women with this genetic mutation have an estimated incidence of 20% to 60% of endometrial cancer (Wallace & Sanford, 2006). The incidence of endometrial cancer is 36.5 cases per 100,000 women aged 40-49 years (Hsu et al., 2008). It is the most prevalent gynecologic cancer and is the fourth most common cancer in women (Wallace & Sanford, 2006). Early detection is linked to a survival rate of 90% (Eisenberg, 2002).

Endometrioid adenocarcinoma is the most common endometrial cancer cell type, accounting for 75 to 80% of cases (Wallace & Sanford, 2006). There are two types of endometrial cancer classified based on cause. Type I, the most common, is caused by exposure to unopposed estrogens. The endometrium will initially exhibit hyperplasia followed by carcinomas. These tumors are usually superficial, minimally invasive and well-differentiated (Wallace & Sanford, 2006). Type I is associated with a good prognosis.

Type II endometrial carcinomas are not as well differentiated and appear spontaneously. There is no associated endometrial hyperplasia. Type II is associated with a poor prognosis. These women are generally thin, multiparous, and often times, African American.

The most common early presenting symptom of endometrial cancer is abnormal vaginal bleeding or spotting. Signs and symptoms later in the disease process include cramping, lower abdominal pressure, pelvic pain, lymphadenopathy, and weight loss (Wallace & Sanford, 2006).

Rhonda's endometrial thickness as measured by ultrasound was 3.5 mm. While carcinoma is less likely to be diagnosed in a woman with an endometrial thickness below 4 to 5 mm, it is possible (Sheikh et al., 2000). Rhonda does have three risk factors: age, hypertension and obesity.

Decision Point #3: Diagnostic tests

The remaining differential diagnoses require further testing to determine the etiology of Rhonda's abnormal bleeding. A saline sonohysterogram is attempted to visualize the inside of the uterus to evaluate the echogenic area that was identified in the ultrasound. Unfortunately, the cervix was too atrophic to pass the catheter through. A dilation and curettage and hysteroscopy were then scheduled with the physician. There was no evidence of endometrial polyp or other endometrial abnormalities identified with hysteroscopy. A tissue sample was taken and sent for study.

Decision Point #4: Suspected diagnosis and management

The presumptive diagnosis is endometrial atrophy. Hysteroscopy is the gold standard in diagnosing abnormal uterine bleeding; the probability of endometrial cancer after a negative hysteroscopy is 0.4% to 0.5% (Cheng, 2006). However, endometrial cancer cannot be completely ruled out until the final biopsy results have returned. It is for this reason that no

treatment is initiated at this time. Endometrial atrophy is benign, and the resultant bleeding that Rhonda is experiencing is harmless, except for the annoyance factor. Expectant management is used for endometrial atrophy. If the biopsy results effectively rule out carcinoma, then a short term, unopposed estrogen regimen may be started to rebuild the endometrium (American College of Obstetricians and Gynecologists [ACOG], 2004). The estrogen therapy would be contraindicated if the patient does have a cancer, so this treatment option is not explored at this time. It is important to note that the estrogen regimen is optional if indicated, and therefore the decision will be left to the patient.

Decision Point #5: Final Diagnosis and Management

The histopathology results show no evidence of cancer, but do show atrophic changes. Hence, the diagnosis of atrophic endometrium is proper. When Rhonda returns to the office to discuss the pathology report, she reports that her bleeding has ceased. She elects not to start on the estrogen regimen at this time. Education on diet and exercise is provided, as obesity and diet are modifiable risk factors for endometrial carcinoma. Rhonda is instructed to follow up yearly for a breast and pelvic exam as well as yearly mammography. She is instructed that the bleeding may recur, and if so, she should follow up with the NP for further evaluation and treatment options.

Case Study Summary

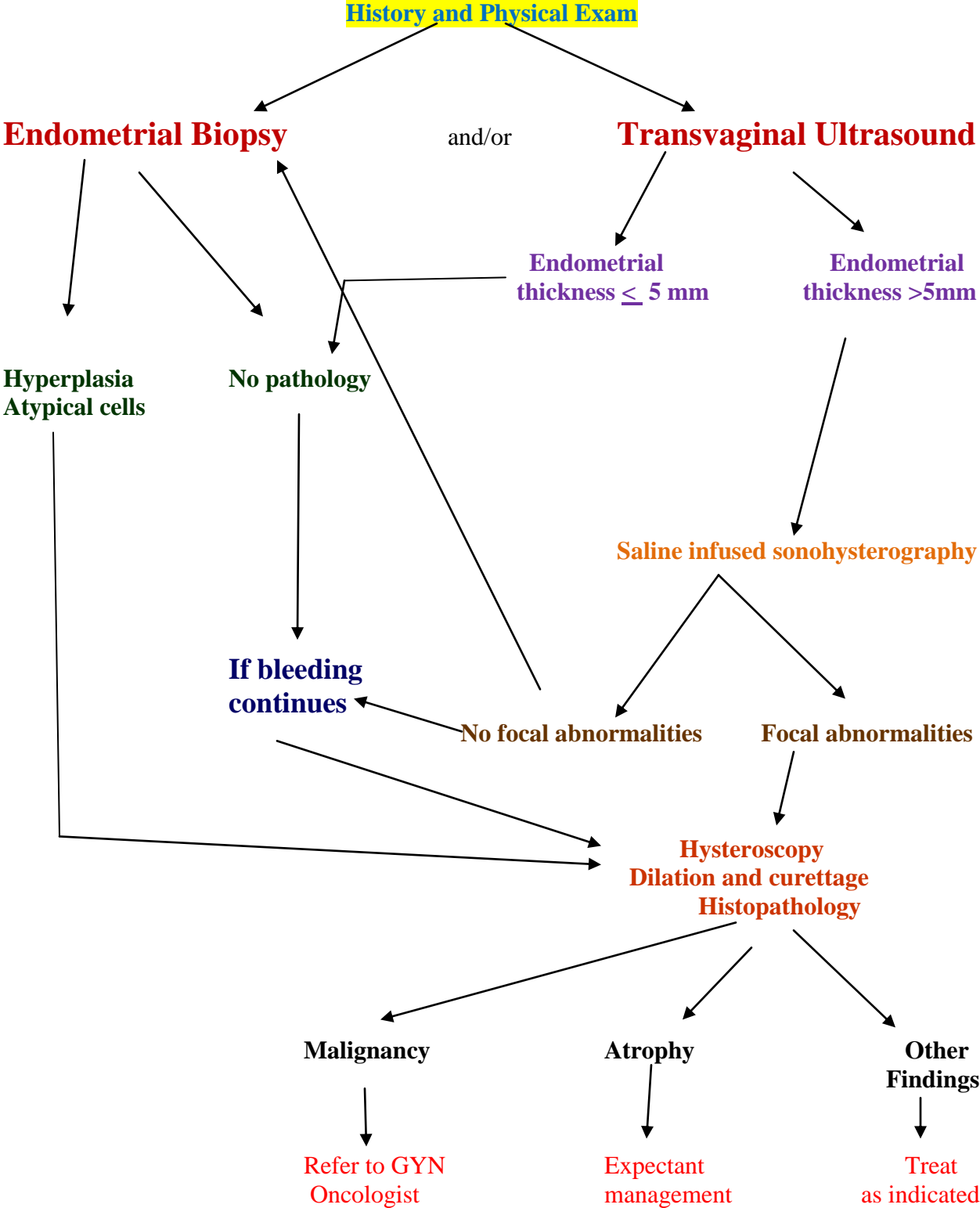
In Rhonda's case, as with all cases of postmenopausal bleeding, endometrial cancer must be ruled out. This patient had been free of menses for three years and then developed a sudden onset of vaginal bleeding. The initial differential diagnoses were many and included endometrial atrophy, endometrial or cervical polyp, emotional stress, trauma, diseases of adjoining structures, exogenous hormone use, vaginal or vulvar lesions, atrophic vaginitis, endometrial hyperplasia,

uterine fibroids, cervical cancer, and endometrial carcinoma. A focused history eliminated emotional stress, diseases of adjoining structures, and exogenous hormone use from the list of differentials. The physical exam findings removed cervical polyp, trauma, and vaginal or vulvar lesions from the list of possible diagnoses. Vaginal pH testing along with history findings eliminated atrophic vaginitis. A normal Pap test ruled out cervical cancer. Endometrial hyperplasia and uterine fibroids were ruled out after the ultrasound. A hysteroscopy and dilation and curettage performed by the physician excluded endometrial polyp and endometrial cancer. The final histopathology confirmed the diagnosis of atrophic endometrium.

Conclusion

While postmenopausal bleeding is most often times caused by an atrophic endometrium, the practitioner should always suspect endometrial cancer until proven otherwise. Endometrial cancers have a high survival rate when detected early. Transvaginal ultrasound and endometrial biopsy are excellent methods of investigating the endometrium. One or the other, or both, should be performed on all postmenopausal women with vaginal bleeding as a first step in the evaluation process. Postmenopausal women should be questioned regarding the presence of vaginal bleeding during routine office visits and instructed to have any vaginal bleeding evaluated.

Decision Tree for Postmenopausal Bleeding



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