The Use of Imaging in Endometrial Cancer

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Introduction

By following a patient through her clinical course, as well as exploring the imaging of others who also have her diagnosis, we will explore the use of imaging in the diagnosis and surgical planning of endometrial cancer.

Let’s begin with a history of our patient, an 84 year old female.
Our Patient, 84 year old female

**CC**: Occasional drop of blood in the toilet

**HPI**: 5 months ago, noticed an occasional drop of blood in the toilet. Bleeding has progressed to “more than a drop” in the toilet and on her underwear with increasing frequency, but not to the amount of a period. Denies dysuria, pain with bowel movements, weight loss.

**PMH**:  
*Medical*: Type II Diabetes, Hypercholesterolemia, Hypertension

**Physical Exam (Pertinent Positives)**:  
*Cervix*: Small amount of pink discharge. No cervical motion tenderness, no lesions.  
*Uterus*: Non-tender. Slightly enlarged.
Differential Diagnosis of Abnormal Bleeding in a Postmenopausal Woman

- Renal
- Urinary
- Lower GI
- Gynecologic
Back to Our Patient: Lab Values

Lab Values: Urinalysis negative for RBCs. Hemoccult negative stools. Pap smear “unsatisfactory for evaluation” due to insufficient cellular material.

Her history, physical exam, and lab values make us suspicious of a uterine etiology of her abnormal bleeding. Let’s continue to discuss common causes of abnormal uterine bleeding.
Differential Diagnosis of Abnormal Uterine Bleeding

**Hormonal**
- Perimenopausal Hormone Change
- Postmenopausal Atrophy
- Hormone Therapy
- Hypothyroidism
- Hyperthyroidism
- Cushing’s Syndrome

**Anatomic**
- Fibroids
- Polyps
- Adenomyosis
- Hereditary Leiomyomatosis and Renal Cell Carcinoma Syndrome

**Cancer/Infection**
- Endometrial Carcinoma
- Uterine Sarcoma
- Endometritis (Chronic)

**Bleeding Diatheses**
- Von Willebrand’s
- Thrombocytopenia
- Acute Leukemia
- Advanced Liver Disease
- Medications
Endometrial Cancer: Clinical Presentation

• **Cardinal Symptom: Abnormal Uterine Bleeding** - occurs in 90% of cases
  • Pelvic Pain - including dyspareunia
  • Mass Effect of Enlarged Uterus
    • Pelvic Pressure
    • Increased Urinary Frequency
    • Difficulty emptying bladder
    • Constipation

**The longer a woman has been postmenopausal, the more likely her abnormal uterine bleeding is due to endometrial cancer. Thus, even one drop of uterine blood for a postmenopausal woman is endometrial cancer until proven otherwise.**

Source: ACOG Practice Bulletin, 2005
Endometrial Cancer: Epidemiology

- Most common gynecologic cancer; 6% of all cancers in women
- Lifetime risk: 2.5%
- Mean age of onset: early 60s. 25% of cases are premenopausal.
- 5-20% of women with postmenopausal abnormal uterine bleeding will have endometrial cancer.
- Stage IA 5-year survival rate is 90.8%; Stage IVB 5-year survival is 20.1%

Endometrial Cancer: Risk Factors

**Risk Factors**
- Increased estrogen exposure
- Exogenous (Hormone Replacement Therapy)
- Endogenous (adipose tissue; functional ovarian tumors)
- Chronic Anovulation (PCOS)
- Obesity
- Nulliparity, EtOH use, early menarche/late menopause
- Age (Older than 60 y.o.)
- Genetics (Lynch Syndrome, ? BRCA, Breast Cancer)
- Hypertension and Diabetes (Obesity, increased insulin-like growth factors)

**Protective**
- OCP use
- Postmenopausal Progestin Therapy
- Smoking

Source:
http://www.uptodate.com/online/content/topic.do?topicKey=gyne_onc/9015&selectedTitle=3~150&source=search_result
Endometrial Cancer: Pathology and Pathogenesis

**Type I**
- Estrogen-related, low-grade endometrioid
- DNA mismatch repair leading to microsatellite instability (K-Ras, P-TEN)
- Risk Factors: Increased estrogen exposure, obesity, nulliparity, etc.

**Type II**
- Higher grade papillary serous or clear cell tumors; poorer prognosis
- Abnormal p53 overaccumulation, High Ki-67 labeling, HER2/Neu overexpression
- Risk Factors: Multiparous, older in age (than Type I)

Source: Bokhman, 1983
Menu of Tests for the Work Up of Endometrial Cancer

**Endometrial Biopsy** - Gold standard and necessary for a definitive diagnosis of endometrial cancer; usually the first test performed in work up; performed in an office setting by a gynecologist

**Transvaginal Ultrasonography (TVUS) and Transabdominal Ultrasonography** - Distinguishes potential anatomical lesions requiring biopsy from atrophy as a cause of postmenopausal bleeding; may be the first test performed in work up or as follow up to an unsuccessful biopsy (e.g., because of a sclerotic cervix)

**Sonohysterography** - Involves placement of fluid in endometrial cavity to enhance endometrial visualization via transvaginal ultrasound; used when endometrium is difficult to visualize via TVUS or when guidance is needed for biopsy of a focal lesion

**Hysteroscopy with Directed Biopsy or with Dilatation and Curettage** - Performed if office biopsy is negative but clinical suspicion remains high; performed under anesthesia in the operating room by a gynecologist

Source: http://www.uptodate.com/online/content/topic.do?topicKey=gyne_onc/9015&selectedTitle=3~150&source=search_result
Illustration of Ultrasound Transducers

Transvaginal Ultrasound

- Ultrasound Transducer
- Vagina
- Sound Waves
- Ovary
- Uterus
- Cervix

Transabdominal Ultrasound

- Ultrasound Transducer
- Sound Waves
- Vagina
- Ovary
- Uterus
- Cervix

Sources:
Testing for Our Patient

First Test Performed

Second Test Performed
Transvaginal and Transabdominal Ultrasound: The uterus is enlarged measuring 9.9 x 5.0 x 6.1 cm. There is a 4-4.5 cm irregular soft tissue mass arising from the anterior endometrium. This contains arterial and venous flow. In addition, there is blood products distending the endometrial cavity. The ovaries are not visualized. No adnexal masses are seen.

“IMPRESSION: Abnormal endometrium with a solid broad-based mass with vascularity surrounded by blood, worrisome for endometrial cancer. Endometrial hyperplasia or a large polyp are felt to be less likely. Biopsy is recommended.”

Source: OMR, BIDMC
Companion Patient I: A Normal Uterine Ultrasound

• “Sandwich Sign” - linear alternating echogenicities representing the meeting of the endometria of the anterior and posterior walls of the uterus. Expect the “sandwich” (total thickness of endometrium) to be less than 5 mm.

• A postmenopausal uterus is expected to be no longer than about 5.5 cm and no wider nor thicker than about 3.0 cm.

Source: Merz, et. al, 1996
Our Patient: Enlarged Uterus on Ultrasound

“The uterus is enlarged measuring 9.9 x 5.0 x 6.1 cm.”
Our Patient: Irregular Uterine Mass on Ultrasound

“There is a 4-4.5 cm irregular soft tissue mass arising from the anterior endometrium. In addition, there are blood products distending the endometrial cavity.”
Our Patient: Blood Flow in Uterine Mass on Ultrasound

“This (the mass) contains arterial and venous flow.”

Source: PACS, BIDMC
The Use of Ultrasound for Detection of Endometrial Cancer in Women with Active Endometria

**Population Affected:** Women who are premenopausal or who are postmenopausal and taking hormone replacement therapy (HRT)

**Detection Issue:** The thickness of their endometria on ultrasound does not correlate well with concern for endometrial cancer and other anatomic anomalies that may be causing abnormal uterine bleeding. *Endometrium as thick as 5mm* on ultrasound has been shown to have *pathologic cytology* as well as *mask fibroids and polyps*.

**Pathophysiology:** Under hormonal influence, endometria naturally grow. Much of the growth seen in these women is more likely to be benign. It naturally masks abnormal growth that would be otherwise immediately concerning in postmenopausal women not on HRT.


Sources: Holbert, et. al, 1997
Breitkopf, et. al, 2004
Endometrial Cancer: Grading

For Our Patient:
Hysteroscopy and D&C revealed Grade 2 Endometrial Carcinoma

Uterine corpus carcinoma grades: degrees of histopathologic differentiation

<table>
<thead>
<tr>
<th>Grade</th>
<th>Description</th>
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</thead>
<tbody>
<tr>
<td>G1</td>
<td>5 percent or less of a nonsquamous or nonmorular solid growth pattern</td>
</tr>
<tr>
<td>G2</td>
<td>6 percent to 50 percent of a nonsquamous or nonmorular solid growth pattern</td>
</tr>
<tr>
<td>G3</td>
<td>More than 50 percent of a nonsquamous or nonmorular solid growth pattern</td>
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</tbody>
</table>

Source:
http://www.uptodate.com/online/content/topic.do?topicKey=gyne&source=search_result
# Endometrial Cancer: Staging

## Staging uterine carcinoma (TNM and International Federation of Gynecology and Obstetrics [FIGO])

<table>
<thead>
<tr>
<th>Primary tumor (T) (surgical-pathologic findings)</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>TNM categories</td>
<td>FIGO stages</td>
</tr>
<tr>
<td>TX</td>
<td>No evidence of primary tumor</td>
</tr>
<tr>
<td>T0</td>
<td>Tumor cannot be assessed</td>
</tr>
<tr>
<td>Tis**</td>
<td>Carcinoma in situ (preinvasive carcinoma)</td>
</tr>
<tr>
<td>T1</td>
<td>Tumor confined to corpus uteri</td>
</tr>
<tr>
<td>T1a</td>
<td>Tumor limited to endometrium or invades less than one-half of the myometrium</td>
</tr>
<tr>
<td>T1b</td>
<td>Tumor invades one-half or more of the myometrium</td>
</tr>
<tr>
<td>T2</td>
<td>Tumor invades stromal connective tissue of the cervix but does not extend beyond uterus*</td>
</tr>
<tr>
<td>T3a</td>
<td>IIIA</td>
</tr>
<tr>
<td>T3b</td>
<td>IIIB</td>
</tr>
<tr>
<td>T4</td>
<td>IVA</td>
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<table>
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<tr>
<th>Regional lymph nodes (N)</th>
<th>Definition</th>
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<tbody>
<tr>
<td>TNM categories</td>
<td>FIGO stages</td>
</tr>
<tr>
<td>NX</td>
<td>Regional lymph nodes cannot be assessed</td>
</tr>
<tr>
<td>N0</td>
<td>No regional lymph node metastasis</td>
</tr>
<tr>
<td>N1</td>
<td>IIC1</td>
</tr>
<tr>
<td>N2</td>
<td>IIC2</td>
</tr>
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</table>

<table>
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<tr>
<th>Distant metastasis (M)</th>
<th>Definition</th>
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<tbody>
<tr>
<td>TNM categories</td>
<td>FIGO stages</td>
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<tr>
<td>M0</td>
<td>No distant metastasis</td>
</tr>
<tr>
<td>M1</td>
<td>IVB</td>
</tr>
</tbody>
</table>

*Used with the permission of the American Joint Committee on Cancer (AJCC), Chicago, Illinois. The original source for this material is the AJCC Cancer Staging Manual, Seventh Edition (2010) published by Springer New York, Inc.
Endometrial Cancer: Common Routes of Metastases

Direct/Local - local extension beyond the uterus, including bladder and bowel

Lymphatic - to pelvic, para-aortic, and rarely inguinal lymph nodes

Hematologic - to lungs, liver, bone, and rarely brain

Peritoneal/transtubal - intraperitoneal implants

Use of Radiography in Staging Endometrial Cancer

This is controversial! Pelvic and abdominal imaging for clinical staging is considered unnecessary if surgical staging is planned. It is indicated only for planning of complex therapeutic surgery or for potential distant metastases. Surgical staging is considered the definitive staging modality.

But if imaging is obtained for staging...

**Contrast-enhanced MRI is the best!**
- Detects invasion of the myometrium, cervical involvement, and lymph node metastases
- 80-90% sensitivity for myometrial invasion and 57-100% sensitivity for cervical invasion.

**CT is also used**
- Myometrial and cervical invasion is less well defined
- Better for locating distant metastases

Our Patient: CT for Clinical Staging

“Impression: Heterogeneous and vascular uterine lesion without evidence of metastatic disease.”

Transverse CT images showing a uterus of heterogeneous intensity.
Our Patient: CT for Clinical Staging, Cont’d

Transverse CT images showing a uterus of heterogeneous intensity.

Sources: OMR and PACS, BIDMC
Companion Patient 2: Endometrial Invasion into the Myometrium on MRI

Coronal T2 weighted MRI with fat saturation showing endometrial invasion of the myometrium at the fundus by more than 50%
Companion Patient 3: Myometrial, Cervical, and Vaginal Invasion of Endometrial Mass on MRI

Axial SPGR post Gadolinium MRI showing endometrial mass through cervix into vagina

Sagittal T2 Weighted MRI showing endometrial mass invading myometrium anteriorly and extending through cervical canal

Source: PACS, BIDMC
Companion Patient 4: MRI Sequence Showing Lymph Node Metastasis

1) Pre-contrast T1 Spoiled Gradient Echo Lava Sequence MRI

2) 60 Second Delay Post Gadolinium MRI enhancing left node with a necrotic part that does not enhance Axial T1 SPGR

3) Subtracted Axial TI SPGR MRI showing an enhancing left node with a non-enhancing necrotic focus

MRI Sequence showing lymph node metastasis with necrosis next to endometrial mass in uterine cavity

Source: PACS, BIDMC
Endometrial Cancer: Treatment

Recommended Treatment:
• Hysterectomy
• Bilateral salpingooophorectomy
• Abdominopelvic washings
• Lymph node evaluation
• Maximal surgical cytoreduction for advanced disease

If the patient is not a surgical candidate for reasons of widespread disease or otherwise, radiation therapy, chemotherapy, or some combination of the two is recommended.

*Our patient underwent the recommended treatment and was found to have the following on pathology:
Histologic Grade: G2 - 6% to 50% non-squamous solid growth
FIGO Stage: IA - Invasion of myometrium of 40% (less than 50%) with no lymph node, local, or distant metastases.

Sources: Pecorelli, 2009; OMR, BIDMC;
http://www.uptodate.com/online/content/topic.do?topicKey=gyne_onc/26018&selectedTitle=2~150&source=search_result#references
Endometrial Cancer: Surveillance

• Postoperative Adjuvant Therapy (vaginal brachytherapy, external beam radiation therapy, chemotherapy) is recommended depending on the patient’s individual risk factors.

• For monitoring of recurrence, following the patient’s symptoms and performing a thorough physical exam are sufficient according to the literature because:
  • Recurrence of stage 1-II is rare and most of the surgical candidates are stage I or II
  • 70% of recurrence is symptomatic
  • There appears to be no statistically significant difference in survival between symptomatic and asymptomatic endometrial cancer survivors

• Thus, imaging in this setting is indicated only for a suspicion of metastasis or for following the progression of non-surgical candidates:
  • CXR for lymphadenopathy
  • MRI/CT as appropriate depending on symptoms.

Sources: Fung-Kee-Fung, et. al, 2006; Cooper, et. al, 2006; Berchuck, et. al, 1995
Take Home Points about Imaging in Endometrial Cancer

(Not imaging related, but) Have a low threshold for suspicion of endometrial cancer in a postmenopausal woman experiencing abnormal bleeding!

**Diagnosis:** Biopsy first, but ultrasound is a good first line alternative. Still, a biopsy follow-up is needed for definitive diagnosis. Also, endometrial thickness on ultrasound for women other than postmenopausal not on HRT is not a reliable indicator of potential malignancy.

**Staging:** MRI only for complicated cases for surgical planning. Staging should happen surgically and pathologically.

**Surveillance:** Image only when suspicious of metastasis.
References


• Estrogen, Progesterone, and Endometrium Image. Tubal-reversal.net. URL: http://www.tubal-reversal.net/images/endometrium-estrogen-progesterone.jpg; accessed 09/20/2010
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