Endometrial and Vulvar Biopsy Practicum

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Disclosures Patty Cason

Advisory Board
Teva (ParaGard, LeCette)
Merck (HPV vaccines)
Actavis (Levosert IUD in development)

Speakers’ Bureau
Teva (ParaGard)
Merck (Nexplanon, Gardasil, NuvaRing, Contraception)
Bayer (Mirena, Skyla)

Learning Objectives

Endometrial Biopsy

Learning Objectives Vulvar Biopsy
Describe characteristics of vulvar lesions that may indicate need for biopsy
Demonstrate punch biopsy technique for obtaining a vulvar biopsy

Learning Objectives EMB
List three indications for endometrial biopsy
Demonstrate spiral technique for endometrial sampling
Identify strategies for sampling the endometrium when cervical stenosis is present

Outline
1) Epidemiology
2) Indications
3) Differential Diagnosis
4) Contraindications
5) Devices
6) Technique
7) Challenging situations
8) Results
9) Follow up
10) Alternative diagnostic strategies
Epidemiology

Endometrial Cancer

4th most common female cancer
Most common female *genital tract* cancer
- 5 year survival 86-93%
  - 86% white; 55% AA
Bimodal age distribution
  - Menopausal women; mean age 61
  - Pre- and peri-menopausal chronic anovulators

Endometrial Cancer: Risk Factors

- Diabetes (RR= 2.8)
- Hypertension (RR= 1.5)
- Personal or family history of breast or colon cancer

Endometrial Cancer: Protection

Combined Hormonal Contraceptives
- Pill, patch, ring
Continuous progestin contraceptive
- Implant, LNG IUC, Progestin-only pills, DMPA

Risk Factors

Age: peak incidence 72 years old
- 3x higher than 50-54 years old
Chronic unopposed estrogen exposure
- E-level and duration of exposure
- High body mass index (BMI)
- Menopause >52
- Low parity (2-3x)
- Exogenous sources: ET, tamoxifen
- Chronic anovulation (PCOS)
Purpose

Detect endometrial hyperplasia in order to prevent cancer
Detect endometrial cancer as early as possible

Routine screening not recommended for:

- Asymptomatic perimenopausal or postmenopausal women
- Asymptomatic chronic anovulation
- Women initiating menopausal hormone therapy
- Tamoxifen Users

Menopausal Woman On Hormone Therapy

- Unscheduled bleeding on CS-EPT (continuous-sequential estrogen-progestin therapy)
- Bleeding > 3 months after start of CC-EPT (continuous-combined estrogen-progestin therapy)
- Endometrial stripe ≥ 5 mm (postmenopausal woman only)

≥ 45

- Exclude pregnancy
- Any irregular bleeding
- Any suspected anovulatory uterine bleeding

Menopausal Woman Not on Hormone Therapy

- Any bleeding
- Endometrial stripe ≥ 5 mm (postmenopausal woman only)
- Cervical cytology:
  - Any endometrial cells
  - AGC Pap

Premenopausal Women

- Exclude pregnancy and infection
- Prolonged abnormal uterine bleeding (AUB) intermenstrual bleeding
- Unexplained post-coital or intermenstrual bleeding

Premenopausal Women

- Exclude pregnancy and infection
- Prolonged abnormal uterine bleeding (AUB) intermenstrual bleeding
- Unexplained post-coital or intermenstrual bleeding
Younger Than 45

Biopsy If:

- No response to medical therapy
- Prolonged periods of unopposed estrogen stimulation
  - Obesity
  - PCOS
  - Hx of oligoovulation or annovulation
  - Hx of oligomenorrhea or amenorrhea

Note: Prior use of combined hormonal contraceptives or continuous progestins protective!

Cervical cytology:

Atypical endometrial cells

EMB + ECC (endocervical sampling – for example with endocervical curettage)
→ if neg → colposcopy

Cervical cytology:

Endometrial cells

- Postmenopausal
- Anovulatory (either anovulatory uterine bleeding or amenorrhea)
- Amenorrhea

Cervical cytology: AGC Pap

- Favor endometrial origin
- Any AGC result if patient at higher risk
  - Over 35
  - Obesity
  - PCOS
  - Hx of oligoovulation or annovulation
  - Hx of oligomenorrhea or amenorrhea

Lynch Syndrome

Hereditary Non-polyposis Colorectal Cancer Syndrome (HNPCC)

- High risk
- Annual screening after age 35
- Prophylactic hysterectomy and oophorectomy after childbearing complete
### Differential Diagnosis

Other tests and other diagnostic considerations

#### Other Testing for Abnormal Bleeding

- CT/GC
- Pregnancy test (even with tubal ligation)
- Sensitive β-hCG to exclude trophoblastic disease in patients who were recently pregnant
- Thyroid-stimulating hormone level assessment to exclude hypothyroidism or hyperthyroidism
- Prolactin level testing (if the level is elevated, the test should be repeated in the fasting state.)

#### Contraindications

- Pregnancy
- Recent or active PID
- Active cervical infections
- Clotting disorders

### Postmenopausal Bleeding: Differential Diagnosis

Exogenous estrogens
- HT (therapy formerly known as HRT)

Endogenous estrogens
- Acute stress
- Estrogen-secreting ovarian tumor

Atrophic vaginitis

Endometrial hypoplasia (atrophy)

#### Technique
Caveats

Blind procedure
Many areas of endometrium unsampled
Endometrial polyps and other anatomic variants may be missed

Uterine Anatomy

Technique of EMB

Bimanual exam to evaluate uterine axis, size
• Cleanse cervix with antiseptic
• Choose correct type (rigidity) of sampler
  • Gently advance to fundus; expect resistance at internal os
  • Note depth of sounding with side markings
  • Pull back stylet (inner stiffening rod) to establish vacuum

Use of the sampling device

• Suction developed once device is at fundus by withdrawing inner stiffening rod
• Sampling done by spiraling technique: fundus to internal os and returning to fundus
Use of the sampling device

Rotate in a helical direction from the fundus to the os in order to use the lateral cutting edge of the port
- If the sampler has filled, remove place tissue in fixative
- If the sampler did not fill, repeat 2-3 more passes

Spiral Technique

Image courtesy of Dr. Anita Nelson

Challenging situations

Clinical tips

Tips for Internal Os Stenosis

Pain relief
- Use para-cervical or intra-cervical block
- Intrauterine instillation of lidocaine
Tips for Internal Os Stenosis

Cervical dilation
- Stabilize cervix with tenaculum
- Dilate cervix progressively
- Lacrimal probes
- Cervical os finders
- Use small size Pratt or Hegar dilators

Internal Os Stenosis

- Freeze endometrial sampler to increase rigidity
- Grasp sampler with ring forceps 3-4 cm from tip

Result: Non-Neoplastic

- Proliferative: Einduced growth, but no ovulation
- Secretory: ovulatory or recent progestin exposure
- Menstrual: glandular breakdown, non-neoplastic
- Disordered: out-of-phase glands (often anovulation)
- Chronic endometritis/inflammation: plasma cells + wbc
- Atrophic: hypoplastic glands and stroma

Pain

- Inject 1/2 cc local anesthetic agent
- Paracervical block
- Alternative diagnostic strategy with anesthesia

Result: Non-Neoplastic

- Cystic hyperplasia: hypoplastic glands and stroma
- Insufficient: not enough tissue for interpretation
  - If adequate sampling, atrophic endometrium likely
  - If sounding <5 cm, may not have entered cavity
**Result: Neoplasm**

Endometrial polyp

Simple endometrial hyperplasia
- Gland proliferation and crowding, but no atypia
- Reversible with continuous progestin exposure

Atypical endometrial hyperplasia
- Hyperplasia with nuclear atypia of gland cells
- Premalignant; often not reversible with progestin

Endometrial carcinoma
- Stromal invasion of malignant glands

**Postmenopausal Bleeding: Management**

- Atrophic vaginitis: topical estrogen
- Chronic endometritis: + antibiotics
- Cystic hyperplasia or endometrial atrophy
  - Observe
  - Simple endometrial hyperplasia
  - Continuous high dose progestin, then re-biopsy in 3-4 months

- Endometrial carcinoma
  - Hysterectomy + XRT

**Follow up**

Management

- Persistent spotting after negative sampling
  - On hormone therapy
    - Adjust balance
    - If proliferative increase progesterone/progesterone
    - If atrophic increase estrogen or decrease progesterone/progesterone
  - If persists or if not on hormone therapy
    - diagnostic hysteroscopy or sonohysteroscopy
Alternative Diagnostic Strategies

Hysteroscopy

Hysteroscopy permits full visualization of the endometrial cavity and endocervix. It is extremely helpful in diagnosing focal lesions that may be missed with endometrial sampling. The likelihood of endometrial cancer diagnosis after a negative hysteroscopy result is 0.4–0.5%.

Transvaginal Ultrasonography

- Transabdominal imaging is less sensitive and of limited value in the evaluation of the endometrium.
- Endometrial thickness alone is not considered a clinically robust observation that can be used to determine management.
  - Varies 4-8 mm during the proliferative phase
  - 8-14 mm during the secretory phase
  - 5 mm is usual cutoff to trigger further assessment

Saline Infusion Sonohysterography

Can determine the presence or absence of intracavitary lesions and depth of myometrial involvement with leiomyomas. More accurately evaluates the endometrium compared with transvaginal ultrasonography alone.

VULVAR BIOPSY

Outline

1) Indications and site selection
2) Anesthesia
3) Types of biopsies and technique
Magnification

Colposcope or any mechanism to allow magnification

Thickened Lesions

Thickened lesions to differentiate:
- Vulvar Intraepithelial Neoplasia (VIN)
- Squamous Cell Cancer
- Lichen Sclerosis

Biopsy thickest region

Indications and Site Selection

When and whom to biopsy

Papular Lesions

- Papular or exophitic lesions, except genital warts
- Lesions (even warty lesions) that don’t respond or worsen with treatment

Hyperpigmented Lesions

Black, brown, red, pink, purple

Unless obvious nevus or lentigo

Use melanoma criteria

Biopsy darkest area

Ulcerative or Erosive Lesions

Unless obvious herpes, syphilis or chancroid

Biopsy at edge and include normal tissue

**In summary:**

Biopsy whenever diagnosis is uncertain

**Diagnostic Challenges**

- If the area is eroded can pose a diagnostic dilemma if epidermis missing
- If area has advance scarring may get a nonspecific result if active inflammation has subsided
- Multiple biopsies from different regions may be needed to show diagnostic findings

**Where to biopsy**

- Homogeneous lesions: one biopsy in center of lesion
- Heterogeneous lesions: biopsy each different lesion

**Site Selection Considerations**

Choose the most suspicious area
If there is a choice, avoid:
- Periclitoral, urethral or anal areas
- Vascular areas
- Areas under tension
- Curves

**Anesthesia**

**Local Anesthetic**

Topical

4% liposomal lidocaine (30 min) or EMLA (60 min)
Local Anesthetic: Injected

- Most lesions will require ½ cc. lidocaine or less
- Epinephrine typically is unnecessary, unless longer anesthetic duration or less bleeding is critical
- Use *insulin syringe* (smallest, sharpest needle)
- Inject anesthetic s-l-o-w-l-y to minimize pain

Punch

- Obtain adequate specimen (~ 3-4mm)
- No need to include healthy tissue
- Good anesthetic effect
- Use epinephrine in lidocaine
- Arrange tissue so that you are approaching at right angle to your punch
- Stretch skin as needed
- Stabilize your hand against adjacent tissue
- Use twisting motion

Types of biopsy

- Punch
  - Obtain adequate specimen (~ 3-4mm)
  - No need to include healthy tissue
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- Shave biopsy
- Excisional biopsy

To Collect Specimen

- Photo courtesy of Dr. Michael Policar
After Punch

- Lift specimen
  - with forceps or needle
- Snip base
  - With scissors or scalpel

Shave

- Helpful with exophytic lesions and warts
- Hold specimen with forceps
- Shave base evenly; flat against skin
  - With curved scalpel

Control of Bleeding

Pressure and patience
Monsel’s Solution
AgNO₃ stick (Silver nitrate will not cause a tattoo)
Gel Foam pieces
Suturing after punch or excisional biopsy almost never necessary

Excisional

Tailor to size of lesion
Use matching elliptical incisions, so defect will close most securely

Excisional

- Good anesthetic effect
- Excise an ellipse; A canoe
- V the incision from top to base
- Avoid cutting rectangles, squares

Suture

Start with one stitch at the mid-point
Then split the difference
Use a separate pathology container for each morphologically distinct area biopsied

References


References