Clinical Pathologic Correlations – Case Four

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Case 4 — Part I

- 44 y.o. G3 P3 referred with abnormal PAP
  - atypical glandular cells of undetermined significance (AGUS). See comment.
  - Comment:
    - “a metastatic adenocarcinoma cannot be excluded”

Case 4 – AGUS PAP

Your thoughts...

- risk factors
- cervical
- endometrial
- metastatic!?
Case 4 – AGUS PAP

PMH
- no prior abnl PAP
- regular exams
- no known h/o HPV
- + Hypertension
- + menorrhagia

PSH
- C/S x3

FH
- father – +breast CA
- brother – +melanoma

Next?

First Office Visit...

Exam
- slightly obese
- normal breast exam
- no lymphadenopathy

Pelvic
- TNS uterus
- no cervical enlargement
- no adnexal mass
- guaiac negative stool

Colposcopy
- no lesions of the cervix, vagina, or vulva

ECC

Endometrial Biopsy

Pathology — Part I

- ECC
  - fragments of benign endocervical glands and squamous epithelium

- Endometrial biopsy
  - Non-hyperplastic secretory endometrium

Case 4 — Additional Workup

- Labs

- Radiographic Studies

- Review the cytology
Case 4 — Additional Workup

- Review of original cytology
  - AGUS... agreed
- "not worried about metastatic adenocarcinoma"
- Source of "atypia"?
  - Indeterminate
- CA-125 <35
- CXR - negative
- XMG - negative
- CT abdomen/pelvis
  - Slightly enlarged uterus
  - No significant abnormalities

What is the next step?

1. Repeat cytology in...
   - 3 months...
   - 6 months...
2. Cone biopsy
   - Not a LEEP
3. D&C

Second Office Visit... 3 months

- Exam
  - Unchanged
- Pelvic
  - PAP repeated
- Colposcopy
  - No lesions of the cervix, vagina, or vulva
  - ECC repeated
Case 4 – Diagnosis

- ECC
  - highly suspicious for Müllerian (mucinous) type endocervical adenocarcinoma

Next?

- A diagnostic procedure is scheduled
- Cold knife conization
  - Not a LEEP
  - With ECC and endometrial curettage
Diagnosis — Part II

- cone biopsy
  - moderately-well differentiated mucinous adenocarcinoma with superficial invasion. Endocervical margins positive.
- endometrial curettage
  - fragments of mucinous adenocarcinoma
- endocervical curettage
  - fragments of mucinous adenocarcinoma. Hypermucinous endocervical glands

Radical Hysterectomy

- no gross photo available

- gross description
  - 1.3 x 1 cm hemorrhagic area at upper endocervix
  - cervix 5.5 cm in length

Gross Depiction of Tumor

- false negative:
  - Embx sample
  - ECC sampling

5.5 cm
Follow-up: Stage IB Mucinous Adenocarcinoma of the Cervix

- Adjunctive pelvic irradiation
- NED at 3 years
AGUS: Issues to Consider

- what are usual findings with AGUS?
  - false negative initial evaluation
  - what do you do?
- what is appropriate management?
  - Bethesda 2001 recommendations

Outcomes of AGUS*

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<th>Qualifier</th>
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<th>ECCa</th>
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* % of patients

All AGUS – 10% with carcinoma (AIS, ECCa, & EmCa)

Bethesda System 2001

- AGC (atypical glandular cells)
  - atypical glandular cells, NOS
  - atypical glandular cells, favor neoplasia
  - atypical endocervical cells, NOS
  - atypical endocervical cells, favor neoplasia
  - atypical endocervical cells, probably AIS
  - atypical endometrial cells
  - adenocarcinoma in situ (AIS)
  - AGC (any of the above) with squamous abnormality

AGC, “favor reactive” replaced by NOS

NCI Bethesda System 2001

Refs:
- Oncology 1999; 13:550-574
AGC Recommendation

- All women with AGC
- colposcopy
- endocervical sampling
- repeat cytology not acceptable

NCI Bethesda System 2001

AGC Qualifiers That Increase Risk

- favor neoplasia
- probable AIS
- AIS

- Recommendation*
  - diagnostic cervical excisional procedure
    > cold knife conization

* unless invasive cancer on exam, biopsy or ECC

NCI Bethesda System 2001

Why not LEEP?

Thermal cautery effect renders the endocervical glandular epithelium at the margin... uninterpretable!
AGC – Increased Risk of Endometrial Neoplasia

- atypical endometrial cells
- age ≥ 35
- unexplained vaginal bleeding with AGC at any age

Recommendation
- endometrial sampling (papelle or D&C)

NCI Bethesda System 2001

AGC – Negative Initial Evaluation

- AGC, glandular or endocervcal, NOS
  - repeat PAP every 4-6 months
  - continue for 3-4 negative cytologies
- AGC, favor neoplasia, AIS or carcinoma
  - diagnostic cervical excision (CKC)
  - if negative, consult with cytopathologist

NCI Bethesda System 2001

Negative Colposcopy, ECC, EMC, and CKC

Recommendation
- pelvic ultrasound
- abdominal-pelvic CT scan
  - look for non-gynecologic source
- review of cytology
  - original pathologist and second opinion

Case Presentation & AGUS Dilemma: Summary

- uncommon diagnosis
  - limited literature
- "qualifiers"
  - assist in projecting outcome
  - "favor neoplasia" et. al. with high probability for disease
- Bethesda 2001 with consensus recommendations