Glandular lesions in cervical cytology

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Glandular cells in cervical smears

1st ENDOCERVICAL
2nd ENDOMETRIAL
3rd TUBAL

Lower uterine segment
Glandular cells in cervical smears

- Transfomation cone
- “junction cone”
- **Endocervical cells key component of Pap test**
- No sq metaplastic/ endocervical cells

**BETHESDA:**
- Smear sufficient for evaluation
- – comment about the smear quality!!!

Salomon&Nayar. The Bethesda system for reporting cervical cytology; 2001
Glandular cells in cervical smears

- Cervical cytology primarily screening test for squamous intraepithelial lesion and squamous cell carcinoma
- Sensitivity for glandular lesions limited by problems with sampling and interpretation
- Rare findings
- ?Brush, ?Bethesda

Moriarity et al. Diagn Cytopathol 2003
Endocervical glandular cells - architecture

Strips, pallisading

(picket fence, palisade)
Endocervical glandular cells - architecture

Honeycomb pattern
Reactive endocervical cells

- Common
- Hormonal influences
- Inflammation
- Polyps
- DD: neoplastic cells, 3-D groups!!!, elongated nuclei, uneven granular chromatin

BETHESDA: Non-neoplastic changes
Reactive endocervical/endometrial cells with IUD

Clinical data!
BETHESDA: Non-neoplastic changes
Tubal metaplasia
Cilia: when these you divine, it is a fine benign sign! Richard DeMay

BETHESDA: Non-neoplastic changes
BETHESDA: Non-neoplastic changes
Tubar metaplasia - high endocervical cells?

Cilia + terminal plate
Endometrial cells - exfoliated

• Exodus: day 6-10
• Glandular and stromal cells
• ?Endometrial pathology: second half of cycle (anovulatory cycle, atrophy, post-partum, post-abortum, instrumentation, IUD, endometriosis, tuboendometrial metaplasia, endometritis, pyometra, leiomyoma, polyp, HRT, OHC, carcinoma (5% PM))

• Postmenopausal!!!

Clinical correlation advised (menstrual history, age)

BETHESDA: Endometrial cells in women ≥40 yrs
Endometrial cells in cervical smear

**Direct sampling-abrasia of the lower uterine segment**

Not reported....
Atypical endocervical cells

- Benign cellular changes with atypia – mimics of glandular neoplasia
- Inflammation, IUD, RT
- Polyps, microglandular hyperplasia, tubal metaplasia
- HG (squamous) lesions: ~10-50%

DD: tubal metaplasia, cilia?

BETHESDA: Atypical endocervical cells - of unknown significance
BETHELSDA: Atypical glandular cells - favour neoplastic

Histology: CIN 2
Endocervical adenocarcinoma in situ

- Loss of honeycomb
- Nuclear crowding, overlap
- Pallisading, feathering
- Nuclei elongated, coarse chromatin

BETHELSDA: Endocervical adenocarcinoma in situ
Endocervical adenocarcinoma

- Different histologic types – cytology?
- Tumor diathesis, nuclear clearing, nucleoli

BETHESDA: Adenocarcinoma - endocervical
Atypical endometrial glandular cells

- Benign/atypical – ↑nuclear size
- Polyp, IUD, endometritis, endometrial hyperplasia, carcinoma

Pap test is not screening procedure for detection of endometrial carcinoma

BETHESDA: Atypical endometrial cells - of unknown significance
Endometrial adenocarcinoma

- Cytology / grade
- Tumor diathesis – finely granular / watery

Pap test is not screening procedure for detection of endometrial carcinoma

BETHELDA: Adenocarcinoma - endometrial
Other glandular cells - mlg

- Extrauterine adenocarcinoma
  - Ovary
  - Fallopian tube
  - Metastases

*BETHESDA: Adenocarcinoma - extrauterine*
CERVICAL SCREENING FOR GLANDULAR NEOPLASIA

• Major challenge in gynecological cytopathology
• Rare finding: incidence of AGC 0.46%-2.5%
• Limited reproducibility of AGC interpretation
• Significant underlying pathology: 8.2-53% (CIN2/3)
• Non-cervical uterine or adnexal carcinoma

ZORA
slovenian national cervical screening program
Zgodnje Odkrivanje predRAkavih sprememb na materničnem vratu

http://www.onko-i.si/zora/
ZORA

- To decrease incidence and mortality from cervical cancer in Slovenia
- Aim: to screen at least 70% of women between 20 – 64 years of age every 3 years
- Invitations for non-attenders
- Gynecological examination and the Pap test (conventional: Ayre’s spatula and brush)
CERVICAL SCREENING FOR GLANDULAR NEOPLASIA

No. of histologically confirmed new cervical cancers in Slovenia

2003: 210 cases = 20.6
2009: 129 cases = 12.6  ↓39%

CERVICAL SCREENING FOR GLANDULAR NEOPLASIA

- IP FM UL 2008: 42,833 cervical smears
- ZORA Registry: 99 (0.23%) cases, different grades of atypical glandular cells
- AGC: 77/99 - 77.8%
- SA-GC/AIS: 12/99 - 12.1%
- Adenocarcinoma (AC): 10/99 - 10.1%
CERVICAL SCREENING FOR GLANDULAR NEOPLASIA

- HISTOPATHOLOGIC FINDINGS
- In 52/77 (67.5%) AGC biopsy not performed
- Follow-up cervical smears (acc. to cytol guidelines)
- All **negative** for neoplasia in 2011
CERVICAL SCREENING FOR GLANDULAR NEOPLASIA

- HISTOPATHOLOGIC FINDINGS in 32% AGC
- CGIN HG only in one case (1.3%)
- CIN in 12 patients (15.6%), most of them (9 cases, 11.7%) were CIN 2 and CIN3
- Benign: 11 (14.3%)
- EM Adenocarcinoma: 1 (1.3%)
CERVICAL SCREENING FOR GLANDULAR NEOPLASIA

- HISTOPATHOLOGIC FINDINGS in SA-GC/AIS

- **Adenocarcinoma** (2 EC, 2 EM): 4 patients (33.3%)

- **CIN**: 6 patients (50%, 5/6 CIN 2 and CIN 3)

- **Benign**: 2 (16.7%)
CERVICAL SCREENING FOR GLANDULAR NEOPLASIA

- HISTOPATHOLOGIC FINDINGS in ADENOCARCINOMA
- Malignancy confirmed in 7 patients (70%)
  - EM ca: 4
  - Meta ovarian ca: 2
  - SCC: 1
  - CIN: 3 cases (30%), 2/3 CIN3
CERVICAL SCREENING FOR GLANDULAR NEOPLASIA

• **ZORA: HPV triage testing** (SLO Oct. 2010)
• Cervical cytology sample in liquid medium
• HPV DNA Hybrid Capture 2 (hc2): HPV 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 68
• Indications:
  – Atypical squamous cells NOS (5-12% CIN-VS expected)
  – Atypical glandular (endocervical) cells - NOS
  – LSIL after age 35
  – Follow-up of CIN1
  – Follow-up after TH of CIN

Rabelo-Santos et al. Cytopathology 2008
CERVICAL CANCER AUDIT

• **Audit** of interval cervical cancers in the context of all the components of the routine screening process

• **Re-screening** of negative or low grade smears before the diagnosis of invasive cancer presents an important part of the audit.

*European guidelines for quality assurance in cervical cancer screening. 2nd ed., 2008.*
CERVICAL CANCER AUDIT

- Slovenia: only cytopathology part of the audit
- Complete audit of all screening components has not been conducted yet!
- 1\textsuperscript{st} cytology audit 2008 for cervical cancer diagnosed in 2006: negative or low-grade smears reviewed from 2003 (beginning of ZORA) till 2006

CERVICAL CANCER AUDIT

- Underdiagnosed cervical smears were less likely to be found in endocervical adenocarcinomas compared to squamous cell carcinomas
- Inadequate sampling (EAC in cervical stroma or deeper in the cervical canal)

CERVICAL CANCER AUDIT

• Underdiagnosed cases: representative highly atypical glandular cells found on the review but not recognized originally

Glandular lesions in cervical cytology

• Cytotechnologists/screeners and cytopathologists alike very rarely see true premalignant and malignant (endocervical) glandular cells in routine everyday practice

• Continuous medical education in cervical glandular cytology!

Hvala za pozornost!
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in cooperation with
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