Non-neoplastic conditions of the uterine cervix

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Normal structure

Physiologic changes and formation of the transformation zone (TZ)

Squamocolumnar junction (SCJ)
"border between stratified squamous epithelium of ectocervix and glandular epithelium of endocervix"
Mature metaplasia

Congenital Transformation Zone (CTZ)
- Variant of squamous metaplasia
- Peripheral to acquired TZ
- Incomplete maturation
- Always irregularly dentate epithelial-stromal junction
- Absence of cytoplasmic glycogen
- DDx: SCC, wart viral infection

Histogenesis of CTZ
- Identical to DES exposure
- Late squamous change
- Nearly always a single line
- LM ~ squamous metaplasia
- Colposcopy ~ CIN
- DNA ploidy = diploid
- Behavior → benign

Hormonal influences on squamous epithelium
- Basal cell hyperplasia
  - Regular replication of basal layers with nuclear enlargement
  - Absence pleomorphism & hyperchromasia
  - Normal upper half
  - Long-term implication – unknown
  - DDx – HSIL
  - Ki-67 and p16

Basal cell hyperplasia
- Squamous cell hyperplasia
### Squamous cell hyperplasia
- Acanthosis, irregular epithelial stromal junction ~ rete ridges of skin
- Hyperkeratosis ± granular layer
- Condition found
  - Uterovaginal prolapse
  - healed following treatment

### Chronic cervicitis
Clinician – red, inflamed, irregular surface
Colposcopist – “wide transformation zone”, physiologic > pathologic, red & rough TZ, excess mucus production
Pathologist – dense CI in superficial cervical stroma

### Chlamydia trachomatis
- Predominantly endocervical esp. crypt
- Plasma cell predominant
- ± germinal center formation
- No necrosis / destruction of underlying tissue
- Cyto – intracytoplasmic inclusion, ragged cytoplasmic border ± follicular cervicitis

### Tuberculosis
- Rare
- 8% of women with genital tuberculosis
- Clinical - Hypertrophic lesion
- Micro – Typical granuloma

### Syphilis
- Treponema pallidum
- Cervix: 10% - 40% of women with syphilis
- Firm, nodular, ulcer
- Dense plasma cell infiltration
- vasculitis

### Inflammation to regenerative changes
- Chlamydia trachomatis
- Tuberculosis
- Syphilis
- Herpes simplex virus
- Cytomegalovirus
- Human papillomavirus (HPV)
- Schistosomiasis
Herpes simplex virus

- Small painful vesicles
- Acute necrotizing inflammation ± vasculitis
- Enlarged nucleus & nucleoli, cytoplasmic swelling → vacuoles, multinucleated cells, ground-glass nucleus, eosinophilic intranuclear inclusion → necrosis, destruction stroma, glands, vessels

Cytomegalovirus

- Sexually transmitted / systemic infection
- Large, basophilic intranuclear inclusion

Schistosomiasis

- Schistosoma hematobium
- Endemic in tropical / subtropical area
- Ulcerative / nodular lesion
- Inflammatory exudate, giant cell, fibrosis
- Sensitive Dx – cervix biopsy crushed between 2 glass slides → ova (terminal spike)

Cytomegalovirus

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Healing and regenerating epithelium

Clue

- Uniform nuclei
- Generally prominent macronucleoli
- Inflamed stroma

Non-neoplastic change

Mullerian metaplasia

- Mullerian (paramesonephric) duct
- 21% - 62%, incidental finding
- Premenopausal women
- Rarely found grossly
- Pap smear esp. cytobrush used
- Negative for CEA
- Individual cell positive for p16
- Negligible Ki-67
- Positive for vimentin (endometrioid metaplasia)

Transitional metaplasia

Intestinal metaplasia

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- Generally prominent macronucleoli
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Transitional Metaplasia

- Peri- and post menopause
- Exogenous hormone / androgen
- Multilayer epithelium, uniform, oval to spindled nuclei
- Vertical → streaming superficially
- IHC: positive CK13, CK17, CK18 negative CK20
  p16 only in superficial "umbrella cell"
- DDx squamous dysplasia

Intestinal metaplasia

- Rarest form of metaplasia in cervix
- Most common associated with AIS / ADC
- Careful sampling & examination

Lesions of the endocervical glandular epithelium

Tunnel clusters
- Multigravid, over age 30
- Multifocal, incidental finding
- 2 types
  - Type A:
  - Type B: more expansive
- Negative CEA
- DDx – AIS / ADC / MDA

Deep Nabothian Cysts
- Multiparous women
- Asymptomatic / chronic cervicitis
- Multiple mucin-filled cysts
- Single layer of columnar / flat endocervical cells
- DDx - MDA

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Lobular endocervical glandular hyperplasia

- Uncommon,
- Suggestive of pyloric gland metaplasia
- 37-71 years (mean 45 y)
- Asymptomatic / discharge / ± mass
- Pap : AGC
- Gross: polypoid mass / multiple cyst
- Micro: single layer of columnar, mucin producing cells, bland and basal nuclei, ± mitosis (up to 2/10 HPF
- IHC: neutral mucin (PAS+), HIK1083 and MUC6 positive, CEA+
**Diffuse laminar endocervical glandular hyperplasia**
- Uncommon
- Premenopausal women (22-54 years)
- Incidental finding / watery or mucoid discharge
- Gross: no specific finding
- Micro: clearly demarcated, diffuse proliferation of round or abnormal shaped, small- or medium-sized glands confined to inner endocervical wall, bland & mucin containing columnar epithelium, rare mitosis
- DDx: MDA

**Microglandular hyperplasia**
- Reproductive age
- Exposure to progesterone, pregnancy
- Incidental findings
- Gross: ectropion, polyp, friable raised area
- Micro: focal / multifocal, closely packed glands of variable size and shape, little stroma, AI in gland lumens
d - columnar/cuboid, mucin producing, supra- or subnuclear vacuoles, uniform nuclei
- DDx: - clear cell CA
  - endometrioid CA with microglandular pattern

**Arias-Stella reaction**
- 9% - 37% pregnant women
- History of OC use
- Incidental / in polyp
- Focal / extensive, most in upper EC canal
- Micro: large cell with clear/oxyphilic cytoplasm, large atypical nuclei with hobnail appearance, rare mitosis ± decidua
- DDx: - clear cell CA

**Lesions related to exogenous stimuli**
- microglandular hyperplasia
- Arias-Stella reaction
- Decidual change
- Radiation change

**Decidual change**
- Progestin-induced alteration of stromal tissue
- Pregnancy / post partum
- Gross: small, raised, vascular nodule or sessile polyp
- Colpo: ~ CA esp. prominent, rather bizarre vessels
- Micro: enlarge, copious cytoplasm with uniform, small, central nuclei

**Radiation change**
- Acute / long term changes
  - Erosion, cellular swelling, dilated vessel, stroma change (necrosis, edema, CI)
  - Atrophy ± atypia, stroma change (edema, fibrosis, hyalinization, atypical fibroblast, rare giant cell, focal calcification)
- Blood vessel change
- EC change
- Mitosis - absent
- DDx: AIS / clear cell CA
Other non-neoplastic conditions

Endometriosis
Mesonephric duct remnants & hyperplasia
Cervical polyp

Endometriosis
- (Deep) / superficial forms
- Premenopausal (range 20-53 years)
- Incidental / secondary to trauma or procedure
- Gross: thickening, nodule, blood-filled bleb or cyst, granular/hemorrhagic mucosa
- Micro: endometrial tissue, up to 3 mitosis/gland, no abnormal mitosis
- IHC: CD10, p16
- Abnormal Pap smear
- DDx: AIS / EM stromal sarcoma

Mesonephric duct remnant
- 22% of adults, 40% newborn / children
- Abnormal Pap smear
- Lateral, deep in EC wall
- Small group of glands or tubules, ± duct branch
- Single layer cuboid/columnar, scant eosinophilic cytoplasm, round bland nuclei, no mitosis, eosinophilic material in lumen
- PAS negative cell but PAS positive, diastase-resistant luminal content

Mesonephric duct hyperplasia
- 3 types
  - Lobular:
    - Most common, 35 year-old
    - Lobule, larger loosely organized, irregular shaped → incidental finding, indurated cervix
  - Diffuse:
    - Second most common, slightly older
    - Irregular shape, hypertrophy, erosion
    - Diffuse proliferation mesonephric tubules ± ducts, lack atypia, rare mitosis

Mesonephric duct hyperplasia
- Ductal:
  - Least common
  - Prominent duct with papillary tufting, minimal proliferation of tubules
- DDx:
  - mesonephric adenocarcinoma
  - MDA

Cervical polyp
- Common
- Localized overgrowth of EC tissue
- Asymptomatic / spotting / irregular bleeding
- EC tissue, inflammation ± squamous metaplasia
- DDx: EM polyp, submucous leiomyoma
- Caution:
  - CIN
  - embryonal rhabdomyosarcoma
Normal structure
Physiologic changes
Inflammation & infection
Healing and regeneration
Non-neoplastic change
- Mullerian metaplasia
- Transitional metaplasia
- Intestinal metaplasia
Lesions of the endocervical glandular epithelium
- Tunnel clusters
- Deep Nabothian cyst
- Lobular endocervical glandular hyperplasia
- Diffuse lobar endocervical glandular hyperplasia
Lesions related to exogenous stimuli
- Microglandular hyperplasia
- Arias-Stella reaction
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Other non-neoplastic conditions
- Endometriosis
- Mesonephric duct remnants & hyperplasia
- Cervical polyp

SUMMARY

Take Home

- Clinical information & correlation
- Careful gross & microscopic examination
- Keep in mind
  - Physiologic VS pathologic
  - Non-neoplastic VS neoplastic
- IHC: may / may not helpful