Benign lesions of the cervix mimicking neoplasia

Anne-Sophie Van Rompuy
UZ Leuven
Overview

- Deep endocervical glands and Nabothian cysts
- Tunnel clusters
- Microglandular hyperplasia
- Mesonephric duct remnants and hyperplasia
- Lobular endocervical glandular hyperplasia
- Diffuse laminar endocervical glandular hyperplasia
- Arias-Stella reaction
- Tubal/tubo-endometrioid metaplasia
- Endometriosis
- Endocervical adenomyoma
- Ectopic prostatic tissue
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Deep endocervical glands and Nabothian cysts

- Endocervical glands can be **irregularly distributed** in the cervix and extend deep into the outer one-third of the cervical wall.
- May form **large cysts**, creating a mass lesion
- Gross examination: multiple, mucin-filled cysts extending from the mucosa to the deep portion of the wall

Oliva & Tornos, USCAP 2015
Glands and cysts are relatively uniform in contour, not overly crowded, and lined by a single layer of cytologically benign columnar to flattened epithelium without mitotic activity.
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Tunnel clusters

- Occur in **multigravid women**, usually over 30 years of age
- Two types: **type A and type B**. Type B is the most common, can be extensive and macroscopically visible.
- **Multifocal** involvement is common
Tunnel clusters: type B

- Closely apposed, simple cystic glands lined by flattened or low cuboidal epithelium that lacks mitotic activity
- Lobular arrangement
- Can expand deeply into the cervical wall mimicking malignancy
Tunnel clusters: type A

- Often associated with type B
- Well-circumscribed proliferation of oval, round or angulated glands.
- More irregular, angular of pseudo-infiltrative arrangement
- More prominent cells: cuboidal with amphophilic cytoplasm/columnar and mucus secreting. May have enlarged nuclei with small nucleoli
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Microglandular hyperplasia

- Can be diagnostically **challenging**, has the potential for misinterpretation as carcinoma.
- Mostly **incidental findings**, can produce gross abnormalities in the form of ectropion, polyps or friable, raised areas.
- Usually in women of **reproductive age**, but occasionally in post-menopausal women.
- Apparent association with exposure to **progesterone** in the form of oral contraceptives, Depo-Provera or pregnancy. But can also be found in women without this hormonal background.
- Unifocal or multifocal
- **Closely packed glands** of variable size and shape, with little intervening stroma
- Epithelial lining is columnar or cuboidal, mucin-producing, and often containing supranuclear or subnuclear **vacuoles**. Usually uniform nuclei, focal atypia can be encountered
- Usually infiltrated by acute and chronic **inflammatory cells**, with neutrophils in the intraglandular mucinous secretions
- Little mitotic activity (< 1 mitosis/10 HPF).
- **Squamous metaplasia** often present
Microglandular hyperplasia

Unusual growth patterns

- Solid
- Signet-ring cells
- Pseudoinfiltrative
- Prominent stromal hyalinization

*Int J Gynecol Pathol, Vol. 21, No. 4, October 2002. Nucci M*
Microglandular hyperplasia: DD

- **Clear cell carcinoma**
  - Cervical mass
  - Infiltrative pattern
  - Pronounced cytologic atypia
  - Papillary growth pattern, hobnailing, sheets of clear cells

- **Endometrioid endometrial adenocarcinoma with microglandular pattern**

  → Features favoring adenocarcinoma:
    - Postmenopausal age
    - Absence of typical areas of MGH
    - Cytologic atypia > than in MGH
    - Increased mitotic activity (> 1/10HPFs)
    - High Ki-67 index. CAVE inflammatory cells!

*Oliva & Tornos, USCAP 2015*
The diagnosis of microglandular hyperplasia should be made with caution in a postmenopausal women, particularly if there is cytologic atypia > usual and the morphologic appearance is not typical of microglandular hyperplasia
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Mesonephric duct remnants and hyperplasia

- Vestigial elements of the mesonephric/wolffian duct
- Preferentially located in the lateral walls of the cervix
- Small cysts and/or tubules lined by bland cuboidal or low columnar nonciliated epithelium
- Often a dense eosinophilic luminal secretion is present

Nucci, 2002  Blaustein, Chapter 4  Soslow & Longacre, chapter 3
Mesonephric hyperplasia

• Proliferation of mesonephric tubules measuring > 6 mm in single dimension
• Typically an incidental finding, rarely mass-forming lesion
• 3 types (no clinical significance)
  • Lobular mesonephric hyperplasia
  • Diffuse mesonephric hyperplasia
  • Mesonephric duct hyperplasia

Lobular mesonephric hyperplasia

- **Most common** type
- **Lobular** arrangement of small-sized to medium-sized, typically round but occasionally irregularly shaped, tubules separated by varying amount of stroma
Diffuse mesonephric hyperplasia

- **Uniformly** well-spaced, small-sized to medium-sized round to slightly irregular mesonephric tubules separated by stroma.
- The presence of **intervening stroma** is helpful in distinguishing it from mesonephric carcinoma.
Mesonephric duct hyperplasia

- **Least common** type
- Located beneath normal endocervical glands
- Medium-sized to large-sized duct, often with a **clefted contour**, lined by **hyperplastic-appearing epithelium** with **short papillary intraluminal projections**
- Typically **lacks** the intraluminal **eosinophilic secretions**

*Int J Gynecol Pathol, Vol. 33, No. 4, July 2014. Nucci M*
### Immunohistochemistry

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<td>PR</td>
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<tr>
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<tr>
<td>p16</td>
<td>Patchy/focally +</td>
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<tr>
<td>CD10</td>
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<td>GATA 3</td>
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</table>
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Lobular endocervical glandular hyperplasia (LEGH)

- Reproductive and postmenopausal women
- Usually *incidental* finding, may present with symptoms of watery or mucoid discharge
- **Distinctly lobular proliferation** of small-sized to medium-sized rounded glands often centered around a larger gland
- **Well demarcated** and is usually confined to the *inner half of the cervical wall*
- Single layer of columnar *mucinous epithelium* with *bland*, basally located nuclei (*pyloric gland* metaplasia)
- **No** significant *cytologic atypia* or *mitotic activity*

*Nucci, 2014*

*Oliva & Tornos, USCAP 2015*

*Nucci, 2002*
Lobular endocervical glandular hyperplasia (LEGH)

Courtesy of Dr. C. Bourgain
### DD mucinous adenocarcinoma gastric-type

<table>
<thead>
<tr>
<th></th>
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<tr>
<td>Mucinous discharge</td>
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<tr>
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<tr>
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<td>Cervical wall involvement</td>
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<td>Stromal response</td>
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Diffuse laminar endocervical glandular hyperplasia

- Uncommon, mostly **reproductive** women
- Usually **incidental** finding, may present with symptoms of watery or mucoid discharge
- Confined to the **inner third** of the cervical wall
- **Laminar** proliferation of closely-packed glands that appears as a discrete layer that is sharply demarcated from the underlying cervical stroma

*Int J Gynecol Pathol, Vol. 33, No. 4, July 2014. Nucci M*

*Blaustein, Chapter 4*
Diffuse laminar endocervical glandular hyperplasia

- Glands typically have a **round, regular outline**, but irregular, angulated and star-shaped glands frequently occur.
- Lined by tall columnar **mucinous** epithelium with **bland** basally located round nuclei, mitotic activity is uncommon

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Arias-Stella reaction

- Up to 10% of **gravid** hysterectomy specimens.
- Use of **oral contraceptives**
- Usually focal, superficial glands. Occasionally deep glands, more extensive.
- In endocervical polyp
- Histologic features similar as in the endometrium: **enlarged** cells with abundant vacuolated and/or eosinophilic cytoplasm and **enlarged hyperchromatic nuclei**, smudged nuclear chromatin, **hobnail** appearance. **Mitotic figures** are **very uncommon**.

*Blaustein, Chapter 4*  
*Soslow & Longacre, chapter 18*
Arias-Stella reaction DD clear cell carcinoma

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<td>Preserved architecture</td>
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<td>-</td>
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<tr>
<td>Mass forming lesion</td>
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<td>+</td>
</tr>
<tr>
<td>Prominent nuclei</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
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Tubal/tubo-endometrioid metaplasia

- Endocervical glands lined by ciliated cells, tubal type secretory cells, intercalated (peg) cells and reserve cells
- Bland cytological features, sparse mitotic figures
- Pseudostratification
- Secretory features with apical snouts
- DD adenocarcinoma in situ! → p16
- Ectopic **endometrial glands and stroma** resembling proliferative endometrium (pseudostratification, mitosis)
- Usually confined to the superficial third of the cervical wall, occasionally deep
- Frequently develops following **cervical trauma** (cone biopsy, delivery)
- DD endocervical adenocarcinoma (in situ/invasive)
- CAVE! May express high levels of Ki-67 and expression of p16 (patchy)
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Endocervical adenomyoma

- Rare endocervical counterpart of the adenomyoma of the uterine corpus
- Premenopausal women
- Polypoid lesion, projecting into the endocervical canal
- **Biphasic:** admixture of benign-appearing endocervical-type glands and smooth muscle
- DD mucinous adenocarcinoma gastric type:
  - Gross circumscription
  - Frequent lobular arrangement of glands
  - Lack of infiltrative pattern
  - Lack of desmoplasia
  - Lack of cytologic atypie
Ectopic prostatic tissue

- Usually incidental finding, rarely cervical mass
- No involvement of the mucosal surface
- Double layer of cells: flattened/cuboidal basal cells and eosinophilic/clear luminal cells
- PSA +

Courtesy of Prof. Dr. K. Van de Vijver, UZ Gent
• Be careful with the diagnosis of microglandular hyperplasia in a postmenopausal woman → consider the possibility of endometrioid endometrial adenocarcinoma with microglandular pattern (and ask for more material if necessary...)

• Think about Arias-Stella reaction if you see ‘funny looking high grade atypia’ and check if the patient is pregnant or is using hormonal therapy