Clinical History:
A 72-year-old woman with a history of uterine prolapse and cystocele underwent a hysterectomy.
New Frontiers in Pathology, Case 20

Stephanie L. Skala, MD

November 2, 2019
Case

• 72 year old woman
• History of uterine prolapse and cystocele
Differential Diagnosis

- Adenoid basal hyperplasia
- Ectopic prostate tissue / prostatic metaplasia
- Adenoid basal carcinoma
- Adenoid cystic carcinoma
- Small cell carcinoma
- Squamous cell carcinoma
- Adenosquamous carcinoma
Adenoid Basal Hyperplasia

• Irregular buds “dropping off” tips of rete pegs (<1 mm)
• Normal or mildly atypical overlying squamous epithelium
• Squamous differentiation rare
• p16 and HPV ISH negative
• Reserve cell immunophenotype
  • CK5/6 cytoplasmic positive, p63 nuclear positive, CK7 and CK14 negative

*Hum Pathol. 2012;43(12): 2255-65.*
Ectopic Prostatic Tissue / Prostatic Metaplasia

• Located in cervical or vaginal stroma without involvement of the surface
• Squamous component sometimes >>>> glandular component
  • Squamous component can show ER/PR expression
  • Glandular areas show luminal and basal cells, and stain for prostate markers but not ER or PR
• p16 negative

• Can be microscopic/incidental, or mass-forming
• Patients have female genotype and phenotype
• Developmental anomaly, endocervical gland metaplasia, or derived from mesonephric remnants?
Adenoid Basal Carcinoma

- Round, oval, or lobulated nests composed of small, monotonous basaloid cells
  - Prominent palisading of cells at periphery of nests
  - Nests may have variably dilated central lumens
    - Lumens can be lined by mucinous epithelium, cells with clear cytoplasm, basaloid cells, or flattened cells
    - Rarely more than one mitotic figure per nest*
    - Central areas of squamous or transitional cell-like differentiation
- May merge with associated high-grade squamous intraepithelial lesion

- Infiltrative growth with depth of invasion usually <1 cm
- No associated desmoplasia

- IHC: p16 and p63 diffusely positive; CAM5.2 positive (basaloid cells in periphery of nests); EMA, CK7, and CEA often positive
Adenoid Basal Carcinoma

• Clinical
  • <1% of cervical carcinomas
  • Usually postmenopausal (but case reports as young as 20 yo)
  • **Incidental finding** / abnormal Pap test
  • Typically **HPV** positive (type 16)
  • If pure, **excellent behavior**
Adenoid Cystic Carcinoma

- Tumor with larger, atypical nuclei and brisk mitotic activity
- Prominent cribriform growth with intraluminal hyaline/basement membrane-like material
- 20-40% of cases show areas resembling ABC

- IHC: CD117 may be strongly positive (~5% of cells)
  - Less diffuse staining than what is seen in ACC of salivary glands

- Pure ACC of the gynecologic tract is HPV-negative, and NFIB rearrangements are often seen
Adenoid Cystic Carcinoma

• Clinical
  • < 1% of cervical adenocarcinomas
  • Mostly postmenopausal (average 71 years)
  • More frequent in non-Caucasians
  • Postmenopausal bleeding, endophytic or exophytic mass on pelvic examination
  • Aggressive tumor, even at early stage
    • Local recurrence, lymph node metastases, distant metastases (lungs, abdominal cavity, brain)
    • ABC’s evil fraternal twin
Small Cell (Neuroendocrine) Carcinoma

- Densely cellular tumor composed of hyperchromatic cells with nuclear molding, brisk mitotic activity, necrosis, and crush artifact
- Diffuse, insular, corded, trabecular, or nested growth; occasional rosette formation
- Squamous/glandular differentiation may be present
- May be associated with adenocarcinoma in situ (AIS) or invasive adenocarcinoma (or less often, squamous dysplasia/carcinoma)

- Neuroendocrine IHC markers often but not always positive
Small Cell (Neuroendocrine) Carcinoma

• Clinical
  • ~ 2% of all cervical neoplasms
  • Average 36-42 years
  • Vaginal bleeding, cervical mass, abnormal Papanicolaou smear
  • May have paraneoplastic manifestations
    • Cushing syndrome, syndrome of inappropriate antidiuretic hormone, carcinoid syndrome, hypoglycemia
  • Poor outcome for all stages, high recurrence rate
Invasive Squamous Cell Carcinoma

- Often more abundant eosinophilic cytoplasm
- Focal mucinous differentiation may occur
- No peripheral palisading in nests
- Desmoplastic stroma
- Can have basaloid features
  - Lack of maturation with minimal keratinization
  - High-grade nuclei and frequent mitoses
Invasive Squamous Cell Carcinoma

• Clinical
  • ~11,000 new cases/year and 4,000 fatalities/year in USA
  • Average age 40-55 years
  • Higher incidence in African Americans
  • Abnormal Papanicolaou smear, vaginal bleeding
  • High-risk HPV
  • Prognosis depends on stage
Adenosquamous Carcinoma

• **High-grade malignant squamous and glandular elements** intimately admixed
  - Squamous component may show keratin pearls and intercellular bridges
  - Glandular component may have complex architecture
• ± Adenocarcinoma in situ and/or high-grade squamous intraepithelial lesion

• IHC: CEA (glandular), p63 (squamous), p16 (both) positive
Adenosquamous Carcinoma

• Clinical
  • Much less common than adenocarcinoma
  • Usually peri-/postmenopausal (average: 57 years)
  • **Vaginal bleeding**, abnormal Papanicolaou smear; thickened cervical wall or exophytic or ulcerated **mass**
  • **High-risk HPV** (type 18 > 16)
  • Prognosis similar to other types of cervical (squamous or glandular) carcinomas
Back to our case...
Our case
Our case.
Our case...
Case

• High-grade squamous intraepithelial lesion (CIN 3) with prominent glandular extension, associated with deeply infiltrative small nests composed of relatively uniform cells with ovoid nuclei, scant cytoplasm, and peripheral palisading. Some nests showed keratinizing squamous differentiation.

• Positive for p16, low Ki-67 proliferative index

• Maximum depth of invasion of 0.8 cm

• No gross lesion identified; tumor involved 9 sections
Case

• Adenoid basal carcinoma
References

- van de Vijver KK. Adenoid basal carcinoma. In: ExpertPath.
CASE 20

DIAGNOSIS: Adenoid basal carcinoma

CLINICAL HISTORY:

A 72-year-old woman with uterine prolapse and cystocele underwent hysterectomy.

MICROSCOPIC DESCRIPTION:

At low magnification, there are small nests of cells deeply infiltrating cervical stroma. The infiltrative nests are composed of relatively uniform cells with ovoid nuclei, scant cytoplasm, and peripheral palisading. Some nests show keratinizing squamous differentiation. Overlying this proliferation is an area of high-grade squamous intraepithelial lesion (CIN 3) with prominent glandular extension.

DISCUSSION:

Adenoid basal carcinoma (ABC), also termed “adenoid basal epithelioma” by some authors, is composed of variably sized nests or cords of small basaloid cells with peripheral palisading. ABC shows infiltrative growth, but typically extends to a depth of less than 1 cm. Desmoplastic stromal reaction should not be present; however, edematous or loose stroma with chronic inflammatory cells may surround nests. ABC is frequently associated with high-grade squamous intraepithelial lesion (HSIL). Dysplastic squamous epithelium extending into the basaloid nests can show numerous mitotic figures. The deepest portion of the tumor is composed of bland basaloid nests with absent to rare mitotic activity.

ABC primarily affects postmenopausal women, although it has been reported in women as young as 20 years old. Pure ABC has an excellent prognosis, and can be managed conservatively. However, ABC can be seen in association with malignancies such as squamous cell carcinoma, adenoid cystic carcinoma, small cell carcinoma, and carcinosarcoma. Only a single case of ABC has been reported with distant metastasis (to the lung). The case in question demonstrated anastomosing cords with nuclear atypia that is beyond what is currently accepted for diagnosis of pure ABC. Any tumor component with more aggressive histology should be mentioned, and the tumor should be treated based on that component.
Adenoid basal hyperplasia morphologically resembles ABC but extends less than 1 mm from the basement membrane. The basaloid nests in ABH usually remain attached to the overlying squamous epithelium or endocervical clefts. In contrast to ABC, ABH is negative for p16 and high-risk HPV, and rarely shows squamous differentiation.

Ectopic prostatic tissue can be seen in cervical or vaginal stroma, without involvement of the surface epithelium. Areas with glandular differentiation may show a double layer of luminal and basal cells; only glandular areas stain with prostate markers. In some cases, the squamous component is so dominant that it is difficult to recognize the glandular component.

Adenoid cystic carcinoma (ACC) shows larger tumor cells and a greater degree of nuclear pleomorphism than ABC. Even the solid variant of ACC should show focal PAS-positive extracellular basement membrane-like material. Pure ACC of the gynecologic tract is HPV-negative, and NFIB gene rearrangements are frequently seen. CD117 is positive in ACC, but negative or equivocal in ABC.

Squamous cell carcinoma typically shows more cytologic atypia than ABC. Not all squamous cell carcinomas produce keratin, and other entities in the differential diagnosis (including ABC and small cell carcinoma) may show areas of keratinization. Small ABC-like nests can be seen in adenoid cystic carcinoma, basaloid squamous cell carcinoma, and small cell carcinoma. Small cell carcinoma shows nuclear molding, hyperchromasia, and brisk mitotic activity, and does not typically show peripheral palisading.

REFERENCES


Kerdraon O, Cornelius A, Farine MO, Boulanger L, Wacrenier A. Adenoid basal hyperplasia of the uterine cervix: a lesion of reserve cell type, distinct from adenoid basal carcinoma. Hum Pathol 2012;43:2255-2265.


