Clinical Data

Female
21 years-old
Hematuria and dysuria

Past medical history: passive smoker

Trans-urethral resection of urinary bladder tumor (TURBT)
Received for 2nd opinion: PUNLMP?
DIFFERENTIAL DIAGNOSIS

1. CYSTITIS CYSTICA ET GLANDULARIS
2. CYSTITIS CYSTICA ET GLANDULARIS with INTESTINAL METAPLASIA
3. INTESTINAL METAPLASIA WITH DYSPLASIA and VILLOUS ADENOMA
4. NEPHROGENIC ADENOMA
5. URACHAL REMNANTS
6. MÜLLERIANOSIS (endosalpingiosis, endocervicosis, endometriosis)
1. CYSTITIS CYSTICA et CYSTITIS GLANDULARIS, usual type

Etiology:
- cystic dilatation of von Brunn nests.

Morphology:
- superficial located
- cuboidal to columnar cells surrounded by ≥1 layers of urothelial cells.

very frequent / normal finding

Pitfall:
- florid forms can present as polypoid masses and clinically mimic neoplasia.
2. CYSTITIS GLANDULARIS, INTESTINAL TYPE (intestinal metaplasia)

Clinical:
- hematuria
- mucosuria
- incidence increases with age
- pre-malignant?

Morphology:
- cystitis glandularis with mucin-secreting goblet cells.

Resembles enteric epithelium!

Immunoprofile:
- CDX2 and CK20+
- CK7-

Enteric immunophenotype!
3. INTESTINAL METAPLASIA WITH DYSPLASIA

Clinical:
- elderly patients
- hematuria
- mucosuria

Morphology:
- exophytic papillary growth
- nuclear stratification
- nuclear crowding, hyperchromasia
- prominent nucleoli, and, as in the colon.

Immunoprofile:
- CDX2 and CK20+
- CK7-
- SATB2 (seems not to improve DDx)

similar to intestinal epithelium!
3. VILLOUS ADENOMA

Clinical:
- elderly patients
- male predominance

Morphology:
- long villo-glandular fronds
- epithelial cells with pseudo-stratified columnar arrangement

Risk of associated malignancy!

Immunoprofile:
- CDX2 +
- CK20+
- CK7-
4. NEPHROGENIC ADENOMA (nephrogenic metaplasia)

Clinical:
- younger patients
- renal transplantation
- post-instrumentation / TURBT
- lithiasis
- irritative symptoms
- metaplastic nature
- relative frequent lesion

Location:
- superficial
- replaces urothelial mucosa
- can growth in superficial submucosa
4. NEPHROGENIC ADENOMA (nephrogenic metaplasia)

**Morphology:**
- **polymorphic nature**! papillary, tubular, cystic
- cuboidal-flattened cells
- eosinophilic cytoplasm
- prominent nucleoli
- hobnail
- associated with inflammation
4. NEPHROGENIC ADENOMA (nephrogenic metaplasia)

Immunoprofile:
- PAX2 / PAX8 +
- Racemase +
- ER / PR –
- WT1-
- PSA weak+ / -
- p53 weak+
- Ki-67 low
5. URACHAL REMNANTS

**Clinical:**
- vestigial
- presente in 1/3 adults
- located in bladder dome
- asymptomatic

**Morphology:**
- epithelial canal surrounded by connective tissue and bladder detrusor muscle.
- lined by transitional mucosa > goblet cell.
6. MÜLLERIANOSIS (endosalpingiosis, endocervicosis, endometriosis)

Immunoprofile:
- PAX8 +
- ER / PR +
- CDX2 –
- racemase –
CASE
IMMUNOHISTOCHEMISTRY

ER

PAX8

CDX2
DIAGNOSIS

• Cystic and complex architecture glandular structures predominantly consistent with tubaric / serous epithelium, and endocervical epithelium.
• No morphological evidence of dysplasia and/or invasive growth.
• PAX8 and ER stains are positive.
• Intestinal epithelium marker (CDX2) stain is negative.

MÜLLERIANOSIS OF THE URINARY BLADDER
MÜLLERIANOSIS

**DEFINITION** – “normal endometrial, tubaric, and endocervical tissue - *singly or in combination*, incorporated within other organs during organogenesis.”

**CHORISTOMA** – “normal tissues, heterotopically placed, giving the impression of a tumor.”

Eugen Albrecht. Über Hamartome. (1904) - Frankfurt a. Main, Germany
MÜLLERIANOSIS: DIAGNOSTIC CRITERIA

- presence of 2, preferably the 3 Müllerian tissue-types: endometrial, endocervical, and tubaric-type epithelium;
  
  Young and Clement, 1996

- endometrial stroma might not be present;

- may involve lamina propria and muscularis propria of the urinary bladder.
MÜLLERIANOSIS

**PATHOGENESIS:** not completely resolved question!

- Embriologic / development theory  (Batt, 2013; others)

- Implantation theory  (Young and Clement, 1992)

- Metaplastic theory  (Donne, 1998; Koren, 2006)
CONSIDER A BLADDER MÜLLERIANOSIS WHEN...

**CLINICAL:** women; fertile age. Cyclic symptoms.

- Urothelial neoplasms are very unusual in young patients!
- History of pelvic surgery / cesarean section not required to consider this diagnosis!

**IMAGING:** an exophytic / polypoid / mass-like lesion, small (1 to 4.5 cm).

**MACRO:** cystic structure / dark blue to black cysts.

**MICRO:** bland-looking glandular lesion with Müllerian-type epithelium.

**IHC:** positive for ER, PR, and PAX8. Negative for racemase, NKX3.1, and CDX2.
WHY I SHOULD NOT MISS A BLADDER MÜLLERIANOSIS?

A rare and benign lesion:

- that **can mimic a neoplastic lesion** clinically, and morphologically.

- may benefit from pharmacologic treatments (+ extensive TURBT).

- **radical cystectomy is NOT necessary.**

- **follow-up is recommended!** Malignant transformation is possible!