

# URETHRAL CANCER

## Diagnosis & Management Case Conferences

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### EPIDEMIOLOGY - 1°

- RARE
- 2200 reported cases
- F:M - 4:1



## FEMALE URETHRAL CA

- any age but >60 most common
- Black > white



## PRESENTATION

- Most present with BLEEDING or DISTAL URETHRAL MASS
  - Dysuria, frequency, dyspareunia, obstructive sx
- DDx
- Caruncle
  - Polyp
  - Prolapse
  - Fibroma
  - Hemangioma
  - Diverticulum
  - Urethral vaginal fistula

## DIAGNOSIS

- Urine cytology
- Cystourethroscopy
- Biopsy
- Bimanual exam
- Lymph node survey (palpable inguinal nodes)
- +/-Bone scan (for disseminated disease)

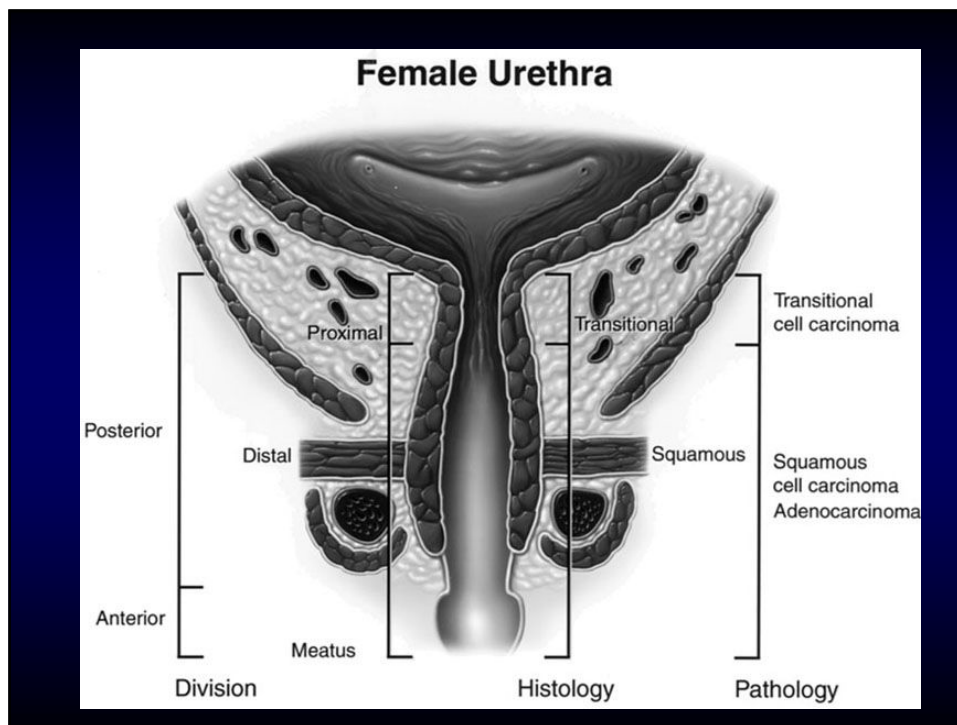
## NO KNOWN RISK FACTORS

### PROPOSED RISK FACTORS

- Viral infection
- Chronic irritation
- Fibrosis
- Caruncle
- Sexual activity
- HPV 16/18

# HISTOPATHOLOGY

- Distribution of types follows the normal histology of the female urethra
- SQUAMOUS CELL - 53%
  - Transitional cell - 15%
  - Adenocarcinoma - 15%
  - Other - 8%
- \*Exception: urethral diverticular Ca = clear cell



## LYMPHATIC SPREAD

- DISTAL (anterior) urethra and labia - superficial and deep INGUINAL nodes
- PROXIMAL (posterior) urethra - deep PELVIC nodes - iliac, obturator, presacral and para-aortic lymphatic chains

## LYMPHATIC SPREAD

- Abnormal nodes - **20 - 50%** at presentation
- Almost always metastatic disease

## HEMATOGENOUS SPREAD

- Liver
- Lung
- Brain
- Bone
  
- Generally occur late
- Most common with adenocarcinomas

## STAGING - AJCC 2002

### ***Primary Tumor (T) (male and female)***

- TX Primary tumor cannot be assessed
- T0 No evidence of primary tumor
- Ta Non-invasive papillary, polypoid, or verrucous carcinoma
- Tis Carcinoma *in situ*
- T1 Tumor invades subepithelial connective tissue
- T2 Tumor invades any of the following: corpus spongiosum, prostate, periurethral muscle
- T3 Tumor invades any of the following: corpus cavernosum, beyond prostatic capsule, anterior vagina, bladder neck
- T4 Tumor invades other adjacent organs

## STAGING - AJCC 2002

### *Regional Lymph Nodes (N)*

- NX Regional lymph nodes cannot be assessed
- N0 No regional lymph node metastasis
- N1 Metastasis in a single lymph node 2 cm or less in greatest dimension
- N2 Metastasis in a single node more than 2 cm in greatest dimension, or in multiple nodes

## STAGING - AJCC 2002

### *Distant Metastasis (M)*

- MX Distant metastasis cannot be assessed
- M0 No distant metastasis
- M1 Distant metastasis

## STAGING WORKUP

- CXR
- CT scan (abdo/pelvis)
- +/- MRI

## Case: Female Urethral Cancer

- 57 y/o female from the Okanagan
- Obstructive predominant LUTS x 3/12 – presented w/ acute retention; catheter
- Otherwise well - Hx C-section x 2
- Cysto - N (?inflammation at bladder neck due to catheter)
- Ultrasound N
  
- DIAGNOSIS: ?acontractile bladder
- TREATMENT: alfuzosin + CIC



## Case

- Referred to gynecologist
- EUA - fibrotic urethra with a periurethral vaginal nodule
- Vaginal biopsy - fibroepithelial polyp
  
- Referred to 2nd urologist 3 months later because of difficulty w/ CIC

## CASE

- Bimanual- dumbbell-shaped urethral mass from meatus to bladder neck w/ extension to side wall
- Cysto - irregular, rigid proximal urethra, friable mucosa
- Biopsy - transurethral and transvaginal
- CT - no gross local extension, N0M0
- **DIAGNOSIS: invasive well differentiated adenoCa - enteric type**

## MANAGEMENT

- Planned anterior pelvic exenteration
- ?adjuvant chemo
- ?adjuvant radiation

## TREATMENT

- Level 4 & 5 evidence - case reports/series and expert opinion
- SURGICAL

## STAGE IS THE PREDOMINANT DETERMINANT OF TREATMENT & OUTCOME

### DISTAL

- often low stage
- accessible
- THEREFORE, *often* amenable to local excision

### PROXIMAL

- often high stage
- THEREFORE, *rarely* amenable to local excision

## LOW STAGE

- Bladder preservation often possible
- T0, Tis, Ta
  - Local excision, fulguration, TUR, laser
- T1 or 2
  - Non-exenterative surgery (e.g. distal urethrectomy)
  - And/or radiation (interstitial and/or external beam)

## HIGH STAGE

- Anterior exenteration ± neoadjuvant radiation
  - Distal: Node dissection not required for non-palpable nodes
  - Proximal: Pelvic LND ± inguinal LND
  - ± Inferior pubectomy to reduce +ve margins

## ROLE OF RADIATION

- BCCA - multimodal therapy for T2 or >
- CONTROVERSIAL
- Adjuvant or neoadjuvant with bulky disease
- Definitive treatment for low grade lesions
- Downsize tumors before surgical tx (consider multimodal therapy)

(Sailer et al, J Urol 1988)

## RESULTS

- 5 yr survival - definitive radiotherapy- 35% for advanced dx
- Side effects: edema, fistulas, damage to bowel
- Successful tx reported for low stage lesions

Dalbagni et al, 2001

## CHEMO AND COMBINED THERAPY

- Limited experience - anecdotal
- Chemo - radiation sensitizer (cisplatin based, 5- FU)
- ? Useful as an adjuvant in advanced disease
- Multimodal therapy best for advanced disease (Gheiler et al, Urology 1998)

## METASTASES

- 50% of cases of advanced disease present with lymph node mets
- Inguinal node dissection indicated for palpable nodes
- Pelvic node dissection for PROX urethra and for + inguinal nodes

## METASTASES

- NO THERAPEUTIC BENEFIT FOR PROPHYLACTIC INGUINAL NODE DISSECTION

## PROGNOSIS

- Long-term survival related to STAGE - size and depth of invasion
- Independent of histology or grade

## PROGNOSIS - POOR

- Few large series
- **Overall 5 yr survival 12 - 32%**
- 5 yr overall survival - 32% (81 pts)
- <2cm diameter and distal urethra- improved survival - Bracken et al (1976)

## Prognosis

- Based on SIZE
  - <2cm - 60% 5 yr survival
  - >2cm - 13% 5 yr survival
- Based on STAGE
  - 45% T1
  - 25% T3, T4
  - 18% distant mets
- Entire urethra involved - 5 yr survival 11%

## MALE URETHRAL CA





## CASE OF MALE URETHRAL CANCER

- 54 y/o male from Trail
- Progressive difficulty emptying his bladder
- Hx of condyloma
- Px - indurated distal urethra
- CIS of distal urethra
- laser ablation/fulguration

## CASE

- Tissue overgrowth on urethra - partial penectomy performed
  - **invasive squamous cell carcinoma**  
- moderately differentiated
- ? Lymph node staging

## MALE URETHRAL ANATOMY

- ANTERIOR: fossa navicularis, pendulous, bulbar
- POSTERIOR: membranous, prostatic, bladder neck

## HISTOLOGY

- Meatus/fossa navicularis - non-keratinized stratified squamous epithelium
- Pendulous/bulbar/membranous - stratified or pseudostratified columnar epithelium
- Prostatic/bladder neck - transitional epithelium

## MALE URETHRAL CARCINOMA

- 90% squamous cell carcinoma
- 5th to 7th decade
- **50 - 75% - bulbar urethra (SCC)**
- Remainder in fossa navicularis

## ASSOCIATIONS

- Urethral stricture
- Chronic inflammatory process
- Sexually transmitted diseases
- HPV 16
- Adenoca from glands of Littre

Farrer et al, 1984

## PRESENTATION

- Proximal - **obstructive symptoms**
- Distal - **urethral bleeding** and palpable mass
- Perineal pain, dysuria, freq, decr. Stream, fistula

## DIAGNOSIS

- Hx
- Physical:
  - bimanual to delineate local extent
  - palpation of inguinal region
- **CRITICAL** - lymph node mets

## INVESTIGATIONS

- Urine Cytology - + in 80%
- Urethral washings
- Retrograde urethrogram (stricture, luminal filling defect, fistula)
- Cysto +/- biopsy
- CT or MRI

## LYMPHATIC DRAINAGE

- Fossa/pendulous urethra - superficial inguinal nodes
- Bulbar/membranous/prostatic urethra - iliac, obturator and presacral nodes
- May be crossover at prepubic lymphatic plexus

## URETHRAL SEGMENT POST-CYSTECTOMY

- 10% recurrence in urethral segment post-cystectomy
- Transitional cell ca
- Monitor with urethroscopy + cytology

## STAGING - AJCC 2002

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## STAGING AJCC 2002

### *Urothelial (Transitional Cell) Carcinoma of the Prostate*

Tis	pu	Carcinoma <i>in situ</i> , involvement of the prostatic urethra
Tis	pd	Carcinoma <i>in situ</i> , involvement of the prostatic ducts
T1		Tumor invades subepithelial connective tissue
T2		Tumor invades any of the following: prostatic stroma, corpus spongiosum, periurethral muscle
T3		Tumor invades any of the following: corpus cavernosum, beyond prostatic capsule, bladder neck (extraprostatic extension)
T4		Tumor invades other adjacent organs (invasion of the bladder)

## TREATMENT

- SURGERY
- RADIATION (if pt refuses surgery)



## TREATMENT - Distal Lesions

T0, Tis, Ta, T1

- low grade/stage - TUR or laser fulguration (bx first), partial urethrectomy

T1, T2, T3

- **partial penectomy** (2 cm margin) +/- total penectomy for high grade lesions



## TREATMENT - Proximal

- AGGRESSIVE MANAGEMENT
- T1, T2, T3, T4: radical cystoprostatectomy, total emasculation, pelvic lymphadenectomy, +/- inferior pubectomy
- +/- preoperative radiotherapy
- +/- inguinal node dissection

NCI 2006



## LYMPHATIC METS

- Inguinal/pelvic lymph nodes - dissection can achieve cure
- Inguinal node dissection for palpable nodes - 5 yr survival 12 - 66%
- If no palpable nodes - Serial groin exams and pelvic CT scans essential f/u
- Prophylactic node dissection not warranted

Hoppman et al, 1978

## METASTATIC DISEASE

- POOR prognosis
- Radiation and chemo as palliation in unresectable pts as adjunct to surgery
- Platinum therapy with some activity against transitional cell ca
- WSAUA 2006, NCI 2006

## PROGNOSIS

- Distal lesions - better prognosis
- Little difference in histopathology - one series worse with adenocarcinoma
- Increasing size and extent of urethral involvement - negative outcome

## SURVIVAL - Independent predictors

- T stage
- Lymph node involvement
- Location of tumor

Dalbagni et al, 2001

## SURVIVAL

- **5 YR - 35 - 45%**
  - superficial (Tis, Ta, T1) - 83%
  - Invasive (T3, T4) - 36%
  - Anterior urethra - 69%
  - Bulbomembranous - 26%
  -

MSK, 1999

## CONCLUSIONS

- RARE - hens teeth
- May be devastating if not recognized
- Early treatment key
- Multimodal therapy for advanced lesions



### STAGE GROUPING

Stage 0a	Ta	N0	M0
Stage 0is	Tis	N0	M0
	Tis pu	N0	M0
	Tis pd	N0	M0
Stage I	T1	N0	M0
Stage II	T2	N0	M0
Stage III	T1	N1	M0
	T2	N1	M0
	T3	N0	M0
	T3	N1	M0
Stage IV	T4	N0	M0
	T4	N1	M0
	Any T	N2	M0
	Any T	Any N	M1

## DISTAL LESIONS

### HIGH STAGE

- T3, T4 (or recurrent lesions) - aggressive tx with anterior pelvic exenteration  
- +/- preoperative radiation

NCI 2006

## DISTAL LESIONS

LOW STAGE (majority)

- T0, Tis, Ta - open excision - TUR, laser vaporization or ifor distal low grade
- T1, T2 - TUR, local excision, interstitial +/- external beam

NCI, 2006

## PROXIMAL LESIONS

TREATMENT: AGGRESSIVE

- Low stage (TIS, TA, T1)
- radiation alone for <2cm or TUR or combo
- T2, T3, T4 - aggressive tx with anterior pelvic exenteration
- +/- neoadjuvant radiation to shrink tumor margins
- Bilateral pelvic node dissection +/- inguinal node dissection
- Present with PROGRESSIVE OBSTRUCTIVE symptoms

NCI 2006