Update on Management of Bladder Cancer

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OBJECTIVES

- Describe the clinical presentation of bladder cancer
- Describe the diagnostic tests used to evaluate and diagnose bladder cancer
- Describe standard of care treatment options after diagnosis
- Describe recent changes to management of bladder cancer
Bladder Cancer = urothelial Ca

- Transitional cell epithelium = urothelium
  - Lines renal pelvis, ureter, bladder, proximal urethra (M), majority of urethra (F)
- Tumor can occur anywhere along path from upper to lower tract (field-change disease)
- Hematuria mandates upper and lower eval
  - Renal U/S/IVP/CT and cystoscopy
Bladder Cancer - epidemiology

- 5400 new cases annually in Canada
- 1300 deaths estimated per year
- 4\textsuperscript{th} most common cancer in men, 8\textsuperscript{th} in women
- 2\% of all cancers
- Male:female 3:1
- Lifetime risk 3\% men, 1\% women
Bladder Cancer - Risk factors

- **SMOKING** - number 1 risk factor
  - RR increase 10-20% (up to 50% if unfiltered cigarette)
  - Likely result of aromatic amine toxins in smoke and excreted at high urinary concentration
Risk factors- TCC (90-95%)

- Occupational exposures-dye, textiles, painters, hairdressers- associated with volatile chemical exposure
- Analgesic abuse- phenacetin, NSAIDs?
- Cyclophosphamide treatment- leukemias, etc
- Pelvic XRT
- GU tuberculosis
Presentation

- Gross or microscopic hematuria (85%)
  - Hematuria screening?
  - 14-21% of men over 50 will have gross or microscopic hematuria (≥3 rbc’s/hpf)
  - 8-22% with GU malignancies
  - 67% of these are bladder cancers
AMH evaluation algorithm

- History of vigorous exercise, trauma to urethra, menses
  - Yes
  - No
  - Yes: Findings of glomerular disease (proteinuria, incr creatinine, red cell casts, dysmorphic)
  - No: Recollect/Retest once contributing factors cease

  - Yes: Refer to Nephrology
  - No: Proceed to Renal ultrasound & urinary cytology

    - No: Any risk factors for urinary disease
      - No: No Further evaluation
      - Yes: Proceed to cystoscopy
    - Yes: Proceed to Renal ultrasound & urinary cytology

    - Age >40 yrs
      - No: Any risk factors for urinary disease
        - No: No Further evaluation
        - Yes: Proceed to cystoscopy
      - Yes: Proceed to Renal ultrasound & urinary cytology
Symptoms

- Irritative voiding sx’s- suggests CIS or invasive disease
  - Frequency
  - Urgency
  - Dysuria
- Obstructive voiding
- Flank pain- hydronephrosis
Diagnosis

- **Hematuria** (gross or micro) merits full upper and lower tract evaluation to rule out cancer
- Urine cytology - overall specificity 90%, sensitivity 70% (best for G3)
- Renal U/S - cheap, noninvasive, sensitive and specific for renal masses greater than 1 cm
- IVP - filling defect of renal pelvis, ureter, bladder
- CT IVP - CT with delayed imaging of Upper tracts
- Cystoscopy
Imaging
Cystoscopy

Flexible Cystoscopy

Flexible telescope

Light shining into bladder

External sphincter

Bladder

Tumour

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TURBT

- Diagnostic and therapeutic
- Permits accurate staging/grading
- Requires general or spinal anaesthesia
- Stratify to:
  - low grade vs high grade
  - Superficial vs deep
Treatment- superficial TCC (Ta,T1)

- Papillary - low grade (70%)
  - TURBT and surveillance cystoscopy q 3-6mo (low risk of progression)

- HG Superficial disease-
  - TURBT and immediate intravesical chemo (prevents local recurrence >20%)
  - Post resection immunotherapy - BCG
CIS

- Flat, red, velvety lesion
- Present in 10% of patients with bladder ca
- May produce irritative voiding sx’s
- 50-60% progress to muscle invasiveness
- Usually positive cytology
- Treatment- intravesical BCG (induction & maintenance) (70% RR and 50% DFS at 5 yrs)
- If fails primary BCG \(\rightarrow\) BCG/Inf α; Valrubicin
- If fails intravesical therapy \(\rightarrow\) cystectomy
Treatment for HG superficial (T1G3)/Muscle invasive TCC (T2-4)

- 25% of patients will present with muscle invasive TCC
- Radical cystectomy – 50% 5yr OS
  - bladder, prostate, +/- urethra in men; urethra, uterus, ovaries, ant vagina, bladder in women (anterior exenteration) and extended pelvic lymphadenectomy
- Urinary diversion- Conduit vs neobladder
Neobladder  Ileal Conduit
Neoadjuvant Platinum-based chemotherapy MVAC/GC

- Pooled meta-analysis 11 trials over 2500 pts
- Absolute survival benefit 5% at 5 yrs
- Absolute disease-specific survival 9% at 5 yrs
- Now standard of care prior to cystectomy especially with large tumors, T3/4, N1, young pts, ECOG 0-1
Gross specimen - cystectomy
Other treatments for Muscle invasive/locally advanced disease

- **EBXRT**
  - poorer survival (30%) vs surgery (usually reserved for non surgical candidates)
- **EBXRT and chemo** (used as radiosensitizer) 10% -15% improvement in LRDFS at 2 yrs
- **Bladder preserving strategies**
  - Radical TURBT with chemo/XRT- if persistant tumor then cystectomy
  - Survival inferior to cystectomy and only 41% of survivors have bladder in situ at 5 years
Metastatic Bladder cancer

- Chemotherapy regimens
  - MVAC
  - CMV
  - CISCA
  - Cisplatin and gemcitabine

- CR - 30-40%
- PR - 20-30%
- 17% tumor free at 3 years
Stage based survival

- Superficial disease (Ta) - 85%
- Superficial invasion (T1) - 70%
- Muscle invasion (T2) - 65%
- Fat invasion (T3) - 50%
- Contiguous organ (T4) - 30%
- Nodal disease - 30%

5 yr survival
CONCLUSIONS

- Smoking cessation very important!
- Bladder cancer is a common malignancy with high mortality rate if diagnosed in advanced stage
- Algorithm for AMH
- Early referral to urology with hematuria
- Intravesical immunotherapy should include consideration of induction and maintenance for 3 yrs
- Advances in management of muscle invasive disease with neoadjuvant chemo
“Urology department. Can you hold?”