Management of muscle invasion bladder cancer (MIBC)

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2022.12.04

Incidence

- Bladder cancer is the second most common cancer of the GU tract.

- Bladder is the 8th most common cancer in Taiwanese male (the 5th common is prostate cancer). Cancer registry annual report, 2019, Taiwan

Risk

- Smoking is the most important risk factor (approximately 50%), because the aromatic amines and N-nitroso compounds induce DNA damage (double-stranded breaks).

  Eur Urol 2016;70:458–66.

  Cancer Res 2009;69:6857–64.

- Occupational exposure

  Aluminium production. Rubber production industry. Dye industry.

  Coal-tar pitch. Dry cleaning. Hairdressers and barbers. Printing.

  Textile manufacturing.

  Eur Urol 2018; 74: 784-795.

Histopathology

- Urothelial bladder cancer
  Papilloma (rare benign)
  Urothelial cell carcinoma (90%)

- Non-urothelial bladder cancer
  Adenocarcinoma including urachal Carcinoma (<2%)
  Am J Clin Exp Urol. 2015; 3(2): 51–63.
  Squamous cell carcinoma (2-5%) Arab J Urol. 2016 Sep; 14(3): 183–191.
  Small cell carcinoma (or neuroendocrine features)
  Orphanet J Rare Dis. 2011; 6: 75.
  Mixed Histology

Symptoms

- Intermittent gross or microscopic hematuria (85-90%).
- Lower urinary tract symptoms (frequency, urgency and dysuria).
- Flank pain if retroperitoneal metastasis or ureteral obstruction.

Signs

- Bimanual palpable mass : if large-volume or invasion tumor.
- Lymphedema : tumor metastasis induced occlusion of pelvic lymphadenopathy.
- Hepatomegaly and supraclavicular lymphadenopathy : if tumor metastasis.

Laboratory finding

- Uranalysis
- Urinary cytology
- Urinary biomarkers (limitations) : Nuclear matrix protein 22 (NMPs), Bladder tumor antigen (BTA). Urol Oncol. 2021 Jan;39(1):41-51.
- Two transcription factors : BLCA-1 and BLCA-4. J Urol, 174 (2005), pp. 64-68

Primary assessment of MIBC

- Diagnostic cystoscopy : histological evaluation of resected tissue.
- Transurethral resection bladder tumor (TUR-Bt) should include a deeper part (detrusor muscle), which has to be sent in separately.
- Prostate urethral biopsies in males and bladder neck biopsies in women is necessary if the orthotopic diversion is considered.

Definition of MIBC

- Tumors invasion to the superficial or deep muscle of urinary bladder : stage T2a and T2b
- Tumors invasion to perivesical fat : stage T3
- Tumors invasion to prostate, uterus and vagina : stage T4a

Image

- Computer tomography urography (CTU) : assessment of local invasion, with the principal aim of detecting T3b disease or higher stage.

- Magnetic resonance imaging urography (MRU) : differentiate ≤ T1 tumors from ≥ T2 tumors before surgery. Radiology, 286 (2018), pp. 502-511

- Bone scan : if suspected bone metastasis.

Neoadjuvant therapy

- Neoadjuvant therapy with cisplatin-based combinations is standard procedure in patients with resectable N0M0-invasive bladder cancer. (better prognosis and surgical morbidity is not increased)

  Eur Urol, 61 (2012), pp. 1229-1238.

  Eur Urol, 45 (2004), pp. 297-303

- Neoadjuvant immunotherapy using checkpoint inhibitors (PD-1/L1, cytotoxic T-lymphocyte associated protein 4 (CTLA-4)) or in combination with chemotherapy.

  Eur Urol, 77 (2020), pp. 439-446

Indication of radical cystectomy

- Patients with MIBC stage T2-T4a, N0-Nx, M0.
- High-risk and unresponsive NMIBC.
- Tumors cannot be controlled with TURB-t and intravesical therapy.
- Salvage cystectomy is indicated in non-responders to bladder-sparing treatment and for palliative reasons fistula, pain, and persisnet hematuria.

Urinary diversion after radical cystectomy

- An ileal conduit or an orthotopic neobladder is mostly used.
- Positive LNs do not exclude an orthotopic neobladder.
- The neobladder is planned with the presence of CIS in the prostatic urethra or bladder neck (females), the frozen sections have to be performed before surgery.
- Glomerular filtration rate (GFR) is no differ significantly after ileal conduit versus neobladder in patients with preoperative impaired renal function.

Int J Urol, 22 (2015), pp. 651-656

Urinary diversion after radical cystectomy

- The ureterocutaneostomy is the simplest cutaneous diversion (less operative time, complication rate, and length of hospital stay than ileal conduit) and is a good option in older and frail patients.

BJU Int, 118 (2016), pp. 521-526.

Urol Int, 94 (2015), pp. 394-400

Outcome after radical cystectomy

- The early complications (within 3 months of surgery) : 58%.

- 5-year recurrence-free survival (RFS) rate is around 60%

Eur Urol, 61 (2012), pp. 58-64

- The 5-year RFS was 76% in patients with pT1 tumors, 74% in patients with pT2 tumors, 52% in patients with pT3 tumors, and 36% in patients with pT4 tumors.

J Clin Oncol, 19 (2001), pp. 666-675

Bladder-sparing treatments for localical disease

- The bladder preservation is candidate for low-volume T2 stage without hydronephrosis or extensive carcinoma in situ.
- TURB-t alone in patients with MIBC is only a therapeutic option in T2 tumors with a negative restaging TURB-t.
- Radiation therapy with concurrent radiosensitive chemotherapy (cisplatin and mitomycin C plus 5-fluorouracil) after TURB-t.
- If nonresponders are identified, salvage radical cystectomy is necessary.

Eur Urol, 66 (2014), pp. 120-137

Outcome of bladder-sparing treatments

- The 5-year cancer-specific survival rate : 50% to 82%
- The overall survival rates : 36% to 74%

Eur Urol, 66 (2014), pp. 120-137

Adjuvant therapy

- In 2014, the very low level of evidence supporting the use of adjuvant chemotherapy. Eur Urol, 66 (2014), pp. 42-54

- In recent , in T3/4 or N+ stage cancer found a benefit for adjuvant chemotherapy versus observation. J Clin Oncol, 34 (2016), pp. 825-832

Follow-up of post cystectomy MIBC

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	1	2	3	4	5	5-10	>10
Imaging	• CTU or MRU (every 3–6 months • CT chest (preferred) or chest x-ray every 3–6 months or • FDG PET/CT if suspected metastatic disease		• Abdominal/pelvic CT or MRI annually • CT chest (preferred) or chest x-ray annually or • FDG PET/CT if suspected metastatic disease			Renal US annually	As clinically indicated
Urinary cytology	• Urine cytology every 6–12 months • Consider urethral wash cytology every 6–12 months		Urine cytology as clinically indicated Urethral wash cytology as clinically indicated				

NCCN Guidelines Version 2.2022

Thank for your attention