UROSURGERY

Bladder cancer

Incidence

Is the second most common cancer of the genitourinary tract. The average age of diagnosis is 65 years, at time of diagnosis 75% of bladder cancers localized to the bladder, 25% have spread to regional lymph nodes or distant metastasis.

Risk factors and pathogenesis

Cigarette smoking accounts for 50% of cases in men and 31% in women, approximately smokers had 2 folds increase risk of bladder cancer than non-smokers, the causative agents are thought to be alpha and beta naphthylamine . Occupational exposure account 35% of cases, workers in chemical,dye,rubber,petroleum are at increased risk, specific occupational carcinogens include benzidine ,beta naphthylamine. physical trauma to the urothelium induce by infection, instrumentation and calculi increase risk of malignancy.

Activation of dominantly acting oncogene such as *ras* and *c-erbB* has reported in bladder cancer, Loss of genetic material on chromosome 9, mutation in *p*53, *p21, p16* tumor suppressor gene, deletion of chromosome17p, has been notes to be increased risk of bladder tumor.

STAGING:

TNM, classification of bladder carcinoma:

Primary tumor(T)

TX: primary tumor cannot be assessed

T0: No evidence of primary tumor

Ta : Noninvasive papillary carcinoma

Tis: Carcinoma in situ(flat tumor)

T1: Tumor invade lamina propria

T2: Tumor invade muscularis propria

pT2a: Tumor invade superficial muscularis propria

pT2b: Tumor invade deep muscularis propria

T3 :Tumor invade perivesical tissue

pT3a: microscopically

PT3b: macroscopically (extravesical mass)

T4: Tumor invade any of the following: prostatic stroma, seminal vesicle, uterus,vagina, pelvic wall, abdominal wall

T4a: tumor invade prostatic stroma, uterus,vagina

T4b : tumor invade pelvic wall, abdominal wall

Regional lymph nodes(N)

NX: lymph nodes cannot be assessed.

NO: No lymph node metastasis

N1: Single node<2cm

N2: Single node2-5cm or multiple node non >5cm

N3: Single or more node>5cm

Distant metastasis

Mx: cannot be defined

M0: no distant metastasis

M1: distant metastasis present

Histopathology

98% of all bladder cancers are epithelial malignancies, with most being transitional cell carcinoma (TCC).

Transitional cell carcinoma

90% of all bladder cancers are TCC, these tumors appear as papillary, exophytic lesion which is mostly superficial (pTa, pT1), that account 70%, or appear as sessile, ulcerated growth often invasive, that account 25%. Carcinoma in situ (CIS) is recognizable as Flat, anaplastic epithelium.

Non transitional cell carcinoma

1. Adenocarcinoma:
   Account 2 % of all bladder cancers, mat be preceded by metaplasia, it appear in glandular, colloid, or signet ring pattern. Muscle invasion usually present at time of diagnosis, 5 years survival <40% despite aggressive treatment.
2. Squamous cell carcinoma:
   Accounts 5-10% of all bladder cancers, often associated here with history of chronic infection, calculi, or chronic catheter use, and also with bilhariziasis, it appear as

nodular mass, and invasive at time of diagnosis.

3. Undifferentiated carcinomas: <2%, no mature epithelial elements, with neuroendocrine feature and small cell carcinoma, aggressive and metastasis at time of diagnosis.
4. Mixed type

Symptoms

Hematuria, in 90% of the cases which is intermittent and painless, small percentage of patient's symptoms of vesical irritability may present, especially with CIS. Bone pain and flank pain are feature of metastasis.

Signs

Large, invasive tumor lead to thickening of the bladder wall and so it can palpate bimanual examination under anesthesia. If the bladder is not mobile indicate direct invasion to the adjacent structure.
Hepatomegaly and supraclavicular adenopathy indicated distant metastasis.

Laboratory findings

Hematuria is the most common finding, pyuria in the presence of concomitant infection, azotemia indicate ureteral occlusion by tumor or enlarge lymph nodes, anemia, owing to chronic blood loss or bone marrow metastasis.

Urine cytology: exfoliated cells from normal urothelium and neoplastic urothelium can be readily identified in voided urine. Detection rates are high for tumors of high grade and stages as well as CIS.

Imaging

Although bladder cancer may be detected by various imaging techniques, their presence is confirmed by cystoscopy and biopsy. Imaging usually used to evaluate upper urinary tract when infiltrating bladder tumor is detected, depth of muscle wall invasion, regional and distant metastasis. Intravenous pyelography remains the most common imaging test to evaluate hematuria. However is increasingly being replaced by CT urography, which is more accurate for evaluation of the entire abdominal cavity.

Superficial bladder tumor with properly performed TUR of the tumor does not require additional imaging, but it must in high stage tumor. CT ``and MRI are beneficial to the asses the depth of the tumor in the bladder wall, pelvic enlarge lymph nodes with overall staging accuracy range from 40%-80% for CT and from 40%-90% for MRI. Staging of advanced lesion completed with chest x ray and bone scan.

Cystourethroscopy and tumor resection:

The diagnosis and initial staging of the bladder cancer is made by cystoscopy and transurethral resection(TUR), superficial low grade tumor appear single or multiple papillary lesion , high grade lesion larger and sessile while CIS , flat area of erythema and mucosal irregularity.

Natural history

Related to the tumor recurrence and tumor progression, progression including metastasis represents the greater biological risk while recurrence represents the substantial patient's morbidity. Required periodic evaluation by cytology, cystoscopy and often intravesical chemotherapy. Treatment decision depend on tumor stage and grade, staging is performed using tumor node and metastasis. There is strong correlation between tumor stage, grade and tumor recurrence and progression, patient with low grade, low stage have low risk of progression to invasive disease, while patients with low stage, high grade tumor had higher risk of progression in follow up period. In patients with organ confined disease, the presence of pelvic lymph node metastasis appears the most important prognostic value. Tumor recurrence related to the grade, size of the tumor and number of the tumor.

Treatment selection:

Patients with superficial bladder tumor can be treated with TUR alone followed by selective intravesical chemotherapy. Ta: treated by TUR alone ,Tis usually treated by TUR followed by Intravesical BCG, T1, small low grade tumor can also be treated by TUR alone followed by surveillance, while T1, high grade, large , multiple treated by TUR

followed by intravesical chemotherapy or immunotherapy. Invasive tumor, but still localized

(T2, T3), are candidate for more local aggressive treatment, including partial or radical, or combination of radiation and systemic chemotherapy. Patients with unreachable local tumor (T4b), are candidate for systemic chemotherapy, followed by surgery or possibly radiation, patients with distances metastasis, are candidate for systemic chemotherapy followed by radiation or surgery.

Tis: complete TUR followed by IVC BCG

Ta(single, low or moderate grade): complete TUR

Ta(large, multiple, high grade): complete TUR, followed by IVC

T1: complete TUR followed by IVC

T2-T4: radical cystectomy

Neoadjuvant chemotherapy

Followed by radical

Cystectomy

Radical cystectomy followed

Adjuvant chemotherapy

Neoadjuvant chemotherapy followed by concomitant chemotherapy and irradiation

Any T, N+,M+: systemic chemotherapy followed by selective surgery or irradiation.

Intravesical chemotherapy:

Can be instilled into the bladder directly via Catheter, thereby avoiding the morbidity of systemic chemotherapy. It had 3 rules: adjuvent at TUR to prevent transplantation of tumor cells after TUR, prophylactic after complete TUR to prevent or delay recurrence or progression, or therapeutic to cure residual disease. It administer in weekly for 6 weeks, then maintenance monthly. Local toxicity is common, systemic toxicity is rare.

Example of intravesical chemotherapy:

1. Mitomycin C
2. Thioptepa
3. BCG: attenuated strain of *mycobacterium bovis*, the mechanism of action thought to be immunologically

mediated, it appear to be effective both therapeutically and prophylactically, it appear to be the most effective Intravesical agent in the management of the CIS, it given weekly for 6 weeks, then maintenance in high risk patients 3-6 months interval by 3 instillation, weekly for 3years after the TUR. Side effects of IVC are relatively common, but severe complications are uncommon.

Partial cystectomy

Patients with solitary, infiltrating Tumor (T1-T3) localized along the posterior lateral wall or dome of the bladder are candidate for partial cystectomy.

Radical cystectomy

Is now slandered for the treatment for localized Pt2-pt3 disease without evidence of secondary disease without evidence of secondary spread or of CIS that has not respond to BCG