Upper Tract Tcc

Mohan Arianayagam FRACS (Urology)
Epidemiology

- Peak incidence 75 to 79 years
- 2x more common in men
- 7% of all renal tumours
- 5% of all urothelial tumours
- Synchronous bilateral is rare ~ 1.6%
  - Preceded by bladder UC in 80% of cases
- 2-4% may develop upper tract TCC after bladder UC at 7 years
Aetiology & risk factors

- Balkan nephropathy
  - Degenerative interstitial nephropathy
  - 100-200x increased risk in affected families
  - No familial inheritance identified
  - Multiple, low grade, bilateral tumours
  - Blaeer UC rate not increased
Aetiology & risk factors

- Smoking – 3 to 7x increased risk
  - Ureteral >> renal pelvic
- Coffee – 1.3x (after corrected for smoking)
- Analgesics – phenacetin 3.6x RR
  - If associated with papillary necrosis >20x RR
  - Thickening of BM & papillary scarring are pathognomonic
Aetiology & risk factors

- **Chemicals – long lag time**
  - Petroleum, plastics, coal, tar, asphalt, aniline dyes, beta napthylamine, benzidine

- **Inflammation**
  - Chronic irritation (infection, stones, obstruction)
  - Cyclophosphamide

- **Lynch syndrome II**
  - Colon Ca without polyps with upper tract UC in younger women
Location

- More common in lower ureter
  - 70% distal
  - 25% mid
  - 5% proximal
  - Bilateral ~ 1.6%

- With upper tract UC bladder surveillance is mandatory
  - 15 – 75% may develop bladder UC
Location

- 2-4% develop upper tract UC after bladder UC

- Risk factors – stage, grade, multiplicity, reflux, CIS post BCG, CIS at cystectomy, tumour near UO

- Up to 30% who have cystectomy for refractory CIS can develop distal upper tract UC
Prognosis

- 19% may present with metastatic disease
- Prognosis related primarily to stage & grade
- 5 year survival
  - Ta, Tis – 100%
  - T1 – 91%
  - T2 – 72%
  - T3 – 40%
- Stage & age are also predictors of survival
- CIS is a poor prognostic sign
Progression

- Thin muscle layer allows earlier invasion
- Prognosis better for renal pelvic tumours
- T3 five year survival
  - Ureter 25%
  - Pelvis 54%
May invade

- Renal parenchyma or surrounding structures
- Epithelial – direct spread or seeding
  - Monoclonal or field change
  - Antegrade or rarely, retrograde
- Lymphadenectomy is controversial
- Vascular – renal vein & IVC are invaded rarely
- May metastasise to lung, bone, liver
Histology

- Pelvis & calyces
  - Fibrous connective tissue with 2 layers of SM (spiral, helical), lined with transitional cell epithelium

- Ureter
  - Upper 2/3 – two, thin continuous layers
  - Lower third has additional layer
  - 3 layers merge with layers of bladder (outer longitudinal, middle circular, inner longitudinal)
Pathology

- >90% are TCC
  - Papillary or sessile
  - Uni/multi focal
  - CIS – epithelial hyperplasia or red patch

- Minority
  - Adeno ~ 1%
  - SCC ~ 7%
Symptoms, signs

- 98% have micro/ macro haematuria
- 30% have flank pain due to obstruction
- Clot colic
- Advanced disease
  - Anorexia, weight loss, mass, bone pain
Evaluation

- CT urography 100% Sn, 60% Sp
  - Filling defects in 75%
  - 46 HU (10 – 70 HU) vs radiolucent uric acid stones 100HU (85 – 200HU)

- Cystoscopy, retrograde studies +/- flexible ureteroscopy & biopsy, cytology – 75% Sn

- Contralateral upper tract & bladder must be evaluated
Main issue

- How to stage accurately?
- Endoscopically it’s easy to get grade but not stage
- Low grade tumours are usually low stage
  - 80% with G1 or 2 are Ta/T1
  - 70% with G3 are T2 or 3
- Ureteral tumours – 75% are low grade & stage
- Renal pelvic tumours – 50% are invasive
cytology

- Voided urine cytology – 25% Sn for G1, 75% Sn for G3
- Selective cytology more accurate but false positive/neg in 35%
- Brush biopsy Sn & Sp 90%
- Exposure of cells to contrast – more cytologic abnormalities
Staging

- Ta – papillary, noninvasive
- Tis – CIS
- T1 – invades subepithelial connective tissues
- T2 – invades muscularis

- T3 – invades perireteral fat.
  For renal tumours – perinephric fat or parenchyma
- T4 – adjacent organs
Staging

- N1 – single node <2cm
- N2 – single /multiple nodes between 2 & 5cm
- N3 – nodes over 5cm
- M0 – no mets
- M1 – distant mets
Treatment - endoscopic

- Lower morbidity
- Small instruments limit size of tumour that can be treated

Options
- Bulk excision & ablation of base
- Diagnostic biopsy & ablation
- Resection to base using resectoscope

Complications – ureteral perforation or stricture formation
Endoscopic resection/fulguration

- Retrograde is less invasive but is limited by smaller instruments
- Difficult to get stage
- Recommended in solitary kidney, bilateral disease, renal failure, poor surgical candidates
- Best for low grade, low stage
Endoscopic resection/fulguration

- Recurrence rates after endoscopic mx
  - Renal pelvis – 31%
  - Ureter – 33%
  - Bladder – 40%
- Usually ipsilateral and distal
Open/ Lap

- Nephron sparing
- Segmental ureterectomy
- Distal ureterectomy
- Subtotal ureterectomy
- Nephroureterectomy
Nephron sparing

- Large localised tumour with solitary kidney or synchronous bilateral tumours, analgesic abuse
- Open pyelotomy with removal of tumour & coagulation of base or partial nephrectomy
- High recurrence rate for T2
Segmental ureterectomy

- Grade 1 & 2 non invasive tumours of proximal/ mid ureter too large for endoscopic mx
- High grade tumours with solitary kidney
- 5 year survival
  - T1 – 65%
  - T2 – 50%
- 50% risk of ipsilateral recurrence requires lifetime surveillance
Segmental ureterectomy

- Ureteroureterostomy can be done in defects up to 4cm
- 1cm clear margin on either side
- Spatulate
- Tension free anastomosis over a stent
- Nephropexy may be done to psoas tendon
Distal ureterectomy

- Distal tumours that can’t be removed endoscopically
  - Low grade or renal preservation
- Lower midline/pfannenstiel
- Direct reimplant or psoas hitch/boari flap
Subtotal ureterectomy

- Long segments for multifocal tumours with renal preservation
- Ileal interposition or spiral flap
- Narrow a length of ileum over 14F catheter discarding antimesenteric tissue
- Last resort – auto transplant
Nephroureterectomy

- Gold standard due to high recurrence rate and low rate of contralateral disease (<5%)
- Entire ureter must be removed with bladder cuff – stump recurrence 75%
- Lymphadenectomy is recommended in open nephroureterectomy based on bladder data but there is no therapeutic benefit yet
- No difference between lap and open
Nephroureterectomy

- Nephroureterectomy with dialysis offers best chance of cure with large, invasive, high grade, organ confined renal pelvis tumours with single kidney
Open/Lap - Results

- Outcome strongly correlates with stage & grade
- Grade 1 & 2 non invasive have good 5 year survival (Ta, T1 ~ 65%)
- T2 – 50% 5 yr survival
- T3 – 7% cancer specific 5 yr survival with 83% death due to tumour
Topical/immunotherapy

- Instill via percutaneous tube, stent, ureteric catheter or iatrogenic reflux
- Low pressure essential to minimise systemic absorption
- No data to suggest it actually improves survival
- BCG may cause granulomatous involvement of kidney
Chemotherapy

- Neo adjuvant or adjuvant is reasonable but there is no evidence at this time
- Adjuvant radiotherapy does not decrease local relapse or protect against distant failure
- Combination chemotherapy is required
  - Methotrexate, vinblastine, cyclophosphamide, gemcitabine
  - Gemcitabine with taxanes
Surveillance
Isolated upper tract cytologic abnormality

- By definition – normal cystoscopy & urogram
- Ureteropyeloscopy is required as direct visualisation has a higher yield than retrogrades
- Biopsy is required prior to definitive treatment