Urinary System 2
Tumours of the kidney, urinary tract and prostate

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Kidney, urinary tract and prostate - the important “tumours”

• Kidney
  – nephroblastoma (Wilms’ tumour) – children
  – renal cell carcinoma - adults

• Urinary tract
  – transitional cell (urothelial) tumour
  – squamous carcinoma of the bladder

• Prostate
  – (prostatic hyperplasia)
  – prostatic carcinoma
Putting them into perspective -

- kidney and urinary tract tumours are generally less common in Africa, than in Europe, N America & Australasia
  - part of that difference is due to differences in age expectations
  - the rest? - ? genetic ? environmental
- prostate hyperplasia and carcinoma common in races other than orientals
Tumours of the kidney

• benign tumours clinically unimportant
  – almost always small, so just incidental findings - e.g. cortical adenoma found in 20% autopsies
• metastatic tumours surprisingly uncommon, despite massive renal blood flow
Malignant tumours of the kidney

The only important ones are -

• nephroblastoma (Wilms’ tumour)
• renal cell carcinoma
• transitional cell carcinoma of renal pelvis (essentially part of urinary tract)
Where would malignant tumours of the kidney spread to?
Nephroblastoma (Wilms’ tumour)

- one of commonest intra-abdominal tumours < 10 yrs age, but still not common
- occasionally bilateral
- mostly 1-5 years (can even be congenital)
- highly malignant tumour of mesoderm (renal blastema) – often already spread to lungs at time of diagnosis
Nephroblastoma
Nephroblastoma (Wilms’)  

• usually quite big tumour  
  – often presents as abdominal mass  

• extension through renal capsule common  

• despite malignancy, excellent results if it can be treated aggressively  
  – combination of radiotherapy, nephrectomy and chemotherapy
Renal cell carcinoma
(adenocarcinoma of the kidney)

• commonest (~90%) renal malignancy in adults, but < 3% all malignancies in countries where it is commonest (less common in Africa)
• ages 50s+ and male:female 2:1
• usually large bulging tumour at renal pole (upper > lower)
• yellowish cut surface, often with cysts and haemorrhage
• often apparently sharp margins, due to pseudocapsule
Histology of renal cell CA

• derived from renal tubular cells
• 80 % are “clear cell” adenocarcinomas
  – abundant clear or granular cytoplasm - contain glycogen and fat
• (other histological types (“papillary” and “chromophobe”) have better prognoses)
• (classification of renal cell CA can now be based on correlation of genetic and histological changes)
Spread of renal cell carcinoma

- **local, lymphatic and blood**
- may invade perinephric fat
- can invade pelvi-calyceal system
- lymphatic – first to para-aortic nodes
- often invades renal vein........
  - blood spread most often to lungs (50%), bones (33%), adrenals and brain
Presentation of renal cell CA

usually late – so often CA has already spread

• most often, haematuria
• abdominal mass +/- loin pain

but, one of the great “mimickers”
• metastasis (classically cannonball metastases in lungs)
• fever of unknown origin/night sweats
• weight loss, malaise
• paraneoplastic phenomena -
  - secretion of erythropoietin, renin, parathormone, corticosteroids, eosinophilia, amyloidosis etc
What could be the effects of secretion of erythropoietin, renin or parathormone?
Prognosis of renal cell CA

5-yr survival rate overall ~ 50%
• 70 % if no metastases
• 15-20% if renal vein involved
Risk factors for renal cell CA

• cigarette smoking is only definite association – e.g. 30-40% occur in smokers in UK, where <20% population smoke

• (rarely, genetic factors – e.g. in the very rare von Hippel-Lindau disease)
URINARY TRACT TUMOURS

• the only common *intrinsic* tumours of the urinary tract are those of transitional epithelium (urothelium)

• variety of names -
  – *transitional tumours*
  – *or transitional epithelial tumours*
  – *or transitional cell tumours*
  – *or urothelial tumours*
Transitional tumours

- common
- spectrum of “benign” to malignant
- behaviour can change with time, i.e. to become more malignant
- malignancy preceded by dysplasia/CA in situ
- sometimes multiple
  - suggesting field change in epithelium
- tract contents promote tumour development
Does *that* remind you of tumours anywhere else?
Transitional tumours

- age 50s - 70s: men > women
- white > black >> oriental populations
- arise anywhere in urinary tract, but bladder (especially bladder base) >> pelvis/calyces > ureters > urethra
- often polypoidal & papillary/fronded, especially at first - if sessile (flat), more likely to be malignant (*like colon*)
- tumours may be preceded by dysplasia/CIS
- “benign” = transitional papilloma: malign. = transitional carcinoma
Papilloma—papillary carcinoma

Invasive papillary carcinoma

Flat noninvasive carcinoma (CIS)

Flat invasive carcinoma

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Transitional tumours

• presentation
  - most often, haematuria
  - but also urinary infection and/or obstruction
• often prolonged natural history
• carcinomas may present with metastases
  – spread – local, lymphatic & blood – details depend on site of primary
• tumour cells exfoliate into urine, so cytological examination of urine can sometimes help in diagnosis
Aetiological factors

chemical carcinogens

• cigarette smoking
• aniline dyes (dye, rubber, plastic, cable & gas industries) – intermediate metabolites filtered by kidney, then carcinogenic substances released by β-glucuronidase (helped by acidity of urine)
• rarely, analgesic abuse (renal pelvis)

chronic inflammation – not related, but

- schistosomiasis (bladder) and calculi (pelvis and bladder) both associated with squamous CA
What tumours other than those of the urinary tract itself could cause urinary tract obstruction?
Main causes of prostatic enlargement

- benign nodular hyperplasia
- carcinoma
Benign nodular hyperplasia (BNH)

- affects most men, usually starting around age 50
- (after age 40 or so, prostate gradually gets bigger)
- incidence/severity increase with age (75% by 70s)
- hyperplasia of connective tissue and glands – usually 60-100 g (normal = ~30G)
- involves more “central” parts, espec lateral or “median” lobes, which are most sensitive to oestrogen
- probably due to age changes in sex hormone levels (androgen:oestrogen levels) – orchidectomy protective
Effects of BNH

• urinary infection and/or obstruction
• prostatic infection & infarction
• but not premalignant
BNH of prostate

effects/complications
• mainly due to abnormal bladder sphincter, so disturbed micturition ("prostatism")
• partly mechanical effects of the enlarged gland
• but also smooth muscle-mediated contraction of the prostate
  – prostatic smooth muscle tension mediated by α1-adrenoreceptor localized in stroma
  – hence use of α-adrenergic receptor antagonists for relief of urinary obstruction
Prostatism

- frequency
- nocturia
- difficulty in starting and stopping
- overflow dribbling
- dysuria (painful micturition)

- in many cases, sudden, acute urinary retention
Effects of BNH

• inability to empty bladder completely
  – due to raised level of urethral floor causing residual urine
• static fluid vulnerable to infection
• catheterization or surgery can introduce organisms
BNH of prostate

- secondary changes occur in bladder
  - hypertrophy, trabeculation and diverticulum formation
- acute retention
- dilatation of urinary tract
- secondary urinary tract infection
- renal damage, even failure
Carcinoma of the prostate

- in Europe, N America (blacks>whites) and Australasia, commonest male CA
- commoner than any female cancer
- incidence increasing everywhere, but especially in Africa - ? higher than elsewhere?
- family history raises risk ~ x 2 or 3
- uncommon in orientals (but incidence increases if they move to regions with higher incidence)
- age of incidence later than any other CA
  - old age (60s -80s)
  - younger in patients with family history
Carcinoma of the prostate

- adenocarcinoma
  - probably arises from PIN (prostatic intraepithelial neoplasia)
- affects peripheral parts of glands (especially posteriorly)
  - more androgen dependent
Effects of CA prostate

• local = same as those of BNH (prostatism, obstruction, infection etc), but very often no local effects

• distant, due to metastases - local, lymph and blood
  – often presents with metastasis – “occult carcinoma”
Spread of CA prostate

- local – especially seminal vesicles and base of bladder
- blood - chiefly to bones, particularly axial skeleton (lumbar spine, proximal femur, pelvis, thoracic spine) and ribs
  - bony metastases typically osteoblastic/osteosclerotic (in men, highly suggestive of CA prostate)
  - massive visceral dissemination unusual
- lymphatic spread – common, often before blood spread
  - initially to the obturator nodes followed by pelvic, presacral, and para-aortic nodes
Aetiology

• suspected risk factors are age, race, family history, hormone levels and environmental factors

• no proven environmental factors- e.g. increased consumption of fats or lack of protective factors in diet
Aetiology

- like BNH, androgens believed to play role in pathogenesis
  - orchidectomy protective
  - oestrogens sometimes used in treatment
- genetic factors
  1. increased incidence if family history
  2. prostate cells with short repeats of CAG are highly sensitive to androgens
    - shortest CAG repeats are in African-Americans, while longest are in orientals
    - African-Americans have highest incidence of prostate cancer and orientals the lowest
PIN (prostatic intraepithelial neoplasia)

- likely precursor of CA
- focal dysplasia/CIS of the glandular epithelium
- may occur beside CA or on its own
- low grade changes common, even in middle age – not an indication for concern, but ? can evolve
- if high grade PIN, say in a biopsy, surveillance for CA mandatory
- (anti-androgenic therapy can let it regress)
Prognosis

• as with most tumours, variable according to grade and stage of tumour
• Gleason grading = histological grading of prostatic CA
• “latent” CA prostate
  – discovered as incidental finding in prostates removed for BNH or at autopsy
  – very common in autopsies in very old men
Markers of use in CA prostate

- prostate specific antigen
- prostatic acid phosphatase
Prostate specific antigen (PSA)

- produced by prostatic epithelium
  - serine protease which liquefies semen coagulum which forms after ejaculation
- normally tiny amounts in serum
- elevated levels can occur in localised or metastatic prostate CA
- but levels can increase in other conditions of the prostate and in ~ 20% CA cases PSA may be normal, so no value as screening test
Prostatic acid phosphatase

- prostatic acid phosphatase
  - produced by prostate and seminal vesicle
  - present in semen
- serum levels may be raised in prostate disease, especially if CA metastasised
Relationship between BNH and CA prostate

CA not 2ndry to BNH, because -

- repeated TURs (transurethral resections) for BNH don’t affect frequency of CA
- lesions affect different parts of gland
- geographic differences in incidence, e.g.
  - BNH UK > Scandinavia
  - CA Scandinavia > UK
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