Renal Cell Carcinoma

- More common in N Europe and N America
- Lowest in Asian Countries & S America
- M:F 2:1
- Risk Factors: Cigarette smoking 20% cases
  Obesity 30% cases
  Hypertension
  Renal dialysis (acquired cystic kidney disease)
Clinical Features

Classically: Flank pain, renal mass and haematuria

Mostly not however!

Around 1/3 present with paraneoplastic features:

- Fever, malaise, night sweats, anorexia
- Neuropathy, non-metastatic hypercalcaemia (PTH-like peptide)
- Erythrocytosis (increased erythropoietin)
- Non-metastatic hepatic dysfunction
Familial Renal Tumours

Von Hippel–Lindau Disease
  Aut Dominant
  Mutation of VHL gene 3p25-26
  Cap haemangioblastomas of CNS and retina
  Clear cell RCC / Phaeo / Pancreatic tumours

Hereditary papillary renal carcinoma (HPRC)
  Aut Dom
  Late onset of multiple Papillary tumours
  Mutation of MET oncogene on 7q31

Hereditary leiomyomatosis and RCC (HLRCC)
  Aut Dominant
  Cutaneous and uterine leiomyomas
  Uterine leiomyosarcoma
  Renal papillary Ca

Tuberous sclerosis
  Bilateral angiomyolipomas
  skin angiofibromas / cardiac rhabdomyomas
## Genetic Alterations

<table>
<thead>
<tr>
<th>Type of Tumor</th>
<th>Genetic Alterations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clear cell Ca</td>
<td>Deletions of 3p / mutations in VHL gene</td>
</tr>
<tr>
<td>Papillary Ca</td>
<td>Trisomy 7, 17 and loss of Y (others)</td>
</tr>
<tr>
<td>Chromophobe Ca</td>
<td>Extensive chromosomal loss</td>
</tr>
<tr>
<td>Collecting duct Ca</td>
<td>Multiple genetic events</td>
</tr>
<tr>
<td>Oncocytoma</td>
<td>Mix of cells with normal and abnormal karyotypes</td>
</tr>
<tr>
<td></td>
<td>Some show t(5;11) CCND1 is at 11q13</td>
</tr>
<tr>
<td></td>
<td>Some show loss of 1 and 14</td>
</tr>
</tbody>
</table>
Grading

• Always causes problems! Why?

• Fuhrman Nuclear Grading
  • Start at x100. If irregular nuclei and prominent nucleoli then it’s grade 3. If also bizarre nuclei then it’s grade 4
  • If neither, go to higher powers to decide between grades 1 and 2.

• Liebovitch (Mayo)
  • Almost same as Fuhrman but requires 1HPF’s worth for highest grading
Renal Sinus
Sinus invasion correlates with:

- Tumour > 4cm (NB pT1 and pT2 may be pT3)
- Fuhrman grade 3 and 4
- Veins first then fat
  Fat first is less common
- Sinus invasion is more common than capsular invasion
Clear cell
Clear cell
Clear cell
Clear cell bv
Papillary Carcinoma

Approx 10% of renal carcinomas

Papillae and tubules
Foamy histiocytes in cores
Solid variants + /- necrosis

Sarcomatoid dedifferentiation in 5% cases
Papillary Carcinoma

Type 1: small cells, scanty cytoplasm. More frequently multifocal

Type 2: bigger tumours larger cells, higher nuclear grade eosinophilic cytoplasm

Type is correlated with survival

Fuhrman grading used
Papillary (tubulo-papillary)
Papillary (grooves)
Papillary Ca Type 2
Papillary CK7
Chromophobe Carcinoma

• 5% of renal carcinomas
• Mainly solid growth pattern
• Many blood vessels are thick walled
• Perivascular cells are enlarged

• Raisinoid nuclei and well defined cell
• Membranes
• Flocculent cytoplasm
• Eosinophilic variant
• Perinuclear halos
Chromophobe
Chromophobe
Chromophobe
Grading of Chromophobe Carcinoma

Grade 1: Usual range of nuclear appearances

Grade 2: Nuclear crowding AND pleomorphism

Grade 3: Anaplasia or sarcomatoid change

Chromophobe Tumour Grade correlates better with stage and adverse outcome than Fuhrman Grade (for non-sarcomatoid tumours)

At least 2 areas to concur on the grade
Oncocytoma (benign)

Well circumscribed
Tan brown
Central scar

Nests, tubules, cysts in hypocellular stroma

Round nuclei, plentiful eosinophilic cytoplasm
A few clusters of pleomorphic nuclei

Tiny clear cell or papillary areas OK
Can get capsular & vascular invasion
Oncocytoma MOC 31
<table>
<thead>
<tr>
<th></th>
<th>Clear Cell</th>
<th>Pap</th>
<th>Chromophobe</th>
<th>CDC</th>
<th>Oncocytoma</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pan CK</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
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<td>HMWCK</td>
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<td>LMWCK</td>
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<tr>
<td>MOC 31</td>
<td>-</td>
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<tr>
<td>RCC</td>
<td>+/-</td>
<td>+/-</td>
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<td>-/+</td>
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<tr>
<td>Ber EP4</td>
<td>-</td>
<td>+/−</td>
<td>+</td>
<td>-</td>
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<tr>
<td>CD 10</td>
<td>+/-</td>
<td>+</td>
<td>-/+</td>
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<tr>
<td>Vimentin</td>
<td>+</td>
<td>+</td>
<td>-</td>
<td>-/+</td>
<td>-</td>
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<tr>
<td>CK 7</td>
<td>-</td>
<td>+</td>
<td>+(diff)</td>
<td>+/-</td>
<td>+(foc)</td>
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<tr>
<td>AMACR</td>
<td>-</td>
<td>+</td>
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<tr>
<td>CD15</td>
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</table>
# Immunoprofiles

<table>
<thead>
<tr>
<th>Tumor Pair</th>
<th>Antibodies</th>
</tr>
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<tbody>
<tr>
<td>Chromophobe Vs Oncocytoma</td>
<td>MOC31, Ber EP4, CK 7, CK 20, CD10</td>
</tr>
<tr>
<td>Chromophobe Vs Clear cell</td>
<td>MOC 31, CD10, RCC, Ber EP4</td>
</tr>
<tr>
<td>Papillary Ca Vs CDC</td>
<td>Immuno not much use</td>
</tr>
<tr>
<td>Papillary Ca Vs Met adenoma</td>
<td>CK 7, AMACR, CD57, WT-1</td>
</tr>
<tr>
<td>Papillary Ca Vs Mucinous tubular and spindle cell Ca</td>
<td>Immuno not much use</td>
</tr>
<tr>
<td>Sarcomatoid RCC Vs MTS Cell Ca</td>
<td>CK7 + in MTS</td>
</tr>
</tbody>
</table>
Transitional cell carcinoma

Renal pelvis
7% of all renal tumours
5% of all urothelial tumours

Prognostic indicators:
grade
ureteric margin status
vascular invasion
stage (most important)
TCC parenchyma
Collecting duct carcinoma

Rare – less than 1% renal tumours
Can be metastatic at presentation

Centrally located
Tubular / tubulo-papillary
Angulated glands infiltrating renal parenchyma
Desmoplastic stroma

Tubular epithelial dysplasia may be seen

High nuclear grade

Poor prognosis: Two thirds dead within 2 years
Angiomyolipoma

1% renal tumours
Thought to arise from perivascular epithelioid cells
Can lose attachment to kidney and grow in retroperitoneum
Associated with tuberous sclerosis

Fat, blood vessels and smooth muscle – variable

Can be malignant
Epithelioid Angiomyolipoma

The presence of 3 or more of the following are predictive of malignant behaviour:

- > 70% atypical epithelioid cells
- > 2 mitoses per 10hpf
- Atypical mitoses
- Necrosis
Renal Leiomyosarcoma

Rare but is the most common sarcoma

Most patients die within a year
Renal angiosarcoma

Very rare and very aggressive
Mixed Epithelial Stromal Tumours of Kidney (MESTK)

- Age 41 – 75
- Almost always female
- Unilateral
- Do not recur
- Solitary
- Solid and cystic
Microscopy

Multicystic
Hobnail cells
Haemorrhage
Glandular areas
Stroma - Fibroleiomyomatous
    Ovarian like
ER / PgR positive
Re: Cystic Nephroma

1. MESTK

2. Really Cystic nephroma (male)

3. Cystic partially differentiated nephroblastoma
Multilocular cystic renal cell carcinoma (benign)
  3p deletion
  Grade 1 or 2
  Cystic spaces lined by clear cells
  No expansile nodules. Ovarian stroma

Mucinous tubular spindle cell carcinoma
  Polymorphic low grade Ca (CD 10 Neg)
  Favourable prognosis

Papillary adenoma
  5mm or less
  Most common neoplasm of renal tubules
  More common in haemodialysis and acquired renal cystic disease