Neoplastic Kidney Diseases
Agenda

- introduction, epidemiology, etiology
- prognostic factors and specimen dissection
- differential diagnosis of clear cell tumors, papillary tumors, and tumors with eosinophilic/granular cytoplasm

Diagnostic Pathology: Genitourinary
Introduction

- primary or secondary tumors
- renal cell carcinoma originates in the tubules of the cortex
- clinical manifestations: frequently incidental; hematuria, abdominal mass, pain, weight loss
- ~25% of patients present with metastasis or advances locoregional disease

<table>
<thead>
<tr>
<th>Renal Cell Carcinomas (RCC)</th>
<th>80-85%</th>
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</thead>
<tbody>
<tr>
<td>Clear cell RCC (65-70%)</td>
<td></td>
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<tr>
<td>Papillary RCC (~18%)</td>
<td></td>
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<tr>
<td>Chromophobe RCC (5-7%)</td>
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<td>Collecting duct RCC (1-2%)</td>
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<tr>
<td>Urothelial carcinoma of the renal pelvis</td>
<td>8%</td>
</tr>
<tr>
<td>Others</td>
<td>rare</td>
</tr>
</tbody>
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UpToDate.com: Clinical manifestations, evaluation, and staging of renal cell carcinoma
Epidemiology

- 9th most common cancer, 338’000 new cases in 2012
- 70% occurred in countries with high or very high levels of socioeconomic development
- Males affected twice as much as females
- 143’000 deaths from kidney cancer in 2012

Estimated age-standardized rates (World) of incidence cases, both sexes, kidney cancer, worldwide in 2012

IARC: Cancer Today
Etiology

• obesity (mechanism not understood)
• smoking
• hypertension
• acquired cystic kidney disease (3-7% of patients with ESRD)
• occupational exposure (trichloroethylene)
• genetic susceptibility (2-4% of cases with familial cause)
Prognostic factors

- anatomic extent (TNM staging)
- tumor type? (ccRCC does worse than pRCC or chrRCC)
- tumor grade (ISUP grading)
- sarcomatoid component, rhabdoid component (%)
- tumor necrosis (%; generally >10% relevant, in stage I and II >20%)

Stage III: pT1-2, N1, M0
pT3, N0-1, M0

Stage IV: pT4, any N, M0
any T, any N, M1

UpToDate.com: Prognostic factors in patients with renal cell carcinoma
International Collaboration on Cancer Reporting: upcoming dataset for kidney carcinoma
ISUP grading

single high-power field showing greatest nuclear pleomorphism

<table>
<thead>
<tr>
<th>grade</th>
<th>description</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>nucleoli absent or inconspicuous at x400</td>
</tr>
<tr>
<td>2</td>
<td>nucleoli are conspicuous and eosinophilic at x400 and visible but not prominent at x100</td>
</tr>
<tr>
<td>3</td>
<td>nucleoli are conspicuous and eosinophilic at x100</td>
</tr>
<tr>
<td>4</td>
<td>extreme nuclear pleomorphism, ultinucleate giant cells, and/or rhabdoid and/or sarcomatiod differentiation</td>
</tr>
</tbody>
</table>

Cancer-specific survival by the ISUP grading system for 3017 patients with ccRCC

➢ grade ccRCC and pRCC
➢ do not grade chrRCC

Cutting

- open ureter longitudinally up to the level of the pelvis
- place probe into a superolateral calyx push through renal parenchyma and perinephric soft tissue
- place second probe in an inferolateral calyx, push through parenchyma and soft tissue
- bivalve kidney along the line of the probes

Hum Pathol 40:456-463, 2009
Pay attention to ...

- macroscopic infiltration of veins, infiltration of perirenal and/or infiltration of peripelvic soft tissue (relevant for T staging!)
- lymph nodes not identified in >80% of specimen
- take normal kidney tissue as far away from the tumor as possible
Approach to histology

- child or adult?
- clear cell, papillary, eosinophilic, and/or high grade morphology?
- any unusual features?
- possibility of genetic syndrome?

Diagnostic Pathology: Genitourinary
### Renal cell tumours
- Clear cell renal cell carcinoma
- Multilocular cystic renal neoplasm of low malignant potential
- Papillary renal cell carcinoma
- Hereditary leiomyomatosis and renal cell carcinoma
- Chromophobe renal cell carcinoma
- Collecting duct carcinoma
- Renal medullary carcinoma
- Mit family translocation renal cell carcinomas
- Succinate dehydrogenase-deficient renal carcinoma
- Mucinous tubular and spindle cell carcinoma
- Tubulocystic renal cell carcinoma
- Acquired cystic disease-associated renal cell carcinoma
- Clear cell papillary renal cell carcinoma
- Renal cell carcinoma, unclassified
- Papillary adenoma
- Oncocytoma

### Mesenchymal tumours occurring mainly in adults
- Leiomysarcoma
- Angiosarcoma
- Rhabdomyosarcoma
- Osseous sarcoma
- Synovial sarcoma
- Ewing sarcoma
- Angiomyolipoma
- Epithelioid angiomyolipoma
- Leiomyoma
- Haemangioma
- Lymphangioma
- Haemangioblastoma
- Juxtaglomerular cell tumour
- Renal medullary interstitial cell tumour
- Schwannoma
- Solitary fibrous tumour

### Mixed epithelial and stromal tumour family
- Cystic nephroma
- Mixed epithelial and stromal tumour

### Neuroendocrine tumours
- Well-differentiated neuroendocrine tumour
- Large cell neuroendocrine carcinoma
- Small cell neuroendocrine carcinoma
- Phaeochromocytoma

### Miscellaneous tumours
- Renal haematopoietic neoplasms
- Germ cell tumours

### Metastatic tumours

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**key adult types:**
- clear cell RCC
- papillary RCC
- chromophobe RCC
- collecting duct carcinoma
- oncocytoma
- angiomyolipoma

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The morphology codes are from the International Classification of Diseases for Oncology (ICD-O) (917A). Behaviour is coded 0 for benign tumours, 1 for unspecified, borderline, or uncertain behaviour; 2 for carcinoma in situ and grade I; 3 for grade II; and 2 for malignant tumours. The classification is modified from the previous WHO classification (7th ed.), taking into account changes in our understanding of these lesions.

*New code approved by the IARC/WHO Committee for ICD-O.*
Clear cell RCC – macroscopy

- often well circumscribed, unencapsulated
- golden-yellow (lipids)
- necrosis, fibrosis, cystic changes, hemorrhage common
Clear cell RCC – microscopy

- various patterns: nests, solid alveoli, tubules, micro- or macrocystic, solid sheets
- focal papillary growth possible
- fibrovascular septations
- clear cell cytoplasm (low grade), granular/eosinophilic cytoplasm (high grade)

» look for prototypical areas
Clear cell RCC – microscopy

Diagnostic Pathology: Genitourinary
Rhabdoid and sarcomatoid morphology
Clear cell RCC – immunohistochemistry

- CK22+, EMA+, Vimentin+
- **CA9****+, CD10+, 34bE12+, GLUT1+, Pax2+, Pax8+, RCC+
- CK7-, AMACR-, CD117-

[Image: Diagnostic Pathology: Genitourinary]
Differential diagnosis of clear cell RCC

- multilocular cystic renal neoplasm of low malignant potential
- clear cell papillary RCC (CK7+, CD10-)
- chromophobe RCC (CD117+, CK7+, CA9-, CD10-)
- MiT family translocation RCC
- epitheloid angiomyolipoma (HMB45+, SMA+)
- adrenal cortical tissue

Diagnostic Pathology: Genitourinary
Papillary RCC – macroscopy

- well circumscribed with fibrous pseudocapsule
- necrosis, hemorrhage, cystic change common
- papillary adenoma ≤15mm with ISUP grade 1-2
- frequently multifocal
Papillary RCC – microscopy

- various patterns: papillary, tubular, solid
- fibrovascular cores frequently contain foam cells and psammoma bodies
- type 1: smaller cells with scant amphophilic cytoplasm, single cell layer
- type 2 (non-type 1): larger tumor cells with eosinophilic cytoplasm, pseudo-stratification of higher grade nuclei
Papillary RCC – microscopy

- Solid appearance of PRCC
- Clear cell areas in PRCC
- Type 2 PRCC

Diagnostic Pathology: Genitourinary
Papillary RCC – immunohistochemistry

- CK22+, EMA+, Vimentin+
- **CK7+ (type 1>2), AMACR+, CD10+, Pax2+, Pax8+, RCC+**
- CA9-, CD117-
Differential diagnosis of papillary RCC

- mucinous tubular and spindle cell carcinoma
- hereditary leiomyomatosis and RCC-associated RCC
- acquired cystic disease-associated RCC (CK7-)
- collecting duct carcinoma (AMACR-, CD10-)
- clear cell RCC
- clear cell papillary RCC
Chromophobe RCC – macroscopy

- well circumscribe, not encapsulated
- cut surface beige or pale-tan, sometimes mahogany
- central scar in ~15%
- hemorrhage and/or necrosis in up to 35%
Chromophobe RCC – microscopy

- mostly solid growth pattern separated by incomplete fibrovascular septa
- prominent cell borders («plant cells»)
- perinuclear halo
- wrinkled nuclei (raisinoid), frequently binucleated
- large pale, clear appearing or eosinophilic granular cells
Chromophobe RCC – IHC

- CK22+, Vimentin-
- CK7+, **CD117**+, ECad+
- CA9-, CD10-, AMACR-
- Hale colloidal iron+

CD117

Diagnostic Pathology: Genitourinary
Differential diagnosis of chromophobe RCC

- oncocytoma (CK7 with isolated scattered cells only)
- hybrid tumor
- tubulocystic renal cell carcinoma
- clear cell RCC
- SDH-deficient RCC
Angiomyolipoma

- mesenchymal tumor originating from perivascular epitheloid cells (PEComa → HMB45+)
- mixture of adipose tissue, smooth muscle cells, and dystrophic vessels
- association with tuberous sclerosis in <50%
- epitheloid angiomyolipoma with malignant behaviour
Summary

• thorough knowledge of the common types
• look for prototypical areas within the tumor
• recognize unusual features → may hint at uncommon tumor types
References

• Differential diagnosis of renal tumours with clear cell histology (Pathology 42:374-383, 2010)
• Diagnostic approach to eosinophilic renal neoplasms (Arch Pathol Lab Med 238:1531-1541, 2014)
• Morphologic, molecular, and taxonomic evolution of renal cell carcinoma. A conceptual perspective with emphasis on Updates to the 2016 World Health Organization classification (Arch Pathol Lab Med 140:1026-1037, 2016)