RENEAL CELL CARCINOMA EPIDEMIOLOGY (2016)

Stage at Diagnosis
2005 - 2011

5-year Survival
2005 - 2011

RENAL CELL CARCINOMA
ACTIVE SURVEILLANCE

- Favorable
  - Clear, NG 1
  - Papillary, type 1, NG 1
  - Chromophobe
- Intermediate
  - Clear, NG 2
  - Papillary, type 1, NG 2
  - Papillary, NOS
  - Oncocytic neoplasm, NOS
- Unfavorable
  - Clear, NG 3 & 4
  - Papillary, type 1, NG 3 & 4
  - Papillary type 2
  - Sarcomatoid


NEEDLE BIOPSY DIAGNOSIS

Clear cell RCC

Papillary RCC

Mucinous tubular and spindle cell RCC

Medullary RCC

Metanephric adenoma

Trabecular angiomyolipoma
WHO 2016 CLASSIFICATION

EPITHELIAL TUMORS

BENIGN
- Papillary adenoma
- Metanephrin adenoma
- Metanephrin adenofibroma
- Oncocytoma

MALIGNANT
- Clear cell RCC
- Multilocular cystic renal neoplasm of low malignant potential
- Papillary RCC
- Chromophobe RCC
- Collecting duct carcinoma
- Medullary carcinoma

WHO 2016 CLASSIFICATION

EPITHELIAL TUMORS

MALIGNANT
- MiT family translocation carcinomas
  Xp11 and t(6;11)
- Carcinoma associated with neuroblastoma
- Mucinous tubular and spindle cell ca
- Tubulocystic RCC
- Acquired cystic disease associated RCC

WHO 2016 CLASSIFICATION

EPITHELIAL TUMORS

MALIGNANT
- Clear cell papillary RCC
- HLRCC syndrome associated RCC
- SDH deficiency associated RCC
- Unclassified RCC

WHO 2016 CLASSIFICATION

EPITHELIAL TUMORS

MALIGNANT
- Clear cell papillary RCC
- Chromophobe RCC
- Acquired cystic disease associated RCC
**WHO 2016 CLASSIFICATION**

**Tumors Not Ready to be Added**

- Specific hereditary types of RCC
  - Birt-Hogg-Dube Syndrome
- Oncocytic papillary RCC*
- So-called “hybrid” oncocytoma/chromophobe RCC**
- ALK-translocation associated
- Thyroid-like follicular carcinoma
- Others

* left in Type 2 papillary RCC
** include in unclassified RCC category

**DIFFERENTIAL DIAGNOSIS**

**ONOCYTOMA**
**CHROMOPHOBE RCC**
**CLEAR CELL RCC**
**UNCLASSIFIED RCC**
**PAPILLARY RCC**
**COLLECTING DUCT CA**
**TRANSLOCATION CARCINOMAS**
**SDH ASSOCIATED RCC**
**EPITHELIOID ANGIOMYOLIPOMA**

**RENAL ONOCYTOMA**

5% of kidney tumors in adults; wide age range; more common in females (2:3:1); majority are asymptomatic; variable cytogenetics: -1 and –Y most often reported
ONCOCYTOMA - IHC

ONCOCYTOMA - NEEDLE BIOPSY: OUR CRITERIA

ONCOCYTOMA - LIKE

RENAL ONCOCYTOMA
**ONOCYTOMA - LIKE**

**CLEAR CELL RENAL CELL CARCINOMA**

**PAPILLARY RENAL CELL CARCINOMA**

**CHROMOPHOBEE CARCINOMA**

5% of kidney tumors, adults, M=F, excellent prognosis (>90% survival); distinctive cytogenetic profile with -1, -2, -6, -13, -17, -21
CHROMOPHOB CARCINOMA

HALE’S COLLOIDAL IRON

CHROMOPHOB CARCINOMA IMMUNOHISTOCHEMISTRY

CHROMOPHOB CARCINOMA

CK7
VIMENTIN
CD10

CD10
Vimentin

Hale’s
“HYBRID” TUMORS

- **RENAL ONCOCYTOSIS**
  - Bilateral, multiple tumors
  - Oncocytoma, chromophobe RCC and hybrid tumors
- **BIRT HOGG DUBE SYNDROME**
  - Skin tumors (trichofolliculomas, achrocordons), multiple renal tumors and pneumothoraces
  - Oncocytoma, chromophobe and clear cell RCC, and hybrid tumors
  - Autosomal dominant, 17p11.2 (folliculin)
- **DE NOVO**
  - 4/425 cases in recent series

**RENAL ONCOCYTOSIS**

- Hale’s colloidal iron

**RENAL TUMOR OF ONCOCYTOSIS**

- Cytokeratin 7
BIRT HOGG DUBE SYNDROME

ACQUIRED CYSTIC KIDNEY DISEASE

- Examined 66 kidneys from 52 patients
- Identified a variety of tumor types:
  - ACD associated carcinoma 33%
  - Clear cell papillary carcinoma 21%
  - Papillary carcinoma 16%
  - Chromophobe carcinoma 16%
  - Clear cell carcinoma 14%
- Considered the first two potentially unique tumor types


ACQUIRED CYSTIC DISEASE ASSOCIATED RENAL CELL CARCINOMA

- To date have occurred exclusively in patients with acquired cystic disease
- Increase in frequency with increased length of time on dialysis
- Occur at any age
- No specific genetic mutations recognized
- Limited prognostic information but metastases reported in 8% to 22% of patients
AcqCKD ASSOCIATED CARCINOMA

Calcium oxalate crystals

AcqCKD ASSOCIATED CARCINOMA

Calcium oxalate crystals
AcqCKD ASSOCIATED CARCINOMA

- 3 – 4% of resected kidney tumors
- Wide age range; slight male predominance
- 95% T1a (< 4 cm)
- Not genetically related to clear cell or papillary RCC
- Distinctive IHC profile
- Excellent prognosis

CLEAR CELL PAPILLARY RCC

- 3 – 4% of resected kidney tumors
- Wide age range; slight male predominance
- 95% T1a (< 4 cm)
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CLEAR CELL PAPILLARY RCC

Clear cell Papillary RCC

Clear cell Papillary RCC

CLEAR CELL PAPILLARY RCC
CLEAR CELL PAPILLARY RCC

EPITHELIAL KIDNEY TUMORS CLASSIFICATION

The t(X;1)(p11.2;q21.2) translocation in papillary renal cell carcinoma fuses a novel gene PRCC to the TFE3 transcription factor gene

Fusion of the transcription factor TFE3 gene to a novel gene, PRCC, in t(X;1)(p1q21)–positive papillary renal cell carcinomas

EPITHELIAL KIDNEY TUMORS CLASSIFICATION

X:1 TRANSLOCATION ASSOCIATED CARCINOMA: FREQUENCY BY AGE

X:1 TRANSLOCATION RCC

- Because of limited number of published cases, prognostic features are unclear.

Prolonged survival in young patients with recurrence/metastases (4/8 with Xp11 translocation RCC)

Komai et al., Urology 77:842, 2011

54 cases, median age 36
50 TFE3
4 TFEB

Malouf et al., J Urol 185:24, 2011

X:1 TRANSLOCATION CARCINOMA

TFE3
CK AE1/AE3

6:11 TRANSLOCATION CARCINOMA

Type IV collagen
**Translocation associated renal cell carcinoma** is in the differential diagnosis of ALL unclassifiable renal cell carcinomas.

**SDH associated RCC**

- Patients with mutation of *SDHB >> SDHC* (rarely SDHA or SDHD)
- Paraganglioma and GIST
- Wide age range (14 – 76 yrs; median 35)
- Multifocal and/or bilateral in 30%
- Eosinophilic cells in nests and tubules; cytoplasmic inclusions; entrapped tubules; mast cells
- Most low grade but metastases develop in about 10% of patients

Williamson et al. Mod Pathol 28:80, 2015
SDH ASSOCIATED RENAL CELL CARCINOMA

HLRCC SYNDROME

- Patients with mutation of fumarate hydratase gene (1q42.3-q43)
- Cutaneous and uterine leiomyomas
- Wide age range (17 – 87 years)
- More common in females
- Complex solid and papillary histology with macro orangophilic nucleoli and perinucleolar halo
- Aggressive tumors with up to 50% with metastasis at diagnosis

HLRCC SYNDROME ASSOCIATED RCC

THYROID-LIKE FOLLICULAR CARCINOMA OF THE KIDNEY

ONCOYTIC PAPILLARY RCC

UNCLASSIFIED RENAL CELL CARCINOMA