Tumors of kidney and urinary bladder

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Overview of kidney tumors

• Benign and malignant

• Of the benign:
  ..papillary adenoma...-cortical
    - small (0.5cm)
    - in 40% of population
    - clinically insignificant

• The most common malignant:
  *Renal cell carcinoma
  ..followed by Wilms (nephroblastoma)
  ..followed by pelvicalyceal malignant tumors

• Tumors of the lower urinary tract are about twice as common as renal cell carcinomas
Benign kidney tumors, oncocytoma

- Arises from the intercalated cells of collecting ducts
- 10% of renal tumors
- Characteristic genetic changes: loss of chromosomes 1, 14, and Y
- Abundant mitochondria
  - tan color grossly
  - finely granular eosinophilic cytoplasm microscopically
- Central stellate scar seen grossly and on imaging...characteristic

Can occur in the syndrome of tuberous sclerosis (TS) (like any other renal tumor)...but remember that the renal tumor most presenting in TS is: angiomyolipoma

- Large size and clinicoradiologically nondistinguishable from malignant tumors...so nephrectomy is needed...and to avoid spontaneous hemorrhage
Oncocytoma, morphology
Malignant kidney tumors, clear cell renal cell carcinoma

• The most common...65% of renal cancers

• Most are sporadic...also familial cases are present

• Seen in 40-60% of von Hippel-Lindau (VHL) disease...autosomal dominant
  ...hemangioblastomas of the cerebellum and retina
  ...hundreds of bilateral renal cysts
  ...bilateral, often multiple, clear cell carcinomas

*In VHL disease, the second allele is lost by somatic mutation
VHL gene product (VHL protein)

• Degrades (inhibits) HIFs (hypoxia-induced factors)

• HIFs are transcription factors that induce VEGF production (angiogenesis) and other genes that increase cell proliferation

Other genetic changes: loss-of-function mutations in SETD2, JARID1C, and UTX, all of which encode proteins that regulate histone methylation
Clear cell RCC, morphology

- Usually solitary and large

- Yellow to orange to gray-white cut surface, with prominent areas of cystic softening or of hemorrhage, either fresh or old

- Well-defined margins...sometimes infiltration is visible

- Sometimes, the tumor invades the renal vein and grows as a solid column within this vessel, sometimes extending in serpentine fashion as far as the inferior vena cava and even into the right side of the heart

- The cells may appear almost vacuolated or may be solid...according to glycogen and lipid amount

- The nuclei are usually small and round (low grade)

- The cells may form abortive tubules or may cluster in cords or disorganized masses

- The stroma is usually scant but highly vascularized
Malignant kidney tumors, papillary renal cell carcinoma

• 10-15% of renal cancers

• Frequently multifocal and bilateral

• Appear as early-stage tumors

• Sporadic and familial forms

• MET proto-oncogene (tyrosine kinase receptor for hepatocyte growth factor) increased activity...on chromosome 7

  ...in familial cases and a subset of sporadic cases

• From proximal tubular epithelial cells
Papillary renal cell carcinoma, morphology

• Grossly:
  ...hemorrhage, necrosis and cystic degeneration are common
  ...less vibrantly orange-yellow because of their lower lipid content
Malignant kidney tumors, chromophobe renal cell carcinoma

• The least common renal cancer (5%)

• Arise from intercalated cells of collecting ducts

• Unique in having multiple losses of entire chromosomes, including chromosomes 1, 2, 6, 10, 13, 17, and 21...extensive hypodiploidy

• Good prognosis
Chromophobe renal cell carcinoma, morphology

• The cells usually have clear, flocculent cytoplasm with very prominent, distinct cell membranes

• The nuclei are surrounded by halos of clear cytoplasm

• Ultrastructurally, large numbers of characteristic macrovesicles are seen
Renal cell carcinoma, clinical notes

• The most frequent presenting manifestation is hematuria, occurring in more than 50% of cases
  …macroscopic and intermittent on top of steady microscopic hematuria

• Less commonly: palpable mass

• Extrarenal effects:
  …fever & polycythemia
  …the polycythemia is seen in 5-10% due to erythropoietin from tumor cells

The triad of painless hematuria, a palpable abdominal mass, and dull flank pain is characteristic and alarming

Other paraneoplastic syndromes:
Hypercalcemia-hypertension-Cushing syndrome-feminization or masculinization

Metastasis mostly to: lungs & bones
Childhood malignant renal tumors, Wilms tumor

= nephroblastoma

• The most common primary tumor of the kidney in children

• Mostly between 2 & 5 years of age
Wilms, associated congenital malformations

1) WAGR syndrome (i.e., Wilms tumor, aniridia, genital abnormalities, and mental retardation)
   ...approximately one in three will go on to develop this tumor

2) Denys-Drash syndrome (DDS)
   ...extremely high risk (approximately 90% will have Wilms)
   ...gonadal dysgenesis and renal abnormalities

   • Both of these conditions are associated with abnormalities of the Wilms tumor 1 gene (WT1),
     located on 11p13
   • The WT1 gene is critical to normal renal and gonadal development

3) Beckwith-Wiedemann syndrome (BWS)
   ...enlargement of individual body organs (e.g., tongue, kidneys, or liver) or entire body segments
   (hemihypertrophy)
   ...enlargement of adrenal cortical cells (adrenal cytomegaly) is a characteristic microscopic feature

   In addition to Wilms tumors, patients with BWS also are at increased risk for the development of hepatoblastoma,
   adrenocortical tumors, rhabdomyosarcomas, and pancreatic tumors
Wilms tumor, morphology

- Large, solitary, well-circumscribed mass
- 10% are either bilateral or multicentric at the time of diagnosis
- Soft, homogeneous, and tan to gray, with occasional foci of hemorrhage, cystic degeneration, and necrosis
- Nephrogenic rests
  - can be found adjacent to tumor
  - precursor lesions
  - a clue for risk of developing Wilms also in the contralateral kidney

Triphasic combination

- Blastemal component (small round blue cells)
- Abortive tubules or glomeruli
- Stromal cells

5% of tumors contain foci of anaplasia (cells with large, hyperchromatic, pleomorphic nuclei and abnormal mitoses)
...acquired TP53 mutation & resistance to chemotherapy

Elsevier. Kumar et al. Robbins basic pathology 9th
Wilms tumor, clinical notes

• Palpable abdominal mass incidentally found by parents...may extend across the midline and down into the pelvis

• Fever

• Hypertension

• Occasionally intestinal obstruction

- Prognosis is very good
  - Diffuse anaplasia is worse than focal one
  - Extrarenal spread is worse
Urinary bladder cancer

• 7% of cancers and 3% of cancer deaths in the United States

• 90% are urothelial carcinomas

• More common in:
  ...males
  ...old adults (80% are between 50 & 80 years of age)
  ...smokers
  ...industrialized countries

• Schistosomiasis & chronic inflammation...squamous cell carcinoma

• Adenocarcinoma...urachal remnants & on top of intestinal metaplasia
Urinary bladder cancer, pathogenesis

• Superficial papillary urothelial carcinoma: p53 mutation is a late event...associated with invasion

• Carcinoma in situ: p53 is an early event and so: high risk of invasion

• FGFR3 & RAS...more in superficial tumors

• p53 & RB...more in invasive tumors
Transitional cell carcinoma in situ

- Commonly is multifocal and sometimes involves most of the bladder surface or extends into the ureters and urethra.

- Without treatment, 50% to 75% of CIS cases progress to muscle-invasive cancer.
Urinary bladder cancer, grading

WHO/ISUP grading

(1) Papilloma...not cancer
(2) papillary urothelial neoplasm of low malignant potential (PUNLMP)
(3) low-grade papillary urothelial carcinoma
(4) high-grade papillary urothelial carcinoma
Bladder cancer, clinical notes

• Intermittent painless gross hematuria

• Recurrences are common

...more with:

Tumor size, stage, grade, multifocality, mitotic index, and associated dysplasia and/or CIS in the surrounding mucosa

Recurrences are common at different sites and with higher grades

Treatment: surgery & immunotherapy
...follow up by cytology

Radical cystectomy for:
(1) Tumor invading the muscularis propria
(2) CIS or high-grade papillary cancer refractory to BCG
(3) CIS extending into the prostatic urethra and down the prostatic ducts, where BCG cannot contact the neoplastic cells
Thank You