Renal tumors

دکتر بهزاد لطفی
استادیار دانشگاه علوم پزشکی تبریز

History

- First nephrectomy: 1861
- Harris: 1882 : 100 nephrectomies
- Grawitz: 1883: Adrenal rest origin □ corrected by: Albarran & Imbert
- Radical nephrectomy: 1960s
- The incidence of RCC: increasing
- Mortality rate: high

Classification

- Malignant
- Benign
- Inflammatory

Classification

Malignant:

- **RENAL CELL CARCINOMA (RCC)**
  - Clear cell RCC
  - Multilocular cystic clear cell renal cell neoplasm of low malignant potential
  - Papillary RCC
  - Chromophobe RCC
  - Hybrid oncocytic chromophobe tumor
  - Carcinoma of the collecting ducts of Bellini
  - Renal medullary carcinoma
  - MiT family translocation RCC
  - Mucinous tubular and spindle cell carcinoma
  - Tubulocystic RCC
  - Acquired cystic disease–associated RCC
  - Clear cell (tubulo) papillary RCC
  - Hereditary leiomyomatosis RCC syndrome–associated RCC
  - RCC, unclassifed

Classification

- **UROTHELIUM-BASED CANCERS**
  - Urothelial carcinoma
  - Squamous cell carcinoma
  - Adenocarcinoma

- **SARCOMAS**
  - Leiomyosarcoma
  - Liposarcoma
  - Other sarcomas
- **NEPHROBLASTIC TUMORSa**
  - Nephrogenic rests
  - Nephroblastoma (Wilms tumor)
  - Cystic partially differentiated nephroblastoma

Classification

- **CARCINOMA ASSOCIATED WITH NEUROBLASTOMA Neuroendocrine Tumors**
  - Carcinoid (low-grade neuroendocrine tumor)
  - Neuroendocrine carcinoma (high-grade neuroendocrine tumor)
  - Primitive neuroectodermal tumor
  - Neuroblastoma
  - Pheochromocytoma

- **Hematopoietic and Lymphoid Tumors**
  - Lymphoma
  - Leukemia
  - Plasmacytoma

  Germ Cell Tumors
  - Teratoma
  - Choriocarcinoma

- **METASTASIS**

- **INVASION BY ADJACENT NEOPLASM**

Classification

Benign

- **CYSTIC LESIONS**
  - Simple cyst
  - Hemorrhagic cyst

- **SOLID LESIONS**
  - Angiomyolipoma
  - Oncocytoma
  - Papillary adenoma (renal adenoma)
  - Metanephric tumors (adenoma, adenofibroma, stromal tumor)
  - Congenital mesoblastic nephroma
  - Cystic nephroma/mixed epithelial stromal tumor
  - Reninoma (juxtaglomerular cell tumor)
  - Renomedullary interstitial tumor
  - Leiomyoma
  - Fibroma
  - Hemangioma
  - Lymphangioma
  - Schwannoma
  - Solitary fibrous tumor

Classification

Benign

- **VASCULAR LESIONS**
  - Renal artery aneurysm
  - Arteriovenous malformation
- **PSEUDOTUMOR**
- **INFLAMMATORY**
  - Abscess
  - Focal pyelonephritis
  - Xanthogranulomatous pyelonephritis
  - Infected renal cyst
  - Tuberculosis
  - Rheumatic granuloma

Imaging and Clinical Risk Stratifcation of Renal Masses

Models and nomograms

- Predict the likelihood of malignancy
- Generally in the range 0.55 to 0.65

The strongest predictors of malignancy

- male sex
- increasing tumor size

Imaging and Clinical Risk Stratifcation of Renal Masses

- Sex:
  - Men: **threefold** increased risk of malignancy compared with women.
  - Although benign histology is more common in women, RCC still predominates in both genders.

Imaging and Clinical Risk Stratifcation of Renal Masses

- Size:
  - The likelihood of malignancy increases (**1.3 per cm**) of tumor diameter.
  - Tumors smaller than 1 cm: 46% benign - 2% high-grade RCC
    Tumors larger than 7 cm: 6% benign - 58% high-grade RCC
  - Less than 2% of patients with tumors 4 cm or smaller had or developed metastatic disease

RCC

- **Incidence**
  - 2-3% of all adult malignancies
  - The most lethal of the common urologic cancers
  - **16** new cases per 100,000 population per year, with a **male-to-female** predominance of **1.9 to 1**
  - Disease of **older adults** (55 and 75 years of age)
  - Diagnosis of renal cancer has increased more rapidly in **<40** years of age than any other age group
  - The incidence and death rates are about 50% lower in Asian-American
  - Majority of cases of RCC are sporadic; **4% to 6% : familial**

Imaging and Clinical Risk Stratifcation of Renal Masses

- The incidence of RCC has increased since the 1970s by an average of 3% per year (use of ultrasonography and CT)
- incidentally discovered: ↑
- localized tumors: ↑
- 5-year survival: improved for patients with this stage of disease

- steadily **increasing mortality** rate from RCC per unit population: since the 1980s (all ethnic -groups and both genders)

Imaging and Clinical Risk Stratifcation of Renal Masses

- **Childhood renal tumors: 7% of all pediatric cancers**
- **RCC is relatively uncommon in this population**
- 90% of renal tumors in children: Wilms tumors or nephroblastomas
- RCC representing only 1% to 6%

- RCC = Wilms tumor during the **second decade** of life.

- Mean age for RCC in children is 8 to 9 years, boys = girls.
- RCC in children and young adults is more likely to be **symptomatic**, locally **advanced**, **high grade**, and of **unfavorable histologic** subtypes

Etiology

- **Tobacco exposure**
- **Relative risks: 1.4 to 2.5**
- All forms of tobacco use
- Risk increases with cumulative dose or pack-years
- Relative risk is directly related to duration of smoking
- begins to fall after cessation
- Tobacco use accounts for 20% to 30% of cases of RCC in men and 10% to 20% in women

Etiology

Obesity

- Increased relative risk of **1.07** for each additional unit of body mass index

- RCC is more prevalent in patients with higher BMI
- Increased BMI is associated with lower stage RCC at presentation, a so-called "**obesity paradox**"
- Potential mechanisms:
  - increased insulin-like growth factor-1 expression
  - increased circulating estrogen levels
  - increased arteriolar nephrosclerosis
  - local inflammation

Etiology

- **Hypertension**
- Third major causative factor for RCC
- Diuretics and other antihypertensive medications have also been implicated, particularly for papillary RCC
- It is the underlying disorder, **hypertension**, rather than the treatment that increases the risk of RCC
- The proposed mechanisms:
  - hypertension-induced renal injury
  - inflammation or metabolic or functional changes in the renal tubules that may increase susceptibility to carcinogens

Etiology

- In animal models
  - Viruses
  - lead compounds
  - more than 100 chemicals such as aromatic hydrocarbons

No specific agent has been definitively established as causative in human RCC

Increased relative risks for RCC:

workers in the metal, chemical, rubber, and printing industries

those exposed to asbestos or cadmium

but the data are not particularly convincing

Etiology

- RCC is more common among individuals with **low socioeconomic** status and urban background

- The typical modern **Western diet**, increased intake of **dairy products**, and increased consumption of **coffee** or **tea** have been associated with RCC

- A **family history** of RCC: relative risk of **2.9** for individuals with a first- or second-degree relative with RCC

Etiology

- Regular usage of **NSAIDs** was associated with a relative risk of 1.51
- aspirin and acetaminophen were not associated with increased risk
- Retroperitoneal **radiation** therapy: appears to be a risk factor for RCC, although the relative risks are low
- Patients with **end-stage renal disease**

Familial Renal Cell Carcinoma and Molecular Genetics

- ***von Hippel-Lindau Disease,* VHL *Gene, and Genetics of Clear Cell RCC***

  - RCC
  - Pheochromocytoma
  - retinal angiomas
  - hemangioblastomas of the brainstem, cerebellum, or spinal cord

- **RCC** develops in about **50**% of patients with VHL disease
- early age at onset (often in the third to fifth decades of life)
- Bilateral
- Multifocal

Familial Renal Cell Carcinoma and Molecular Genetics

Hereditary Papillary Renal Carcinoma Syndrome

Autosomal dominant

Median age at diagnosis: **45 years**
Most patients developed **multifocal** and **bilateral** papillary RCC
Type 1 papillary RCC
Typically do not develop tumors in other organ systems

Mutations: the tyrosine kinase domain of c-MET

Tumors in HPRC tend to be less aggressive

Familial Renal Cell Carcinoma and Molecular Genetics

Hereditary Leiomyomatosis and Renal Cell Carcinoma

cutaneous and uterine leiomyomas and type 2 papillary RCC

Mean age at diagnosis: early 40s.

Often **solitary** and **unilateral**, more **aggressive** than other forms of familial RCC.

Mutation: fumarate hydratase *(FH)* gene

Prompt **surgical management** of the renal tumors is recommended (in contrast to most of the other familial syndromes of RCC)

Familial Renal Cell Carcinoma and Molecular Genetics

Succinate Dehydrogenase Renal Cell Carcinoma

Shares features with HLRCC

Affected individuals present with **bilateral**, **multifocal**, **early onset** (<40 years) renal tumors

often along with pheochromocytomas and head and neck paragangliomas.

Good prognosis for a subset of patients with SDH-RCC, particularly when **low-grade** features predominate.

Tumors with high-grade, coagulative necrosis, or sarcomatoid features are more likely to behave aggressively

Familial Renal Cell Carcinoma and Molecular Genetics

Birt-Hogg-Dube Syndrome

Birt-Hogg-Dube (BHD) syndrome:

- cutaneous fibrofolliculomas
- lung cysts
- spontaneous pneumothoraces
- renal tumors primarily derived from the distal nephron

The renal tumors typically include chromophobe RCC, oncocytomas, and hybrid oncocytic tumors

when they occur they are often bilateral and multifocal

Familial Renal Cell Carcinoma and Molecular Genetics

Average : 50 years

Most renal tumors in BHD syndrome have limited biologic aggressiveness

Mutation: folliculin

Familial Renal Cell Carcinoma and Molecular Genetics

Cowden Syndrome

mutations of PTEN tumor suppressor gene
Termed PTEN hamartoma tumor syndrome

50% lifetime risk of female breast cancer
34% lifetime risk of RCC
10% lifetime risk of epithelial thyroid carcinoma

Greater than 31-fold increased risk of RCC
should be screened with CT or MRI for RCC
RCC in this syndrome is most often of papillary histology

Familial Renal Cell Carcinoma and Molecular Genetics

Tuberous Sclerosis Complex

autosomal dominant disorder

include AML
cortical tubers
subependymal nodules or subependymal giant cell astrocytomas (SEGA)
pulmonary lymphangioleiomyomatosis (LAM)
cardiac rhabdomyomas
facial angiofbromas

Renal AML are typically multifocal, bilateral, and often large, occasionally requiring angioembolization or partial nephrectomy (PN) to treat or prevent bleeding from larger (>5 cm) tumors.

Mutations: TSC1 or TSC2

Familial Renal Cell Carcinoma and Molecular Genetics

Microphthalmia-Associated Transcription Factor–Associated Cancer Syndrome

Mutation: microphthalmia-associated transcription factor (MiTF) □ greater than **5-fold increased risk** of **melanoma** and **RCC** in affected individuals.

MiTF regulates HIF-1α

پایان