NOTES
RENAL CANCER

GENERALLY, WHAT IS IT?

PATHOLOGY & CAUSES

- Abnormal cell growth → kidney mass (malignant/benign), caused by genetic mutation of tumor suppressor gene
- *Angiomyolipoma:* most common benign renal tumor
- *Renal cell carcinoma:* most common malignant renal tumor in adults
- *Wilms tumor:* most common malignant renal tumor in children

COMPLICATIONS

- Spontaneous hemorrhage, kidney highly vascular
- Malignant
  - Distant metastasis

SIGNS & SYMPTOMS

- Often asymptomatic initially
- Unilateral abdominal mass
- Flank pain, hematuria, systemic symptoms (e.g. fever, appetite loss)
- *Ectopic hormone production:* renin, erythropoietin (EPO), adrenocorticotropic hormone (ACTH), parathyroid hormone-related peptide (PTHrP) → paraneoplastic syndromes

DIAGNOSIS

DIAGNOSTIC IMAGING

CT scan/MRI/ultrasound

- See individual disorders

LAB RESULTS

- Tissue biopsy

TREATMENT

MEDICATIONS

- *Malignant:* chemotherapy

SURGERY

- *Malignant:* surgical resection

OTHER INTERVENTIONS

- *Angiomyolipoma:* embolization, surgery not suitable
- *Malignant:* radiotherapy

ANGIOMYOLIPOMA

osms.it/angiomyolipoma

PATHOLOGY & CAUSES

- Most common benign kidney tumor
- Also found in liver (common), reproductive organs (rare)
- Made of blood vessels (angio), smooth muscle (myo), fat (lipo)
- *Type of hamartoma:* cellular tumor, disorganized architecture
- Genetic mutation in tumor suppressor gene tuberous sclerosis 1 (*TSC1*) for hamartin/ tuberous sclerosis 2 (*TSC2*) for tuberin
  - Usually sporadic
  - Associated with tuberous sclerosis (multiple, bilateral angiomyolipomas)
- *Perivascular epithelioid cell tumor family (PEComa):* epithelial-like cells around blood vessels on microscopy
- More common in right kidney

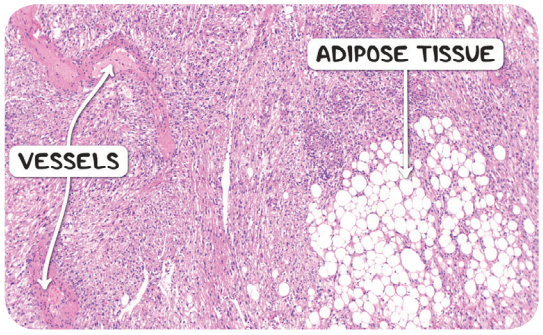

Figure 119.1 Histological appearance of an angiomyolipoma. The tumor is composed primarily of myoid cells with areas of mature adipose tissue and numerous vessels.

RISK FACTORS

- Individuals who are biologically female
- Tuberous sclerosis

COMPLICATIONS

- Spontaneous hemorrhage risk
  - Dysregulated angiogenesis → weak blood vessels → aneurysms

SIGNS & SYMPTOMS

- *Small:* often asymptomatic
- *Large:* mass effect on healthy kidney tissue → chronic kidney disease
- *Extreme cases:* end-stage renal disease (dialysis needed)

DIAGNOSIS

DIAGNOSTIC IMAGING

Ultrasound

- Fat appears hyperechogenic

MRI

- Small lesions with wedge-shaped pattern which grow outward as tumor enlarges; fat appears bright on T1-weighted images, intermediate-dark on T2-weighted images

LAB RESULTS

- Image-guided percutaneous needle biopsy and histological analysis

TREATMENT

- Surgery unlikely to be useful, highly vascular tumors with high bleeding risk

OTHER INTERVENTIONS

Embolization

- Synthetic emboli released into tumor vessels → vessel occlusion → tumor necrosis → tumor shrinkage, haemorrhage less likely
- Adverse effects
  - Postembolization syndrome, fever, flank pain, malaise

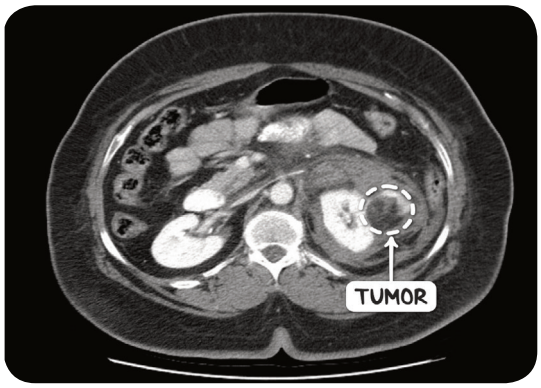

Figure 119.2 An abdominal CT scan in the axial plane demonstrating an angiomyolipoma of the left kidney.

RENAL CELL CARCINOMA (RCC)

osms.it/renal-cell-carcinoma

PATHOLOGY & CAUSES

- Most common malignant kidney tumor in adults
- "Silent cancer," may be asymptomatic until late stage, poor prognosis
- *Spontaneous:* solitary upper pole tumors
- *Inherited:* young adults; multiple, bilateral tumors
  - *Von Hippel–Lindau (VHL) disease:* inherited RCC

TYPES

Clear cell carcinoma

- Epithelial cells in proximal convoluted tubule in renal cortex
  - *Polygonal epithelial cells:* clear cytoplasm, full of carbohydrate, fat
  - Fat in tumor cells → yellow tumor

Papillary carcinoma

Chromophobe carcinoma

RISK FACTORS

- Individuals who are biologically male
- Advanced age
- Lifestyle factors (e.g. smoking, obesity)
- Hypertension
- Environmental exposures (e.g. asbestos, heavy metals)
- Existing kidney disease
  - Acquired renal cystic disease, long-term dialysis, renal transplant
- Genetic mutations in chromosome 3p common in spontaneous, inherited

STAGING

- Tumor, nodes, metastasis (TNM), scored 0–4
  - *T:* size, sites invaded (e.g. renal vein)
  - *N:* degree of spread to retroperitoneal lymph nodes
  - *M:* presence of distant metastasis

SIGNS & SYMPTOMS

- Flank pain
- Hematuria
- Palpable mass in abdomen/lower back
- Systemic symptoms (e.g. fever, weight loss, night sweats, weakness, malaise)
- Ectopic hormone secretion → paraneoplastic syndromes
  - *Erythropoietin:* polycythemia → hyperviscosity symptoms
  - *Renin:* hypertension
  - PTHrP → hypercalcemia
  - ACTH → cortisol release → Cushing syndrome
- Left varicocele (testicular swelling)
  - RCC in left kidney → obstructs left renal vein → drains left testicular vein
- Lung/bone presentations
  - RCC invades renal vein/inferior vena cava (IVC) → quick metastasis

DIAGNOSIS

DIAGNOSTIC IMAGING

- Some of newly diagnosed individuals
  - Metastases on radiology, esp. lungs/bones

CT scan of chest/abdomen with contrast

- CT scan chest to evaluate metastasis

Ultrasound

TREATMENT

- Chemotherapy/radiotherapy resistant

MEDICATIONS

- Immunomodulatory drugs
  - Activate immune system to attack tumor; interferon, interleukin-2 (IL-2), monoclonal antibodies (nivolumab)
- Molecular targeted drugs
  - Inhibit growth receptors; everolimus, temsirolimus

SURGERY

Resection

- If localized

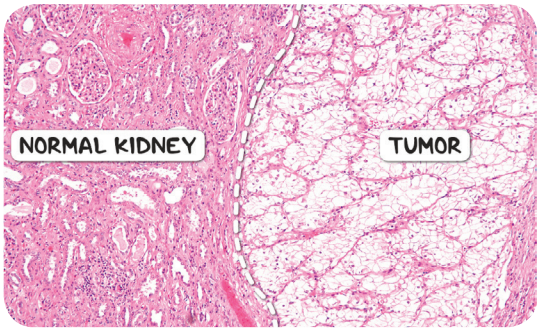

Figure 119.3 Histological appearance of renal cell carcinoma. The tumor is of the clear cell subtype.

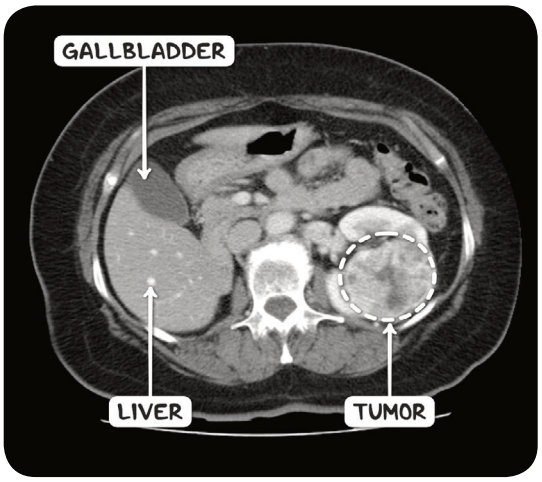

Figure 119.4 A CT scan in the axial plane demonstrating a renal cell carcinoma (RCC) of the left kidney.

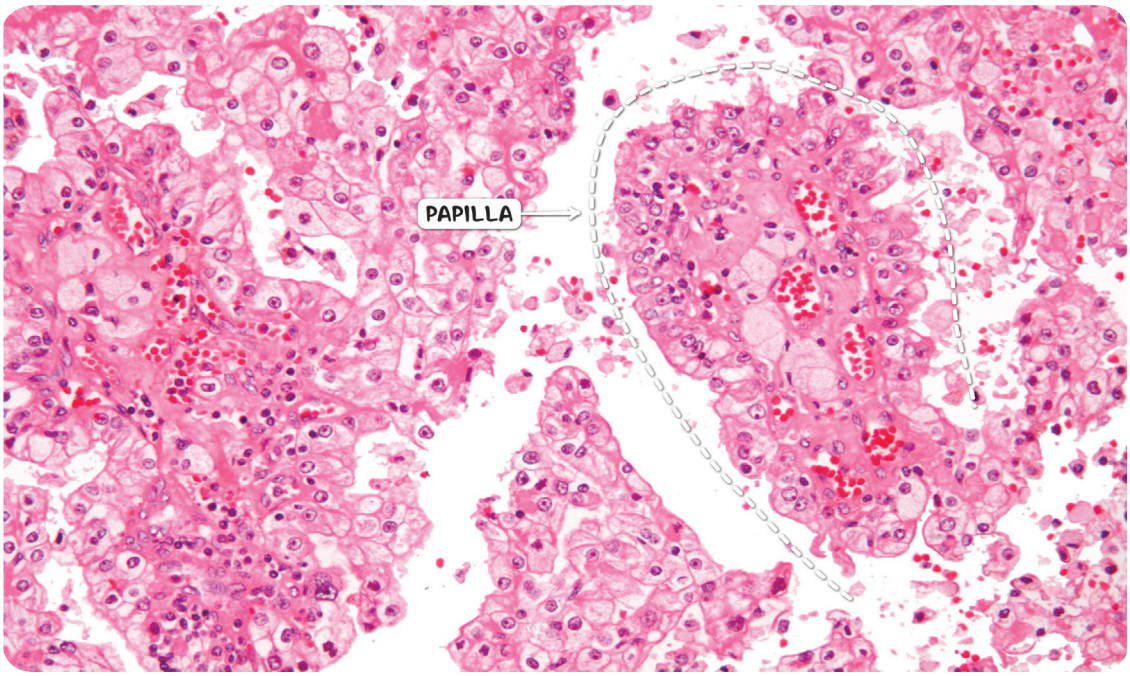

Figure 119.5 Histological appearance of a papillary renal cell carcinoma. The tumor is composed of numerous clusters of malignant cells arranged around fibrovascular cores.

WAGR SYNDROME

osms.it/WAGR-syndrome

PATHOLOGY & CAUSES

- Genetic disorder affecting children predisposed to Wilms tumor
  - Wilms' tumor
  - Aniridia (total/partial absence of iris)
  - Genitourinary anomalies
  - Intellectual disability (previously mental Retardation)
- Sporadic mutation → autosomal dominant inheritance

TYPES

WAGRO (O for obesity) subtype

- Additional deletion of brain-derived neurotrophic factor (*BDNF*) gene → obesity

CAUSES

Contiguous gene deletion syndrome

- Heterozygous deletion of several genes beside each other on p arm of chromosome 11
  - Deletion of WT1 → Wilms' tumor, genitourinary malformations
  - Deletion of PAX6 protein → aniridia
  - Genetic basis for intellectual disability unclear

COMPLICATIONS

- Streak ovaries in individuals who are biologically female; gonadoblastoma

SIGNS & SYMPTOMS

- Few patients with WAGR exhibit all symptoms
- Wilms' tumor (nephroblastoma)
  - Only ⅓ of individuals with WAGR
- Aniridia (since birth)
  - Most common feature
  - Blurry vision, photophobia
- Genitourinary anomalies
  - *In individuals who are biologically male:* cryptorchidism (undescended testes), hypospadias (urethra opens onto underside of penis, not tip)
  - *In individuals who are biologically female:* streak ovaries (undeveloped ovaries; increased risk of gonadoblastoma)
  - Ambiguous genitalia
- Intellectual disability
  - Not always present, often associated with autism/attention deficit hyperactivity disorder (ADHD)
- Other features
  - Progressive kidney failure
  - Growth retardation, small head size, obesity
  - Cataracts, glaucoma, nystagmus

DIAGNOSIS

LAB RESULTS

Fluorescence in situ hybridization (FISH)

- DNA mixed with fluorescently-labeled DNA probe
- Genetic deletion on one chromosome → only one bright spot

TREATMENT

- Each symptom addressed independently

MEDICATIONS

Chemotherapy

- Wilms' tumor

SURGERY

Nephrectomy

- Wilms' tumor

OTHER INTERVENTIONS

Radiotherapy

- Wilms' tumor

Tinted lenses

- Photophobia from aniridia

Medical surveillance

- Wilms' tumor
  - Renal ultrasound, blood pressure
- Genitourinary
  - Pelvic US for gonadoblastoma in individuals who are biologically female

WILMS' TUMOR

osms.it/wilms-tumor

PATHOLOGY & CAUSES

- Most common malignant kidney tumor in children, typically ages 2–5
- AKA nephroblastoma (metaphrenic blastemal cells)
- Wilms' tumor typically appears in otherwise healthy children
  - Beta-catenin mutations in 10% of sporadic Wilms' tumors
- Tumors composed of metanephric blastemal cells
  - Abortive/partly-developed structures of nephron
  - *Triphasic blastoma:* tumor composed of blastemal, stromal, epithelial cells

CAUSES

Genetic mutations

- Chromosome 11, short arm p, region 1, band 3
- Loss-of-function mutation in *Wilms' Tumor 1* (*WT1*); may be part of wider developmental syndrome with additional abnormalities
  - *WAGR syndrome:* genetic disorder affecting children predisposed to Wilms' tumor
  - *Denys–Drash syndrome:* *WT1* mutation → Wilms' tumor, early-onset nephrotic syndrome, male pseudohermaphroditism
- Wilms' Tumor 2 (*WT2*) mutation → developmental syndromes (e.g. Beckwith–Wiedemann syndrome)
- Majority of cases not associated with *WT1*/*WT2* mutations, developmental syndromes

RISK FACTORS

- Ages 2–5
- *Developmental syndromes:* WAGR, Beckwith–Wiedemann, Denys–Drash
- Family history of Wilms' tumor

COMPLICATIONS

- Distant metastasis to brain, lungs, liver, bones
- Paraneoplastic syndrome
  - Renin secretion → high blood pressure → decreased kidney function

SIGNS & SYMPTOMS

- Large, palpable, unilateral flank mass (bilateral tumors)
- Abdominal pain
- Constipation (due to kidney hemihypertrophy)
- Hematuria
- Systemic symptoms (e.g. loss of appetite, fever, nausea, weakness)
- Renin secretion → hypertension

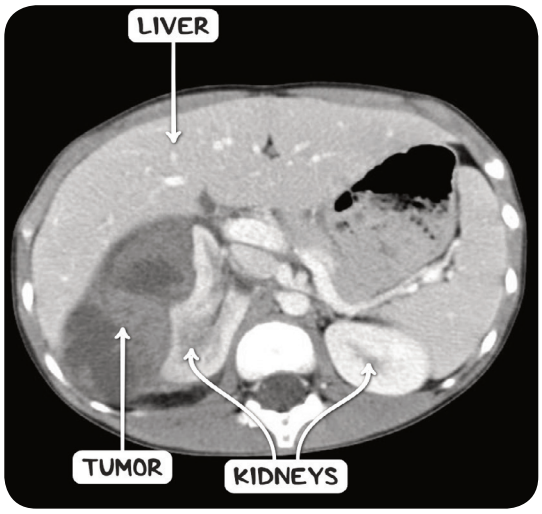

Figure 119.6 A CT scan in the axial plane demonstrating a Wilms' tumor of the right kidney.

- Developmental syndromes
  - *Denys–Drash syndrome:* Wilms' tumor, early-onset nephrotic syndrome, male pseudohermaphroditism
  - *Beckwith–Wiedemann syndrome:* Wilms' tumor, macroglossia, organomegaly, hemihypertrophy

DIAGNOSIS

- Never palpation
  - Risk of tumor rupture, metastasis

Abdominal ultrasound

- Presence of mass, renal vein infiltration

Abdominal contrast-enhanced CT scan/MRI

- Tumor staging; lymph node metastasis penetration of capsule

Chest CT scan

- Detects metastasis

LAB RESULTS

- Image-guided percutaneous needle biopsy and histologic analysis

TREATMENT

- Depends on genetic mutations, tumor aggressiveness, unilateral/bilateral

MEDICATIONS

- Chemotherapy

SURGERY

- Nephrectomy

OTHER INTERVENTIONS

- Radiation
  - Used with care, risk of secondary cancers

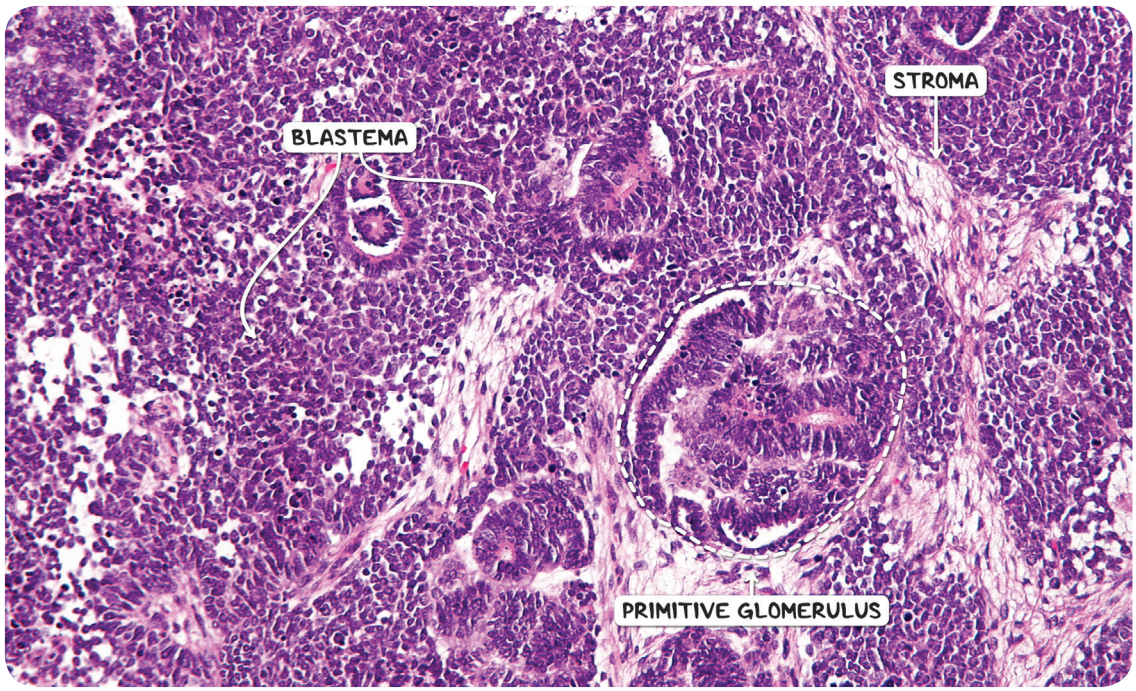

Figure 119.7 Histological appearance of Wilms' tumor. The tumor is triphasic, composed of blastema, stroma and immature epithelial elements (glomeruli and tubules).

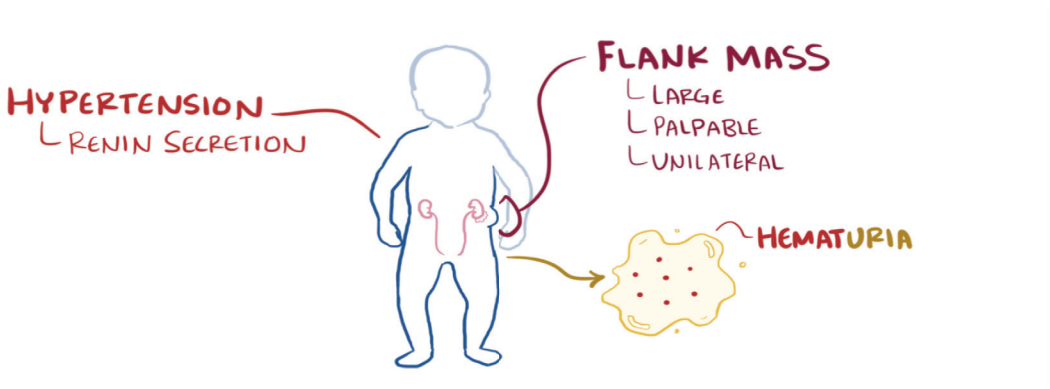

Figure 119.9 Illustration of the signs and symptoms of Wilms' tumor, which most commonly affects children who were otherwise healthy.

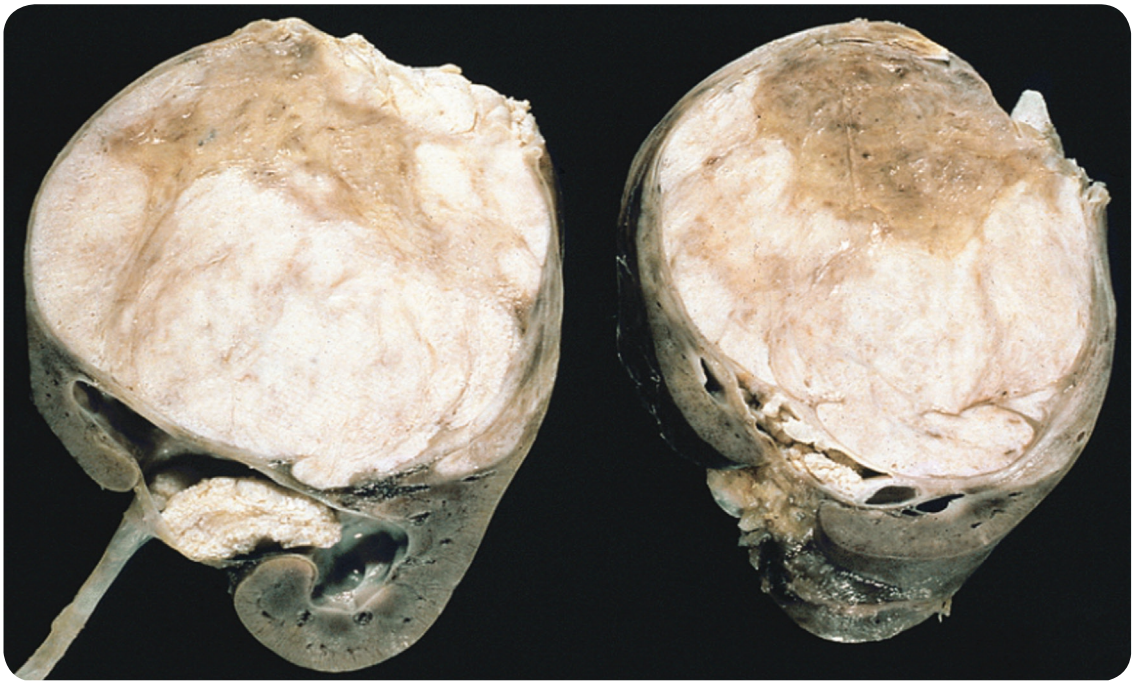

Figure 119.8 Gross pathological appearance of a nephrectomy specimen in a patient with Wilms' tumor.