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TUMORS OF KIDNEY
A. **Benign renal neoplasm include**

1) **Angiomyolipoma** found in 20-25% of patients with tuberous sclerosis, is a benign tumor composed of a mixture of fat, blood vessels, and smooth muscle tissue. These tumors are of significance because clinically and radiologically, they often are misdiagnosed as carcinomas.

• **Tuberous sclerosis** disease characterized by lesions of the cerebral cortex → epilepsy, mental retardation as well as a variety of skin abnormalities. (See 1413 – 1414)

2) **Mesoblastic nephroma** (benign nephroblastoma) is a congenital hamartoma that commonly is confused with Wilm’s tumor. Most mesoblastic nephromas are diagnosed in the early months of life. It has no malignant proportions renal papillary.
3) Adenoma. Traditionally, this tumor has been defined as a renal tubular epithelial neoplasm that is 0.5cm less than 2.5 cm in size. Most of well-circumscribed, yellow these lesions are associated with benign course, found in 7-22% of autopsy.

4) Renal fibroma or hamartoma (Renomedullary interstitial tumor <1 cm, smell of gray white, firm found in the pyramid of the kidney.

5) Oncocytoma:– Epithelial, composed of large, eosinophilic cells having small, round, benign nuclei with large nucleoli. It is thought to arise from the intercalated cells of collecting duct. It account for 15% of surgically resected neoplasm. This esophilia is due to accumulation of cytoplasmic mitochondria. They can achieve large size upto 12cms, well encapsulated. There are some familial that these tumor is multi centeric rather than solitary.
• **B. Malignant renal neoplasm include**

• 1) **Wilm’s tumor** (nephroblastoma) is a mixed neoplasm composed of metanephric blastema and its stromal and epithelial derivatives at variable stages of differentiation. Wilm’s tumor is the most common malignancy of renal origin in children.

  • **a) Etiology and pathogenesis.** Very recent work has located a tumor suppressor gene on chromose 11.

  • **b) Epidemiology.** Wilm’s tumor occurs with equal frequency in both sexes. The tumors appear at any age, but most cases are diagnosed before age 5, with the peak incidence in the second year of life. Familial cases included those in monozygous twins.
c) Clinical features.

1) The most common presenting sign is an abdominal mass, which is seen in almost 90% of patients. Other findings include hypertension, nausea, vomiting, hematuria, and occasionally leg edema. Arteriography reveals poorly vascularized tumors.

2) Nephroblastomas may be combined with several other congenital malformations, such as sporadic aniridia, microcephaly, mental retardation and spina bifida. Another associated condition is hemihypertrophy of the body.
Pathology. Wilm’s tumor can be unilateral, bilateral, or multifocal in its involvement of the same kidney.

1) Macroscopic appearance. The tumors are large, well delineated and well encapsulated. On cut section, they often appear grayish white to tan, with areas of hemorrhage and occasional cystic changes. The renal pelvis is compressed in Wilm’s tumor; and local spread into the perirenal fat, renal vein, and hilar nodes is common.

2) Microscopic appearance. The lesions are characterized by formation of abortive or embryonic glomerular and tubular structures surrounded by an immature spindle cell stroma. The epithelial elements may be scanty or predominantly tubular. The stroma may show different elements, such as skeletal muscle, cartilage, and fat.
e) **Metastases.** The renal hilar and paraaortic lymph nodes are frequent sites of metastatic spread. The lungs, liver, adrenal gland, diaphragm, retroperitoneum and bones also are commonly involved. The presence of metastases usually is discovered within 2 years after diagnosis of the primary tumor.

f) **Prognosis.** Several factors influence the prognosis for patients with Wilm’s tumor.

- 1) **Age of patient.** Patient under age 2 have a good 5-year survival rate.
- 2) **Extent of disease.** Capsular permeation, venous extension and distant metastases are associated with a poor prognosis.
- 3) **Microscopic features.** Marked tubular and glomerular differentiation is associated with a good prognosis. Unfavorable histology includes nuclear pleomorphism and abnormal mitotic figures.

**g) Treatment** consists of surgical resection of the lesion and systemic chemotherapy, supplemented by radiation of the affected area.
2. Renal cell carcinoma account for 1-3% of visceral neoplasm and 85% of renal cancer.; (hypernephroma) is an adenocarcinoma that arises from the proximal or distal convoluted tubule.

- Etiology and pathogenesis. The cause of these tumors remains obscure, but they have been produced in laboratory animals using chemical, physical and viral agents exposure to asbestos, heavy metals, petroleum products, hypertension, estrogen therapy. It accounts for 4% of all cancer, familial incidence account for 4% of renal cancer association with Von-Hippel Lindau syndrome surface. Where 1/2 – 2/3 of patient with V.H.L. characterized by haemangioblastoma of cerebellum and retina, renal cysts and bilateral and multiple RCC.

- Hereditary (Familial RCC) confined to kidney without manifestation of VHL.

- Hereditary papillary carcinoma autosomal dominant manifested by multiple bilateral tumor with papillary histology.
b) Epidemiology: Sporadic, ↑ in smoker either cigarette or cigar. Most cases occur in adults, with the peak C.R.F, acquired cystic disease, incidence around the sixth decade of life. Renal cell carcinoma affects men and women in an approximate ratio of 2:1. Usually, the tumor is not discovered until it is in advanced stage.

c) Clinical features include the characteristic triad of (a) haematuria (b) costovertebral pain and a palpable flank mass although this complete triad is found in only a minority of patients. Other symptoms include fever, fatigue and anorexia. Haematuria is the most reliable but it is usually intermittent and microscopic, thus tumor can remain silent till it reach large size and metastasis.
d) Diagnosis

1) Laboratory studies. Approximately 5% of affected patients have polycythemia with erythrocytosis. Other laboratory findings include leukocytosis, thrombocytosis, hypercalcemia and an elevated erythrocyte sedimentation rate. Anemia is present up to 25% of patients with these neoplasms.

Polycythemia, hypercalcemia, hypertension, hepatic dysfunction, feminization or masculinization, cushing syndrome, eosinophilia, leukaemoid reaction and amyloidosis.

They tend to metastasize widely before giving rise to any local symptom or sign.

2) Arteriography. A selective arteriogram of the kidney demonstrates a mass with increased and irregularly branching vessels.
• **Pathology.** Renal cell carcinoma may
  affect either kidney and has no predilection for a specific location within the organ.

• **1) Macroscopic appearance.** The tumor protrudes from the renal cortex as an irregular bosselated mass, which, on cut section, has a characteristic yellow-orange appearance. Hemorrhage and necrosis are commonly seen. At the periphery of the tumor, the normal parenchyma is compressed, forming a pseudocapsule.

• **2) Microscopic appearance.** Several patterns can be seen, including papillary, tubular, granular, solid or sarcomatoid. However, most tumors are composed of clear cells with distinct cytoplasmic membranes, abundant cytoplasm and eccentric nuclei. The lesions are markedly vascularized, with little stroma between the cells, occasionally clusters of histiocytes and inflammatory cells are present. Renal cell tumors frequently show areas of pleomorphism and giant cells and thus, resemble different types of sarcomas.
• **Classification of RCC:**
  a. **Clear cell type:** Most common accounting of 70-80%. The cells will have clear or granular but not papillary.
  • They can be associated with VHL or in most cases, sporadic (95%).
  • 98% of cases whether sporadic familial or associated – VHL. There is loss of sequence on short arm of chromosome 3 due to deletion of (3P) or by unbalanced translocation (3;6, 3;8 3;11).
  • → loss of chromosome 3 spanning 3P12, 50 3P26 where VHL gene (3P25) is harbored.

b. **Papillary carcinoma** account for 10-15% characterized by papillary growth occurs as sporadic familial but not associated 3P deletion. The most common cytogenetic abnormalities are trisomy 7,16 & 17 & loss of y – in male in sporadic form while in familial form trisomy 7. It is multifocal origin unlike RCC clear type.
c. Chranophobe represent 5% - composed of prominent cell membrane and pale eosinophilic cytoplasm with halo around the nucleus. It exhibits multiple chromosome losses and extreme hapodiploidy.

d) Metastases. Renal cell carcinoma metastasized mainly through the bloodstream although lymphatic spread also is possible. Approximately 95% of affected patients have evidence of metastatic spread at the time of death. The most commonly affected organs are the lungs, brain, bones, liver, adrenal glands, lymph nodes and contralateral kidney.
- **Urothelial Carcinoma of Renal Pelvis:**
- Represents 5-10% of primary renal tumor originating from the urothelium of the renal pelvis. They range from benign papilloma to invasive carcinoma. They become apparent early due to their frequeation with haematuria. They never become palpable unless they cause outlet obstruction → secondary hydronephrosis.
- They may occasionally be multiple, involving the pelvis, ureters, bladder.
- In 50% of renal pelvic tumors have pre-existing or concomitant bladder urothecal tumor. There is increased incidence of this tumor in patients with analgesic nephropathy.
- Infiltration to the wall of renal pelvis and calyces is common and for this reason they have poor prognosis where it is 50-70% for low grade superficial to 10% of high grade infiltration. See (1018 – 1019) (1028-1033)
e) **Prognosis.** Although spontaneous regression of renal cell carcinoma has been reported, these tumors generally are associated with a poor prognosis: 20% 10 year survival rate. The unfavorable prognosis is the result of both the aggressive nature of the tumor and its tendency to be silent until it reaches a large size, frequently having metastasized at the time of presentation.

f) **Treatment.** The treatment of choice is surgical resection of the lesion, with removal of adjacent lymph nodes. Radiation and chemotherapy have not proven to be successful treatment options.
• Malignant tumor of the urinary bladder
• 1. Transitional cell carcinoma of the urothelium has characteristic features that remain the same regardless of the tumor’s location along the urinary collecting system. These tumors typically are multifocal and tend to recur.
• a) Incidence. Malignant tumors of the urinary collecting system account for more than 10,000 deaths per year in the United States.
• b) Etiology. Urinary tract carcinomas, especially those involving the bladder, have been linked to environmental factors, such as industrial carcinogens (e.g., aniline dyes), metabolites of tryptophan, cigarette smoking, mechanical irritation (e.g., due to calculi or diverticuli), and parasites. The longer the duration of exposure, the greater the change that these tumors will develop.
• **c) Clinical features.** Patients experience painless hematuria.

• **d) Pathology.** On cytoscopic examination, the tumors may appear as papillary lesions or plaque-like ulcers. The region of the trigone in the bladder is the most common location. Histologically, the transitional cell epithelium is thickened, with an increased number of layers of cells, which show varying degrees of nuclear atypia and pleomorphism. The tumors are assigned one of three histologic grades, which are significant for estimating prognosis.
• 1) Grade I is composed of a central core of fibrovascular tissue covered by uniform transitional cells. Pleomorphism and mitoses are rare, and necrosis is absent. The epithelium is 7 to 10 cells thick.

• 2) Grade II tumors are characterized by persistence of the papillary configuration but more crowding of cells with enlargement and hyperchromatism of nuclei. The epithelium is 15 to 20 cells thick or more. The number of mitoses varies.

• 3) Grade III tumors have a sessile, cauliflower-like appearance. Necrosis and ulceration are frequent findings. The cell masses form groups; atypia and mitoses are abundant.
• e) Prognosis depends on the histologic grade and the stage of the disease. The more undifferentiated the tumor, the worse the prognosis. Carcinoma of the bladder can be staged according to the depth of penetration of the tumor into the bladder wall and for advanced disease by the location of metastases.
2. **Squamous cell carcinoma** of the urinary tract is rare, representing 5% of all bladder tumors.

a) **Epidemiology.** These tumors occur in persons living in geographic areas (such as Egypt) where close associations between parasitic infections (e.g., schistosomiasis) and carcinoma are known to occur.

b) **Pathology.** Grossly, the tumors appear as ulcerated and necrotic masses. Histologically, they are poorly differentiated, but areas of keratinization may be present.

c) **Prognosis.** Squamous cell cancers are associated with a poor prognosis.
These are normal term infant kidneys. Note the presence of fetal lobulations and the smooth cortical surfaces with some attached adipose tissue.
These fetal kidneys (from a gestation estimated at 25 weeks in the second trimester) demonstrate a normal cut surface. Note the pelvis and the calyces. Note the well-defined corticomedullary junctions.
This infant died soon after premature birth at 23 weeks gestation from pulmonary hypoplasia as a result of oligohydramnios. The oligohydramnios resulted from markedly diminished fetal urine output as a consequence of polycystic kidney disease. Note the bilaterally enlarged kidneys that nearly fill the abdomen below the liver. The histologic appearance in this case, coupled with the gross appearance, was consistent with autosomal recessive polycystic kidney disease (ARPKD).
Here is a cut section of a kidney with autosomal recessive polycystic kidney disease (ARPKD). Note that the cysts are fairly small but uniformly distributed throughout the parenchyma so that the disease is usually symmetrical in appearance, with both kidneys markedly enlarged. The recurrence risk for this disease is, of course, 25% because of the autosomal recessive inheritance pattern. Affected babies usually do not survive long. This disorder is linked to an abnormal fibrocystin protein produced by the PKHD1 gene.
Here is the microscopic appearance of autosomal recessive polycystic kidney disease (ARPKD). Note that the cysts fill most of the parenchyma, and it is hard to find glomeruli. Many of the cysts are elongated and radially arranged from the center of the kidney on the right, much like spokes on a wagon wheel.
You're right, this isn't kidney, but remember that autosomal recessive polycystic kidney disease also manifests with congenital hepatic fibrosis, as seen here in which a portal area is expanded with increased bile ducts radially arranged around the perimeter. The abnormal fibrocysin protein product of the mutated *PKHD1* gene affects liver and pancreas as well as kidney. The many dark clusters of cells in the hepatic parenchyma are islands of extramedullary hematopoiesis typical for fetal liver.
This is a multicystic dysplastic kidney. This condition must be distinguished from ARPKD because it occurs only sporadically and not with a defined inheritance pattern, though it is more common than ARPKD. The cysts of multicystic renal dysplasia are larger and more variably sized than those of ARPKD. Often, multicystic renal dysplasia is unilateral. If bilateral, it is often asymmetric. If bilateral, oligohydramnios and its complications can ensue, just as with ARPKD.
A multicystic dysplastic kidney (also known as cystic renal dysplasia) has been sectioned to reveal the variably sized cysts that replace the renal parenchyma. In this case, the disease was unilateral and presented in infancy as a mass lesion which was removed surgically. Even with one kidney, there is enough renal reserve capacity to live a normal life.
You may see references to polycystic kidney disease that include Potter's classification. Type I is RPKD, type II is multicystic dysplastic kidney, type III is dominant polycystic kidney disease (DPKD), and type IV is cystic change with congenital urinary tract obstructions.
The microscopic appearance of a multicystic dysplastic kidney (cystic renal dysplasia, or Potter type II) is characterized by large cysts lined by flattened cuboidal epithelium and an intervening parenchyma that is fibrotic with islands of bluish cartilage and rare glomeruli.
The contents of the chest and peritoneal cavity have been removed at autopsy here to reveal markedly bilaterally enlarged kidneys in the retroperitoneum in an adult who died from complications of chronic renal failure. This patient had autosomal dominant polycystic kidney disease (ADPKD).
The cut surfaces of these kidneys in a patient with ADPKD reveal that the parenchyma is replaced by large cysts. Note how large these kidneys are in relation to the normal sized transplanted kidney.
This kidney in a patient with ADPKD weighed 3 kilograms! This disease is inherited with an autosomal dominant pattern, so the recurrence risk in the family is 50%. The cysts are not usually present at birth, but develop slowly over time, so the onset of renal failure occurs in middle age to later adult life.
These adult kidneys are about normal in size but have a few scattered small cysts, none of which is over 2 cm in size. This is cystic change associated with chronic renal dialysis.
Cystic change resulting from long-term renal dialysis may rarely give rise to renal cell carcinoma. A large variegated mass is seen here on sectioning of a kidney that has large cysts arranged around the mass.
Simple renal cysts, as seen here, can also be multiple, but they are never as numerous as with polycystic change, and they do not predispose to chronic renal failure or to neoplasia. Such simple cysts become more common as persons become older.
In the bladder removed surgically and opened here can be seen a large urothelial carcinoma. These neoplasms arise from the urothelium. A presenting sign can often be hematuria. Cytologic examination of urine can reveal malignant cells shed from the surface of the neoplasm. Cystoscopy can be performed and biopsies taken.
This bladder was removed surgically from a male who had a long history of smoking. He had presented with hematuria. The opened bladder reveals masses of a neoplasm that histologically proved to be urothelial carcinoma (previously known as a transitional cell carcinoma). Urothelial carcinoma can arise anywhere in the urothelium lining the urinary tract from the urethra to the calyces, but is most common in bladder. Urothelial carcinoma is often multifocal and has a tendency to recur.
The cut surfaces of the kidney removed surgically here demonstrate normal cortex and medulla, but the calyces show focal papillary tumor masses of urothelial carcinoma.
Here is another example of urothelial carcinoma that is more aggressive and is invading into the renal parenchyma, causing obstruction of pelvis and calyces to produce hydronephrosis. Hematuria is a frequent presenting symptom.
A urothelial carcinoma of the urothelium is shown here at low power to reveal the frond-like papillary projections to the left of the tumor above the surface. It is differentiated enough to resemble urothelium, but it is producing a mass effect. No invasion to the right is seen at this point.
At medium power, the urothelial carcinoma does resemble urothelium, but the thickness is much greater than normal urothelium, and the neoplastic cells show more pleomorphism.
The causative factors for urothelial carcinoma typically act upon the entire extent of the transitional epithelium in the urinary tract, and it is common for areas of neoplasia to arise multifocally. Seen here is urothelial carcinoma in situ. The abnormal cells are confined to the epithelium above the basement membrane. This area was present in a random bladder biopsy in a patient who also had a grossly visible lesion on cystoscopy.
This is a renal cell carcinoma arising in the lower pole of the kidney. It is fairly circumscribed. The cut surface demonstrates a variegated appearance with yellowish areas, white areas, brown areas, and hemorrhagic red areas. Though these neoplasms are usually slow-growing, they can often reach a considerable size before detection because there is a lot of room to enlarge in the retroperitoneum, and there is another kidney to provide renal function. Thus, presenting symptoms and signs usually include flank pain, mass effect, and hematuria.
This renal cell carcinoma is very large, as indicated by the 15 cm ruler. A portion of normal kidney protrudes at the lower center. This patient was a physician himself and just didn't have any early symptoms.
Here is a renal cell carcinoma that on sectioning is mainly cystic with extensive hemorrhage. Sometimes large simple renal cysts may develop hemorrhage and mimic this appearance.
Renal cell carcinomas have a tendency to invade into the renal vein, as shown here at the white arrow in a resected kidney surrounded by adipose tissue. They may even crawl up the vena cava and into the heart, but even these can be removed! Here, the tumor extended up the vena cava and occluded the adrenal vein, leading to hemorrhagic adrenal infarction in the adrenal at the top of the specimen. Renal cell carcinomas may invade through the renal capsule. Renal cell carcinomas may metastasize to odd locations, and about a fourth of them first present as metastatic lesions.
This is the classic histologic appearance of a renal cell carcinoma: the neoplastic cells have clear cytoplasm and are arranged in nests with intervening blood vessels. This microscopic appearance is why they are often called "clear cell carcinomas".
The multiple irregular bilateral masses (many of which show central indentations, or "umbilications", from necrosis) here represent metastases of carcinoma to the kidneys. Kidney is not a usual site for metastases.
This small kidney from a 4 year old child contains a lobulated tan-white mass. This is Wilms tumor of the kidney. Many are now known to be associated with genetic defects on chromosome 11. The children with Wilms tumor usually present with abdominal enlargement from the mass effect. Nowadays, treatment gives a better than 90% 5 year survival.
This is a Wilms tumor that is composed microscopically of nests and sheets of dark blue cells at the left with compressed normal renal parenchyma at the right.
Wilms tumor resembles the fetal nephrogenic zone of the kidney. The tumor shows attempts to form primitive glomerular and tubular structures.
This rare neoplasm of the kidney is called angiomyolipoma. Note that it is solid and has a tan to yellowish-tan cut surface. It is also multifocal (a smaller nodule appears in the upper pole. Most of these tumors are incidental findings, but persons with a rare condition known as tuberous sclerosis often have these tumors. [Image contributed by John Nicholls, MD, Hong Kong University]
This is the low power microscopic appearance of an angiomylolipoma. There is normal renal parenchyma at the left. The tumor has a strip of adipose tissue (the "lipoma" part) that then blends in with interlacing bundles of smooth muscle (the "myo" component) in which are scattered vascular spaces (the "angio" component).
This small round white nodule in the medulla is an incidental autopsy finding known as a medullary fibroma, also called a renomedullary interstitial cell tumor, a designation larger in size than its importance. They are generally 0.5 cm in size or less and are not associated with any renal diseases.