Pathology – Tumors of the Kidney and urinary tract

Renal Block

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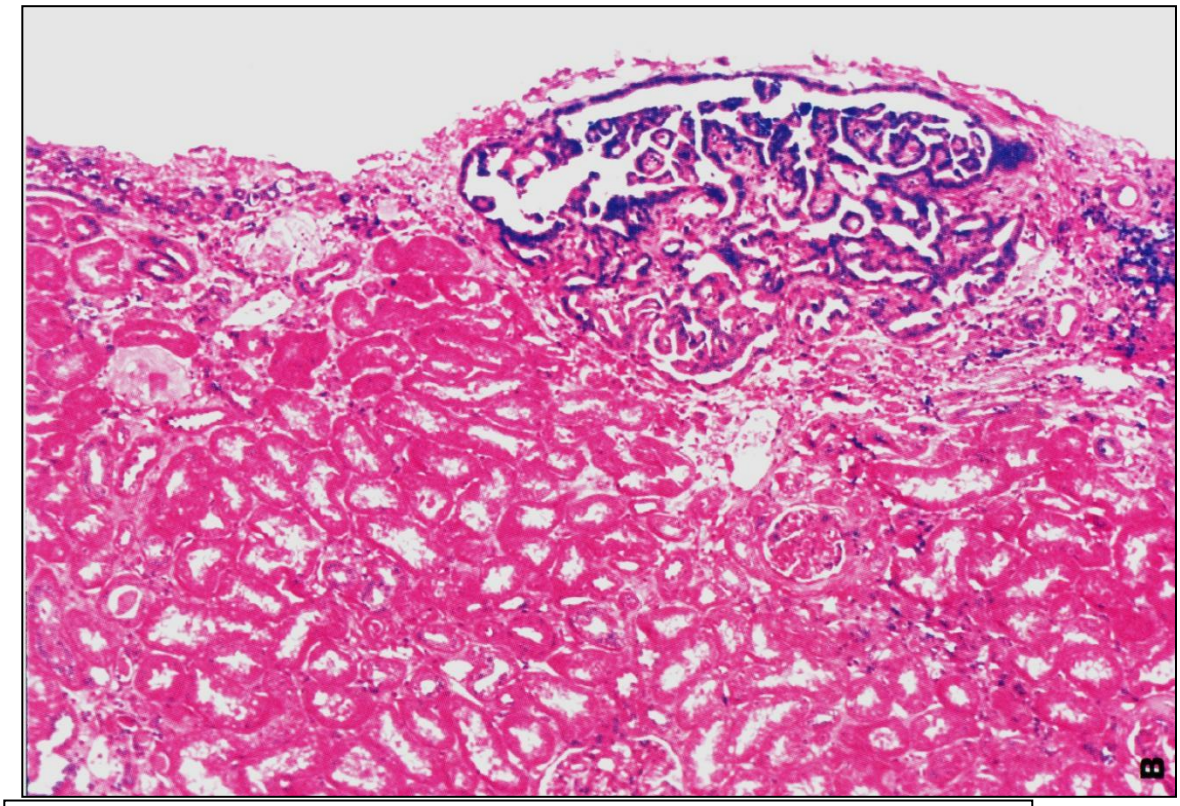
Benign tumors of the Kidney

1. Adenoma

a) This tumor is most often small and asymptomatic. It is derived from renal tubules.
b) The adenoma can either show in a papillary formation or regular tubular epithelium lining.
c) The tumor is cortical, usually subscapular, and is generally well circumscribed.
d) It may be a precursor lesion to renal carcinoma.



H&E slide of renal tissue showing subcapsular papillary **adenoma, where the tubules are arranged in papillary formation.**

2. Angiomyolipoma

a) It is often associated with the tuberous sclerosis syndrome. Tuberous sclerosis is an inherited genetic disorder that affects the skin, kidneys, heart, and mainly brain/nervous system. This disease can cause tumors to grow.
b) The lesion of this tumor consists of blood vessels, adipocytes, and smooth muscle cells.
c) Angiomyolipoma is usually a big tumor where it can be mistaken as Renal Cell Carcinoma RCC. The tumor can enlarge greatly to the extent where it can effect kidney function, or even rupture a vessel causing hemorrhage.

Malignant tumors of the Kidney

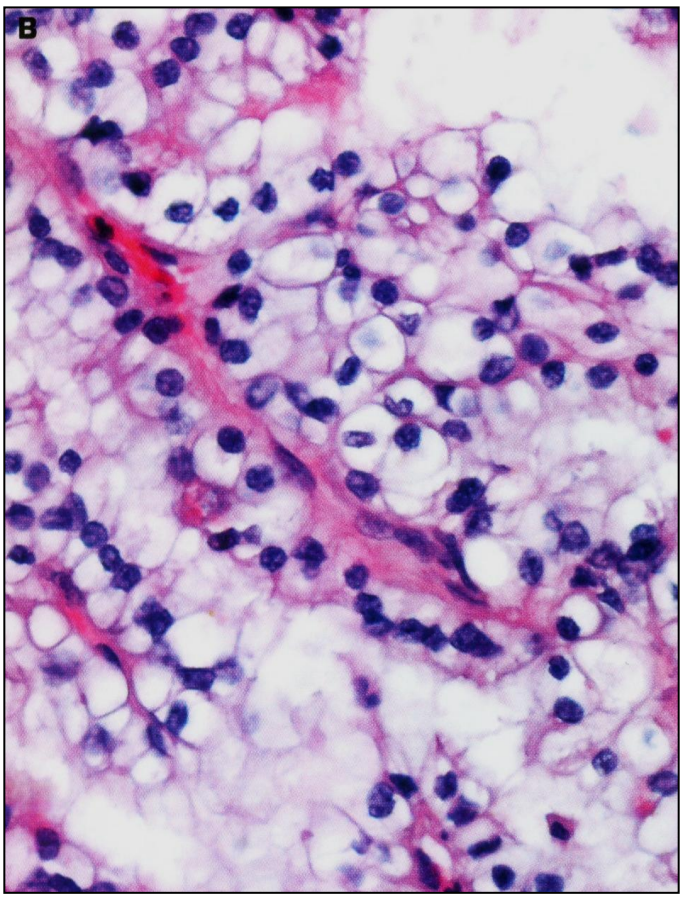
1. Renal cell carcinoma (Clear Cell Carcinoma) (Hydronephroma) has three types:

I. Clear Cell Renal Cell Carcinoma with 70 – 80% of cases (detailed later)
II. Papillary Renal Cell Carcinoma: Doses not occur with association with deletions of chromosome 3, but changes in or with chromosome 7 and trisomies of other chromosomes especially in sporadic cases.
III. Chromophobe Renal Carcinoma: mostly affects the cortical collecting ducts or their intercalated cells. This type of renal carcinoma is associated with loss of multiple and full loss of certain chromosomes; therefore, the affecting loss of locus and gene cant be pinpointed. This type also has a good prognosis.

a. This cancer is the most common renal malignancy.
b. It is more common in men, occurs most often from 50-70 years of age and has a higher incidence in cigarette smokers. Other risk factors include: cadmium exposure (a substance most notably found in zinc batteries) and acquired polycystic disease that results form chronic renal failure.
c. In some instances, it is associated with gene deletions in chromosome 3; renal cell carcinoma can also be associated with von Hippel-Lindau disease, an autosomal dominant disease characterized by predisposition to a variety of neoplasms but particularly cerebellum and retina, which is caused by alterations in a gene localized to chromosome 3. It is thought that these genes may transcribe tumor suppressor factors that help oppose tumor cancer formation.
d. The carcinoma originates in renal tubules. Most often, it arises in one of the renal poles, frequently the upper pole. (This is why it was called hypernephroma). The tumor can also form in lower and middle regions of the kidney, but they are rare in occurrence.

Pathology of Renal Cell Carcinoma:
The tumor is yellow to grayish white with forming cysts that may be accompanied by hemorrhage. It is usually well circumscribed, but some process may project to the renal parenchyma. Frequently the tumor invades renal veins or the vena cava and can extend up the vena cava. Early hematogenous dissemination may occur.

f. Histologic characteristics include polygonal clear cells, filled with lipid and glycogen. Sometimes with vestigial (primitive) tubule formation, (not shown in the next slide)



g. Presenting features may include the triad of flank pain, palpable mass and **hematuria,** which is mostly intermittent and very short. Most individuals present without symptoms, where they are termed to have silent tumors and physicians usually stumble on the tumor. Hematuria is the most frequent presenting abnormality. Renal cell carcinoma may be manifested clinically by any of the following additional findings:

1) Fever
2) Secondary polycythemia (results from erythropoietin production)

3) Renal cell carcinoma mostly metastasizes to the lung and bone, which may cause pathological fractures. The tumor may also spread to the brain localizing to enough extent that would cause a persistent headache or even early morning headaches.

4) Ectopic production of various hormones or hormone-like substances like:

- ACTH a hormone released from the anterior pituitary gland in the brain.
- Prolactin a hormone released from the anterior pituitary gland that stimulates milk production after childbirth.
- Gonadotropins are a group of hormones secreted by the pituitary that stimulate the activity of the gonads.

- Renin: that causes hypertension
- Paraneoplastic parathyroid-like hormone can also cause hypercalcemia.

Other paraneioplastic effects include:

- Cushing syndrome
- Masculinization
- Feminization

2. Wilms tumor (nephroblastoma)

a. This cancer is the most common renal malignancy of early childhood.
b. Incidence peaks in children 2-4 years of age.
c. Wilms tumor originates from primitive metanephric tissue.
d. Histologic characteristics are varied with immature stroma, primitive tubules and glomeruli, and mesenchymal elements such as fibrous connective tissue, cartilage bone, and rarely striated muscle.
e. Most often, the presenting feature is a palpable flank mass (often huge).
f. Wilms tumor is often associated with deletions of the short arm of chromosome 11. The WT-1 and WT-2 genes localized to this chromosome are cancer suppressor genes.
g. The disease can be part of the AGR (or WAGR) complex (Wilms tumor, Aniridia (absence of the choroid layer in the eye), Genitourinary malformations, and mental-motor Retardation). This set of anomalies is associated with deletion of the WT-1 tumor suppressor gene and other nearby genes.
h. It can also be associated with hemihypertrophy (gross asymmetry due to unilateral muscular hypertrophy), macroglossia, organomegaly, neonatal hypoglycemia and various embryonal tumors. This set of anomalies along with Wilms tumor is collectively referred to as the Beckwith-Wiedemann syndrome and is associated with deletion of the WT-2 gene.

C. Transitional cell carcinoma

Usually affects patients from 50 – 70 years of age.

1. This cancer is the most common tumor of the urinary collecting system and can occur in renal calyces, pelvis, ureter, or bladder. It is often multifocal in origin.
2. In the renal pelvis, transitional cell carcinoma has been asscociated with phenacetin abuse. So it would sometimes present as a medullary mass rather than the cortical masses in RCC where it arises from the tubules.
3. This carcinoma is likely to recur after removal.

4. Most often, the presenting feature is hematuria. The hematuria here is intermittent in contrast to a continuous hematuria found in RCC.
5. There is a tendency to spread by local extension to surrounding tissues.
6. Associated toxic exposures may sometimes be involved, including the following:
   a. Industrial exposure to benzidine or p-naphthylamine which is an aniline dye.
   b. Cigarette smoking,
   c. Long-term treatment with cyclophosphamide.
   d. Squamous cell carcinoma constitutes a minority of urinary tract malignancies.

1. This cancer may result from chronic inflammatory processes, such as chronuic bacterial infection or *Schistosoma haematobium* infection,
2. It can also be associated with renal calculi.

Malignant tumors of the bladder

By far the commonest malignant tumour of the bladder in adults is the urothelial-delivered transitional cell carcinoma (TCC).

However, in the paediatric age group a common malignant tumour of the bladder is the rhabdomyosarcoma

Transitional cell carcinoma-in-situ is believed by many authorities to precede the development of TCC in some patients (as evidenced by the presence of TCCis in the majority of cases of TCC), TCCis is characterised by flat and thickened or gently undulating full-thickness dysplastic urothelium (nuclear pleomorphism, abnormal mitoses and apoptotic figures are seen). Often appearing as a red patch, the disease may be multifocal within the bladder.

TCC accounts for about 5% of all malignancies in adults in the U.K. Most patients are over 50 years of age and there are definite risk factors for development of TCQ the most important of which are mentioned in Box I. The tumour may present with painless haematuria, frequency or urgency. TCC may be multifocal within the bladder or the urinary tract.

As in other parts of the urothelium-lined urinary tract the tumour can have a very varied appearance, both macroscopic ally (fronded and seaweed-like to solid) and microscopically (well differentiated and papillary to poorly differentiated and widely muscle-invasive). The grading and staging system for bladder TCC is shown in Box II, together with prognosis.

Numerous cytogenetic and molecular alterations have been found in TCC, including monosomy or deletions of the short (p) or long (q) arm of chromosome 9 and deletions of 17p (which involves the p53 gene).

Squamous metaplasia of the urothelium can occur in a variety of circumstances, for example as a response to bladder stones, indwelling catheters and infection by *Schistosoma* (schistosomiasis is endemic in countries such as Egypt). Under these circumstances, squamous cell carcinoma of the bladder can develop. Often this tumour has invaded the bladder wall at time of presentation.

Box I. Confirmed or suspected risk factors for transitional cell carcinoma

Smoking	Increases risk up to five times
Analgesics, especially phenacitin over periods of time.	Mainly associated with renal pelvis transitional cell carcinoma, but also bladder tumours.
Occupation	Workers in aniline dye, rubber and chemical industries, of textile industries due to exposure to |3~ naphthylanine (which in the liver is converted to a carcinogen that must be activated in the bladder). These workers need regular bladder checks.
Cyclophosphamide used in treats of lymphomas, leukemia, and Polyarteritis Nodosa.	Can cause bladder cancer in the long term (although used for cancer treatment)
Schistosomiasis	Causes chronic inflammation and metaplasia (squamous) of the bladder mucosa (leading to squamous cell carcinoma)
Chronic infections/ inflammation	Some authorities believe that any chronic inflammatory process may predispose to cancer

Box II. Grading and staging of bladder transitional cell carcinoma (TNM)

GRADE	DEFINITION
G1	Well differentiated
G2	Moderately differentiated
G3	Poorly differentiated/ undifferentiated
STAGE	DEFINITION
Tis	In situ carcinoma
Ta	Non-invasive, papillary tumour
T1	Tumour invades subepithelial connecticve tissue
T2	Tumour invades muscularis propia
T3	Tumour invades beyond muscularis propia
T4	Tumour invades prostate, uterus, vagina or pelvic wall/ abdominal wall
N1	Single lymph node metastasis (< 2 cm)
N2	Single metastases (>2 cm) or multiple metastases (< 5 cm)
N3	Multiple metastases (> 5 cm)

- The prognosis of TCC of the bladder depends largely on the grade and stage of tumour but most patients with metastatic bladder TCC die within five years of diagnosi