Renal pathology II.

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Urologic renal diseases

I. Congenital abnormalities

II. Cystic diseases of the kidney

III. Urolithiasis

IV. Obstructive uropathy

V. Pyelonephritis

VI. Tumors of the kidney

I. Congenital abnormalities

1. Agenesis of the kidney

In utero detected bilateral agenesis indicates abortion

2. Hypoplasia of the kidney

Smaller kidney with contralateral compensatory hypertrophy

3. Oligomeganephronia

Reduced number of nephrons leading to end stage renal disease (ESRD) by the time of adolescence

4. Horseshoe kidney

The most common congenital anomaly (1/500-1000) resulting from the fusion of lower (90%) or upper (10%) poles

5. Ectopic kidneys

The kidney lies at the pelvic brim or within the pelvis

I. Congenital abnormalities

6. Duplication of the renal pelvis and the ureter

7. Ureteropelvic junction stenosis

Usually unilateral, leads to hydronephrosis, early operation can save the kidney

8. Accessory renal artery

9. Multicystic renal dysplasia

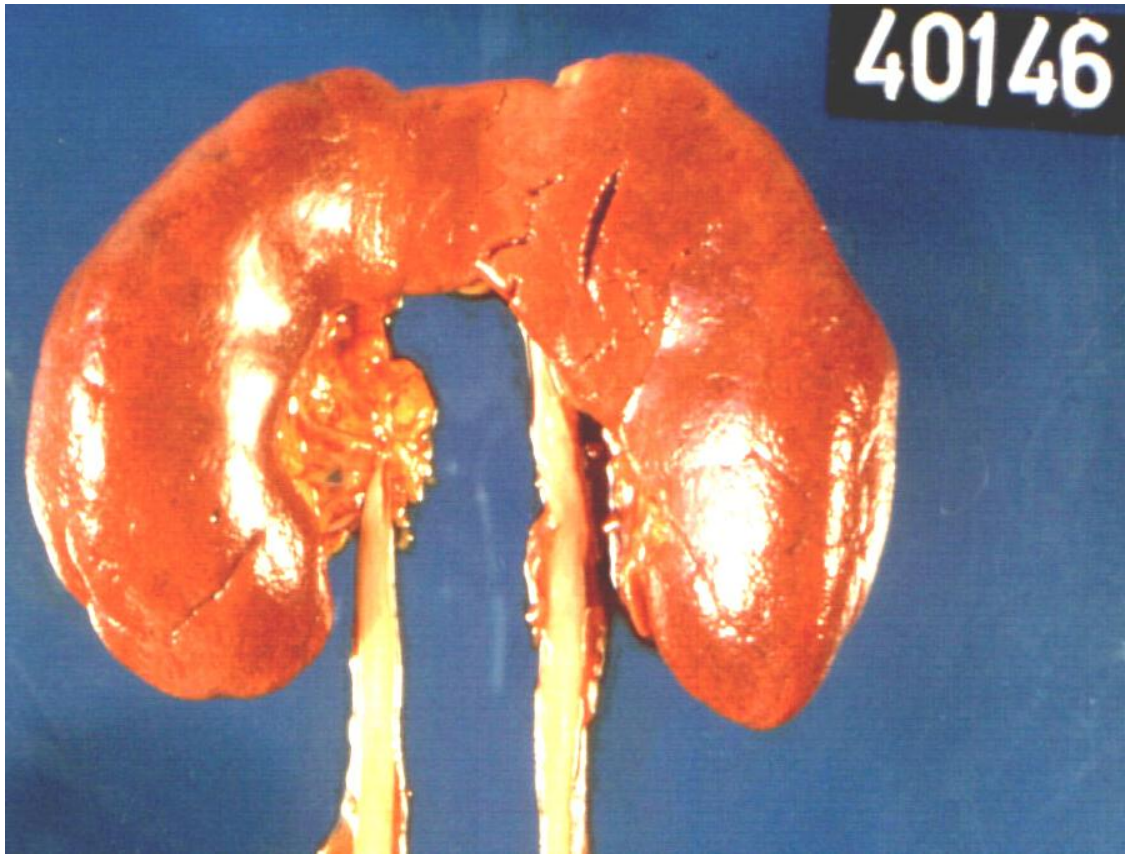
Developmental anomaly, NOT neoplastic process!

Abnormal tissue elements (cartilage, undifferentiated mesenchyme)

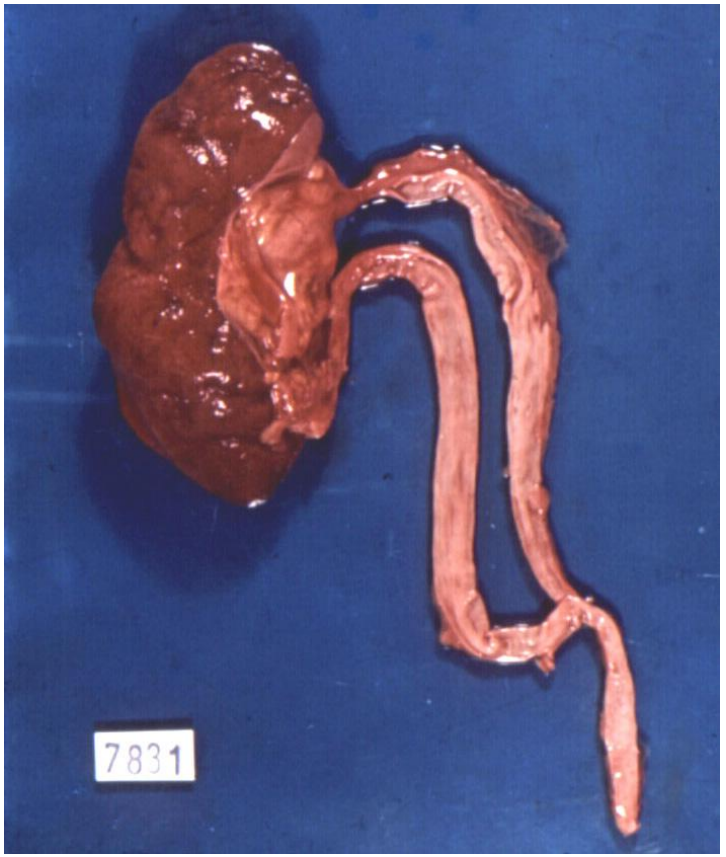
Cysts

Unilateral or bilateral, complete or segmental

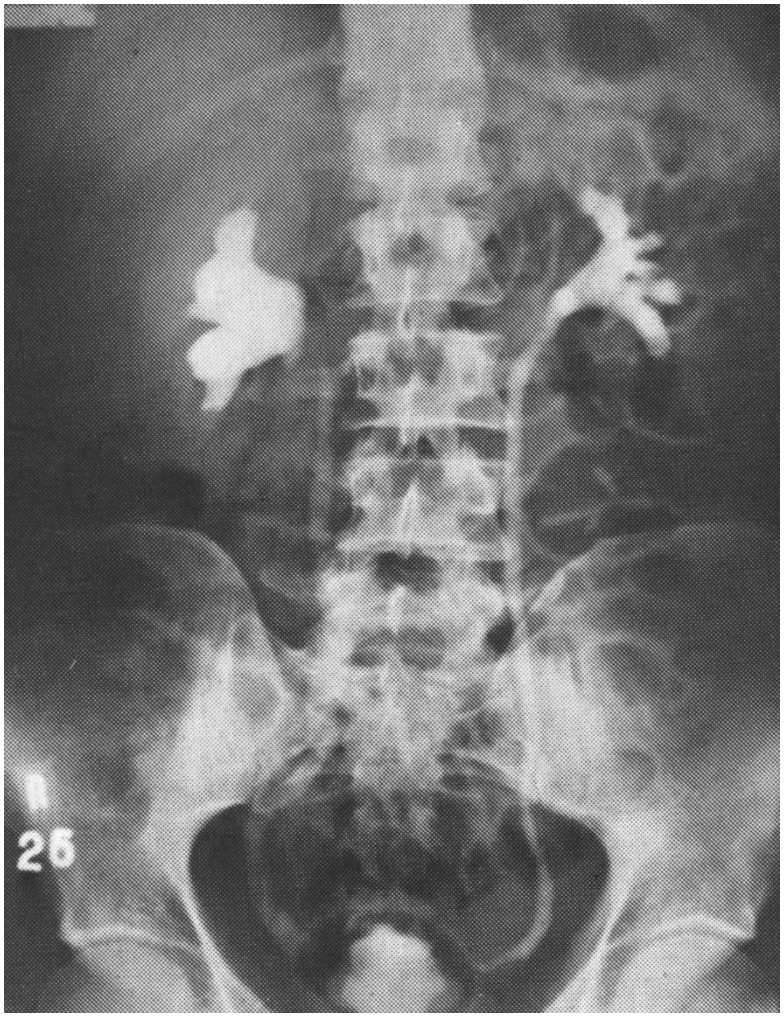
Enlarged kidney with insufficent function

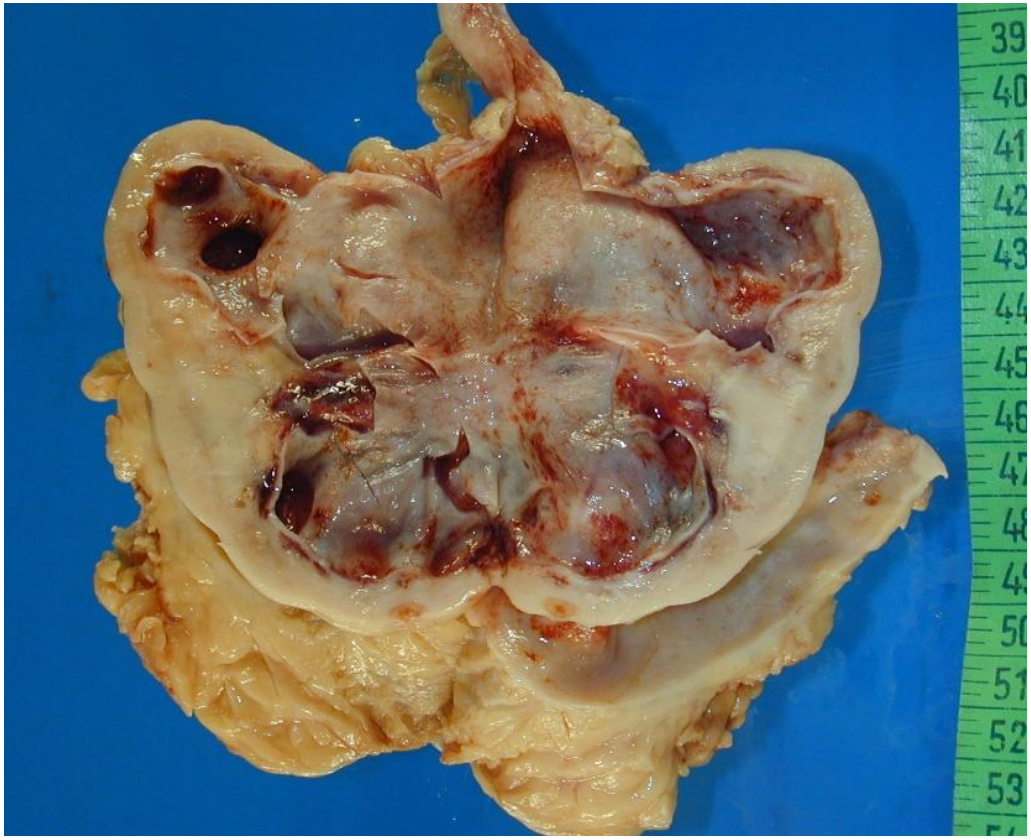


Horseshoe kidney

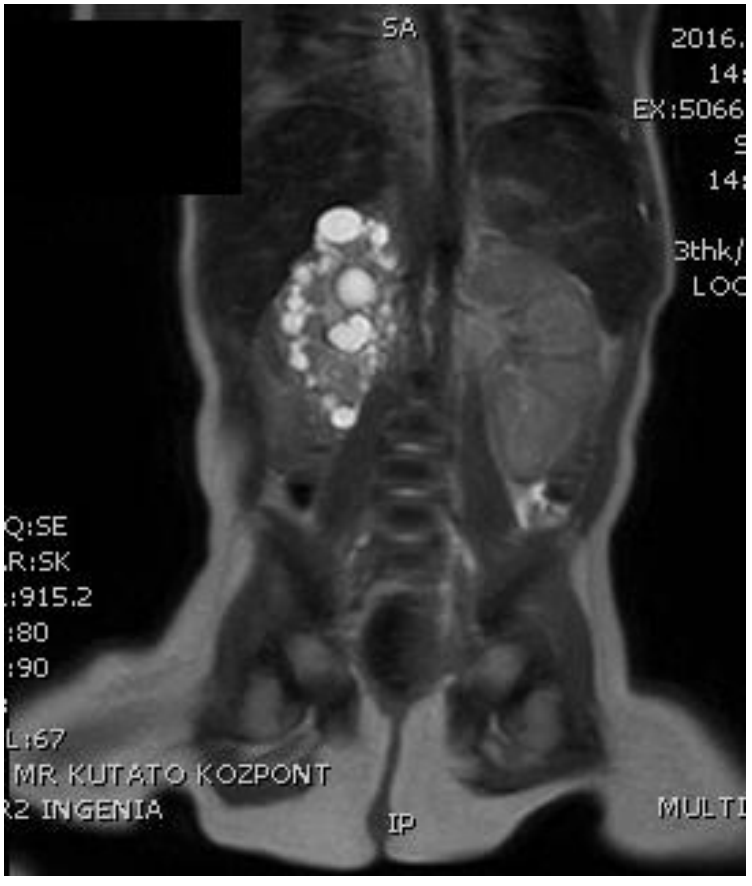


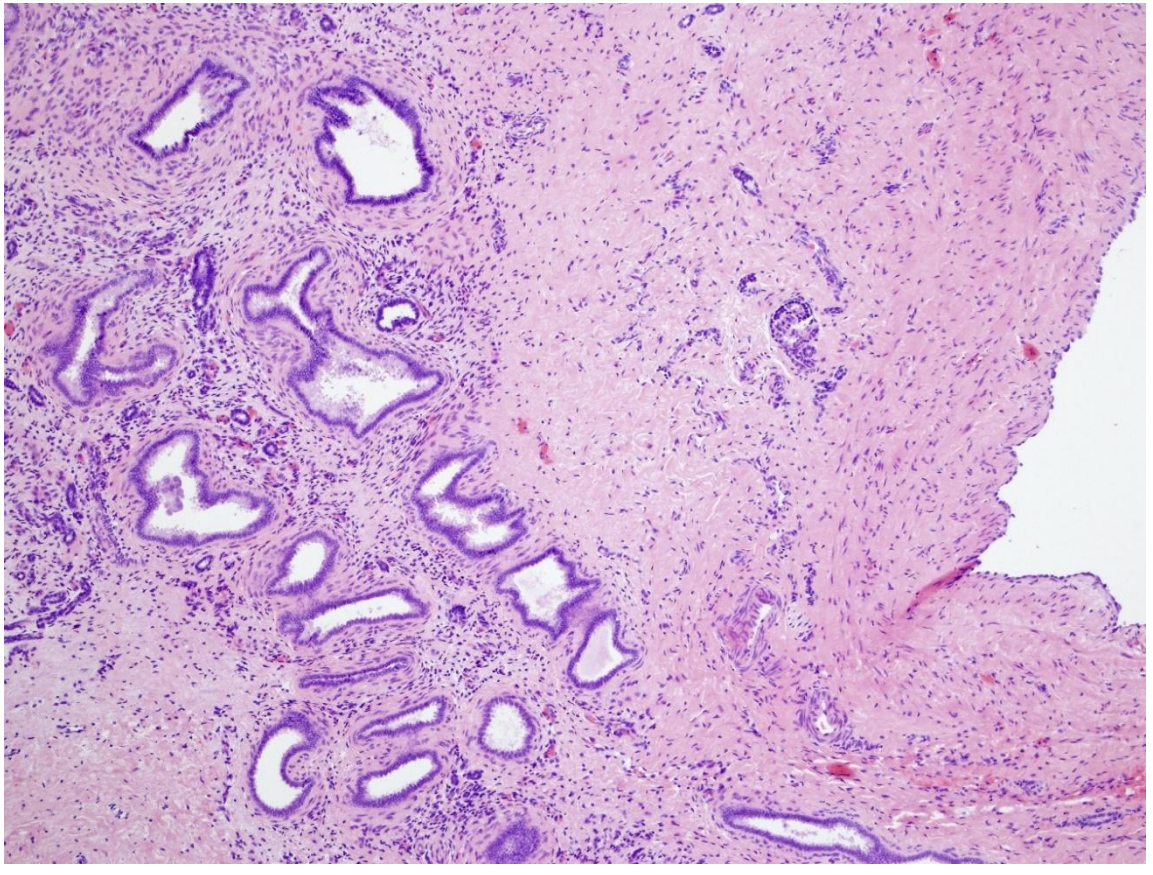
Ureteral duplication





Ureteropelvic junction stenosis





Multicystic renal dysplasia

II. Cystic diseases of the kidney

1. Polycystic kidney disease

A) Autosomal-dominant (ADPKD)

Adulthood

PKD1 and PKD2 genes (Polycystin-1 and -2)

Prevalence 1/400-1000

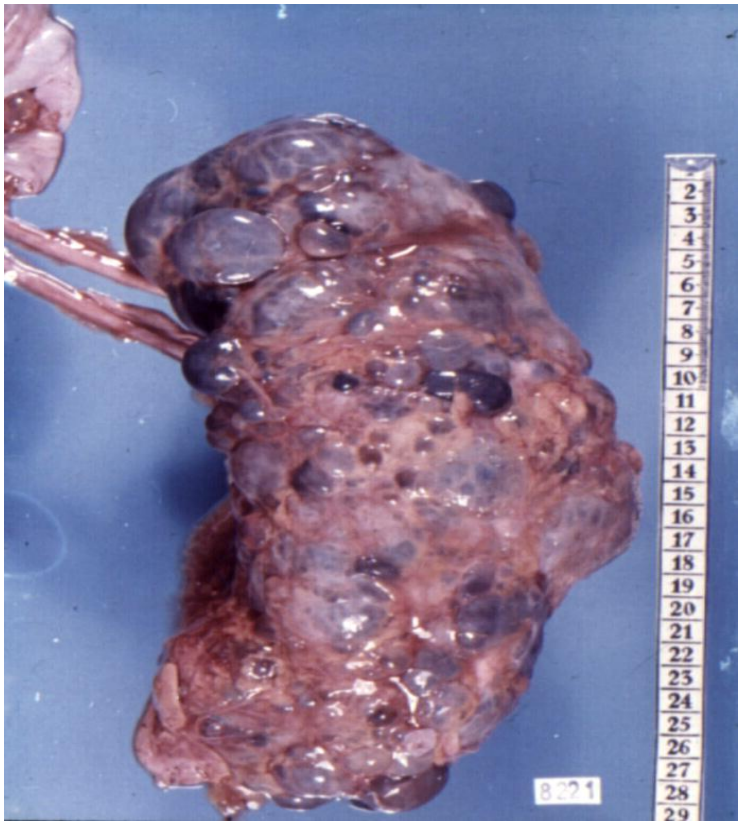
Bilateral and marked enlargement

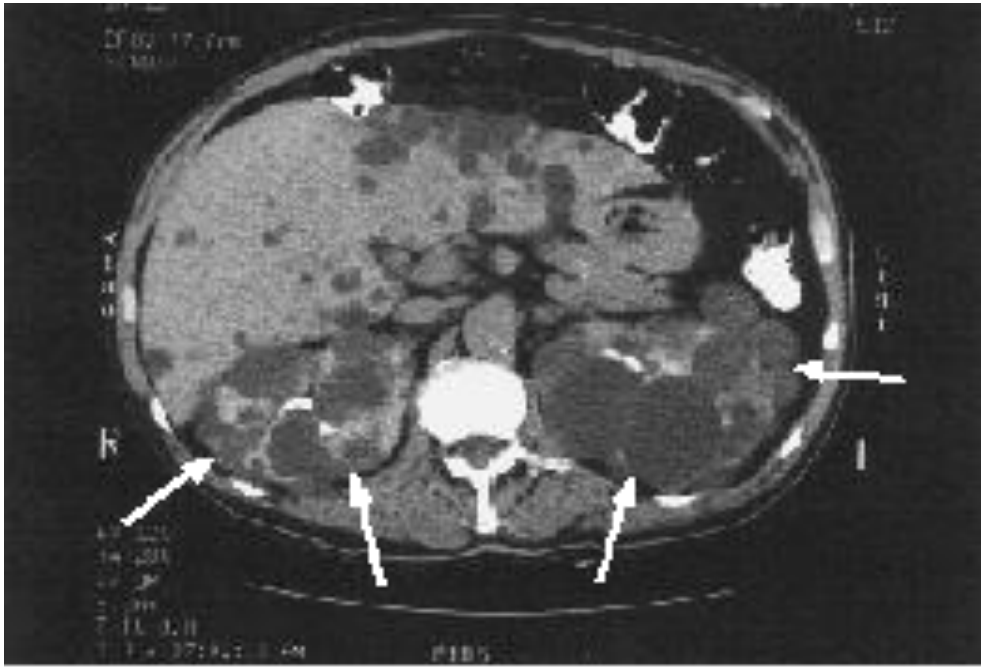
Grape-like appearance

Symptomes begin in early adulthood

It is responsible for 5-10% of chronic renal failures

Liver and pancreatic cysts, mitral valve prolapse, intracranial berry aneurysms





Autosomal-dominant polycystic kidney disease

II. Cystic diseases of the kidney

1. Polycystic kidney disease

B) Autosomal-recessive (ARPKD)

Perinatal, neonatal, infantile, juvenile subcategories

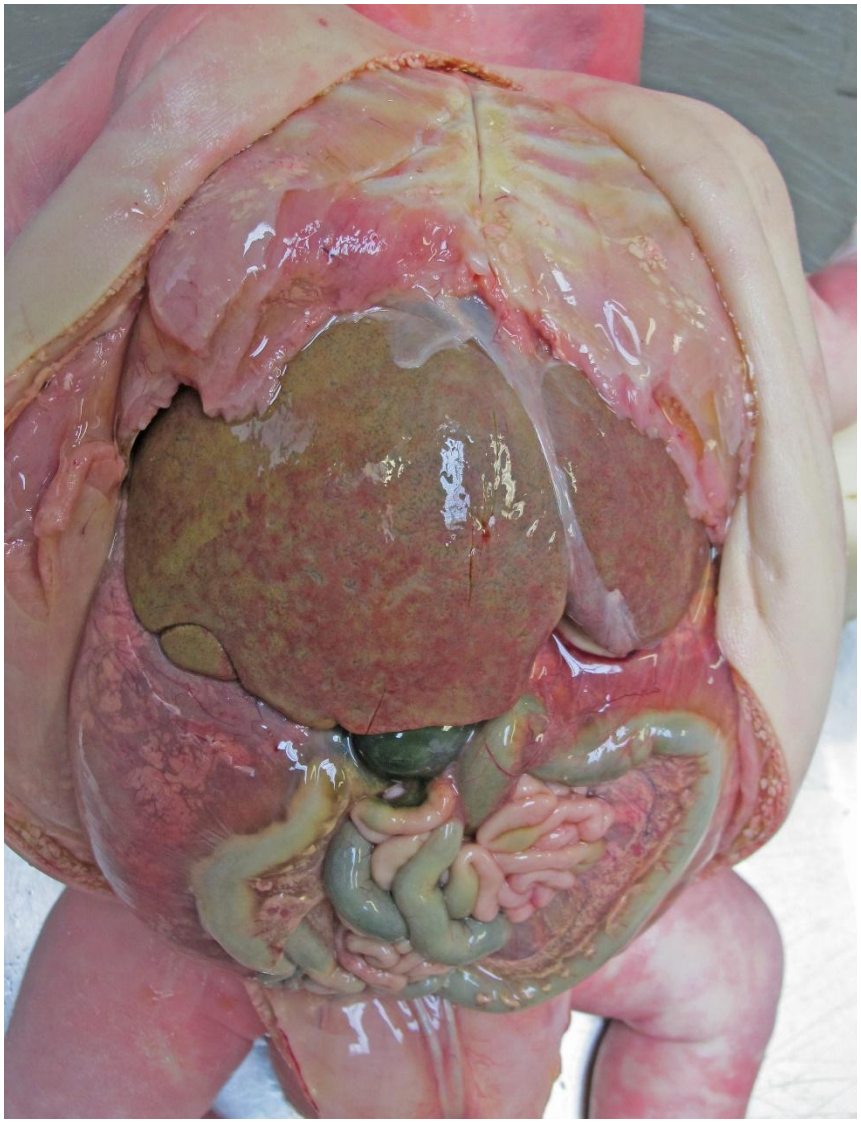
PKDH1 gene (fibrocystin)

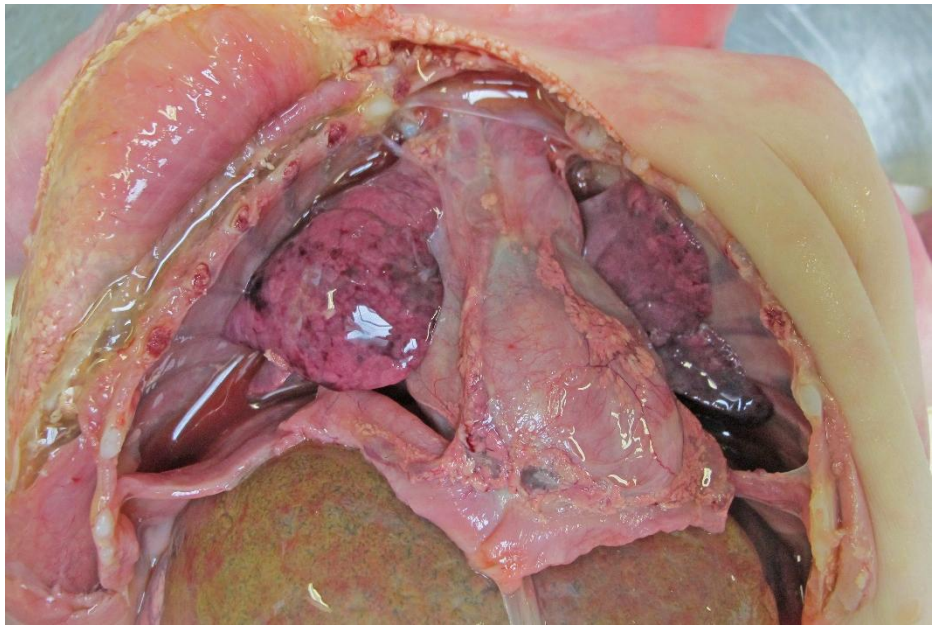
Markedly enlarged kidneys

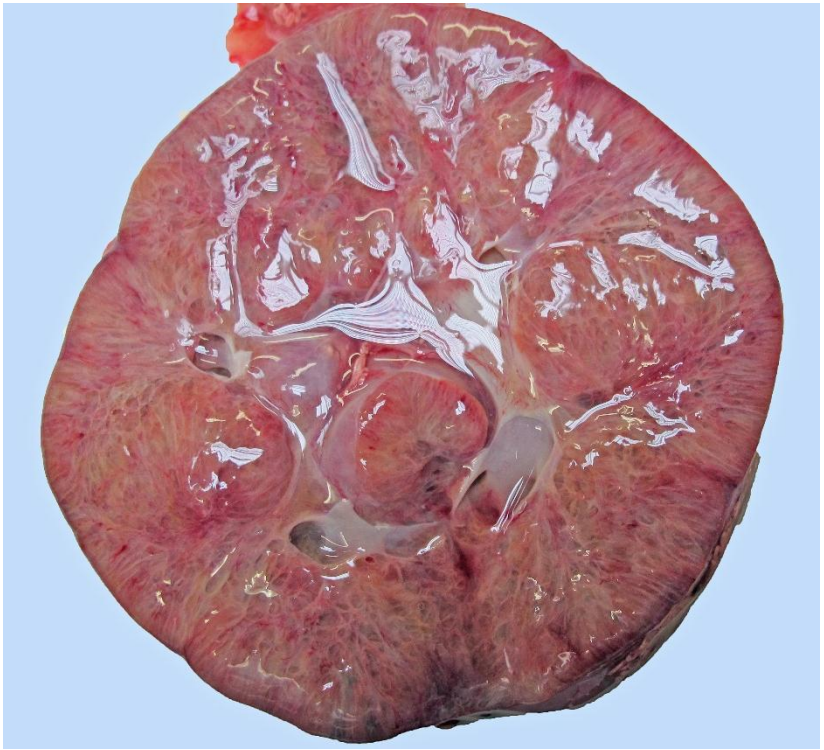
Lung hypoplasia, oligohydramnion

Medullary and cortical elongated cysts, sponge-like appearance

Usually leads to death within the first month of life







Autosomal-recessive polycystic kidney disease

II. Cystic diseases of the kidney

2. Cystic diseases of the renal medulla

A) Medullary sponge kidney

1-3 mm medullary cysts of the collecting ducts

Does not lead to renal failure

B) Nephronophtysis

Sporadic or familial

Atrophic kidneys, cysts at the corticomedullary junction

Leads to ESRD

3. Simple cysts

Common finding, single or multiple, do not influence the renal function

II. Cystic diseases of the kidney

4. Acquired cystic disease of the kidney

In case of long-standing dialysis

5. Glomerulocystic kidney disease

6. Cysts in hereditary syndromes

von Hippel-Lindau syndrome

Tuberous sclerosis

III. Urolithiasis

Three factors:

Salts that are capable of crystallization

Core that triggers crystallizaton (cell debris, urinary cast)

Lack of inhibitors of crystallization

1. Calcium stones

60-70%

Calcium oxalate/calcium phosphate

Hypercalciuria (with or without hypercalcemia), hyperoxaluria

Brown-black, 1-2 cm, visible by X-ray

III. Urolithiasis

2. Struvite stones

15%

Magnesium ammonium phosphate

After infection (e.g., Proteus)

Grey-yellow, staghorn calculi

3. Uric acid stones

15%

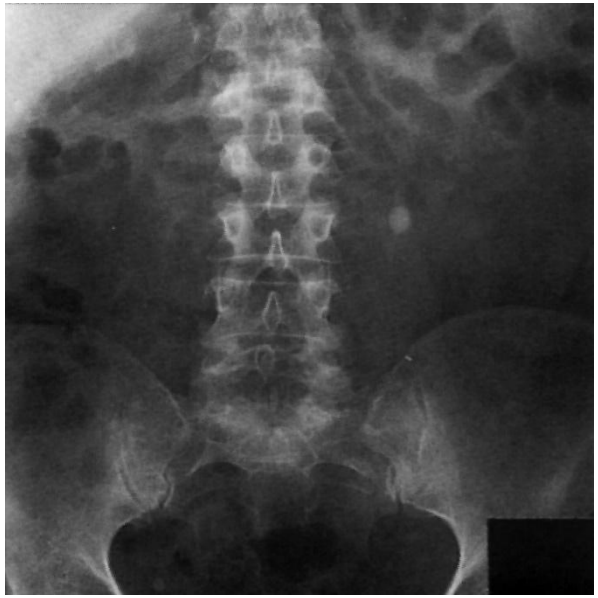
Hyperuricemia (gout, rapid cell turnover e.g., leukemias)

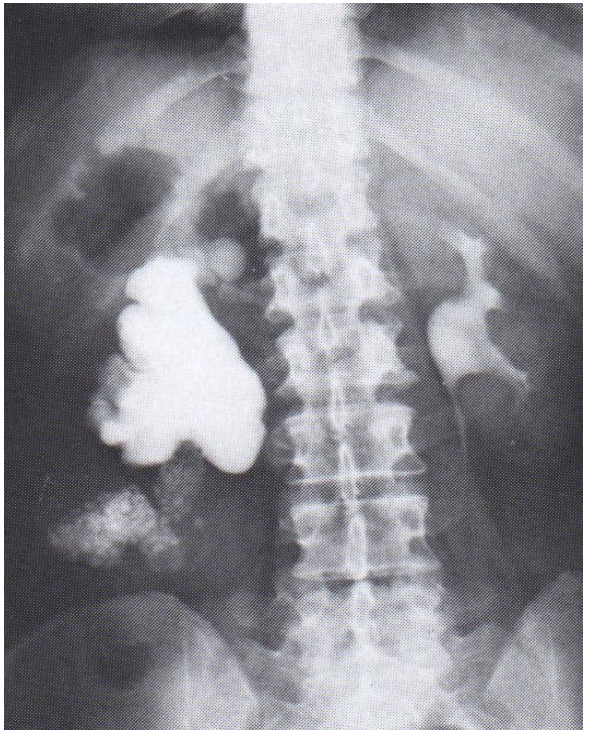
White or orange, radiolucent

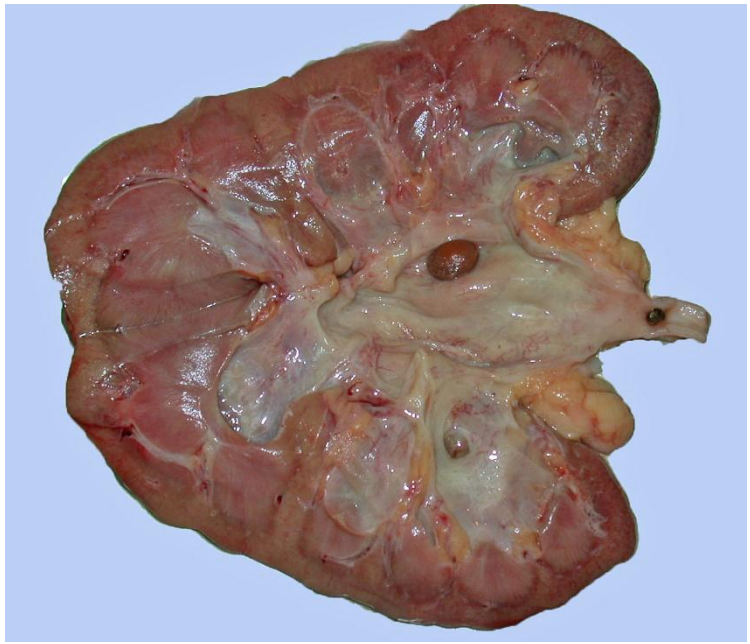
4. Cystine stones

1-2%

Cystinuria







Calcium stone

Staghorn (struvite) stone

III. Urolithiasis

Clinical features

Uni- (80%) or bilateral

Kidney stone attack: agonizing intense pain in the lower back (lumbal area)

extending into the groin area

Nausea, vomiting

Smaller stones are more hazardous

Hematuria

Might be without symptomes

Predisposes for infections

IV. Obstructive uropathy

Obstruction predisposes for infections and stone formation

Unrelieved obstruction leads to hydronephrosis

Hydronephrosis:

Dilation of the renal pelvis and calyces

Progressive atrophy of the kidney

IV. Obstructive uropathy

Causes:

1. Congenital anomalies
2. Calculi
3. Prostatic hyperplasia
4. Tumors
5. Lower urinary tract inflammations
6. Pregnancy
7. Uterine prolapse
8. Functional disorders

IV. Obstructive uropathy

Clinical features:

Acute obstruction usually provokes pain

Partial obstruction may remain silent

Partial bilateral obstruction leads to inabilty to concentrate the urine resulting in polyuria followed by chronic tubulointerstitial nephritis

Complete bilateral obstruction leads oliguria or anuria

V. Pyelonephritis

1. Acute pyelonephritis

Inflammation of the tubules, the interstitium, the calyces and the renal pelvis

Caused by bacterias (**E. coli**, Proteus mirabilis, Klebsiella, Enterococcus)

Usually consequence of an ascending urinary tract infection

Less commonly result of a hematogenous spread

In normal kidneys, or as a complication of urinary tract disorders (e.g. VUR)

Predisposing factors: catheter, diabetes, pregnancy, lower urinary tract obstruction, immunsuppression

V. Pyelonephritis

1. Acute pyelonephritis

Morphology:

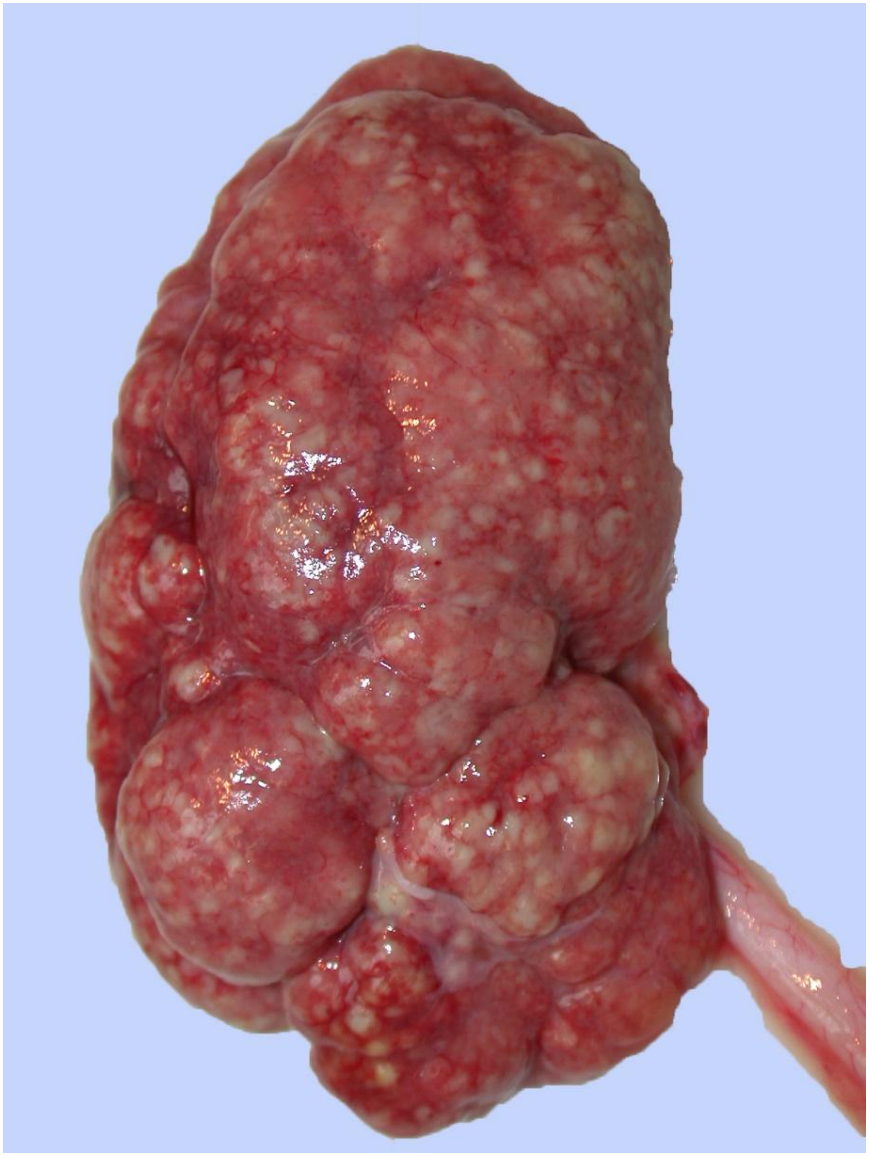
Sligthly enlarged kidney(s)

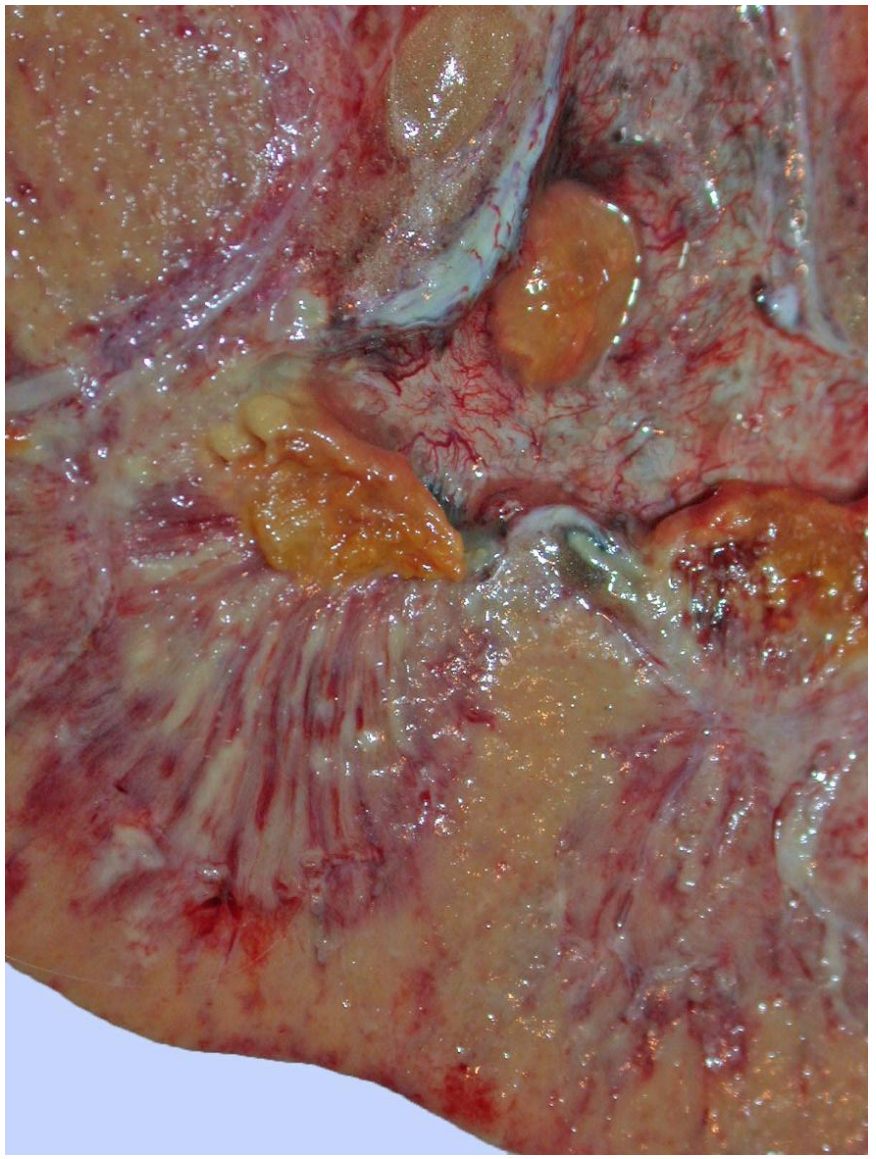
1-3 mm yellowish abscesses on the surface and in the parenchyme (pyelonpehritis apostematosa)

The calyces and the renal pelvis are reddish

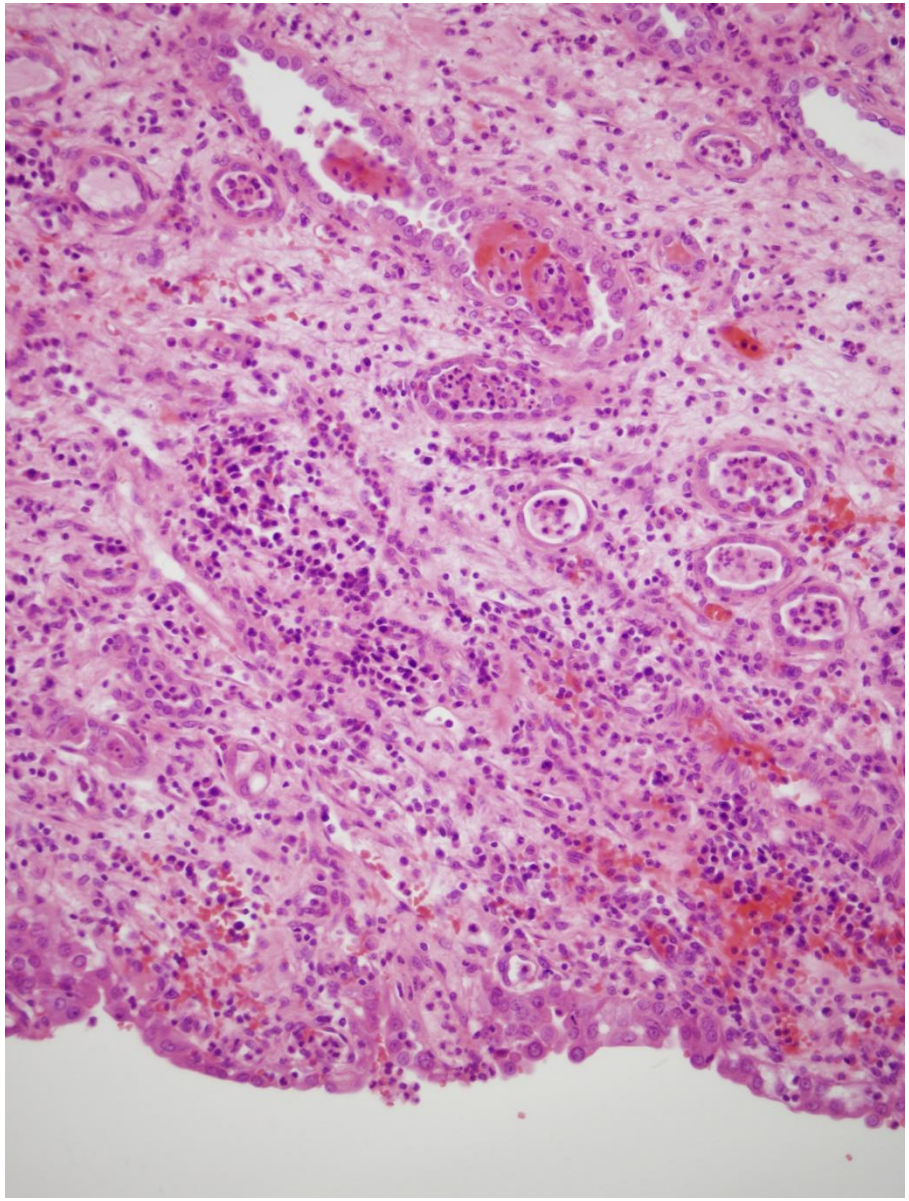
Patchy interstitial suppurative inflammation, aggregates of neutrophils in the tubules, tubular necrosis

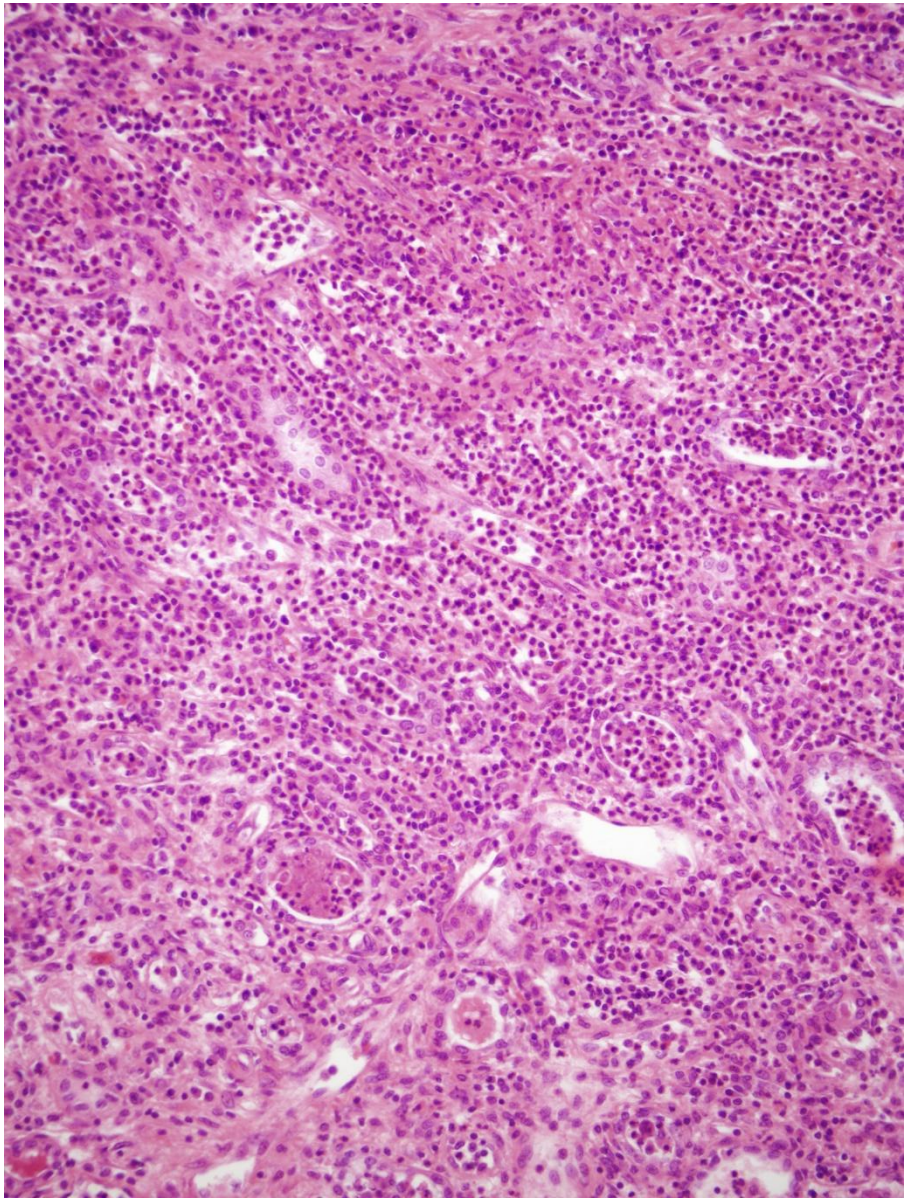
Glomeruli are also affected in case of hematogenous origin





Acute pyelonephritis





Acute pyelonephritis

V. Pyelonephritis

1. Acute pyelonephritis

Clinical features:

Uni- or bilateral

Sudden onset with high fever

Pain at the costovertebral angle

Leukocytosis, high sedimentation rate

Pyuria, bacteruria

Usually follows a benign course (with appropriate antibiotic therapy)

Complicated cases can be fatal

V. Pyelonephritis

2. Chronic pyelonephritis

Chronic injury of the interstitium and the tubules resulting in scar formation

The renal pelvis and the calyces are also affected

Causes: reflux nephropathy, chronic obstruction

Recurrent infections

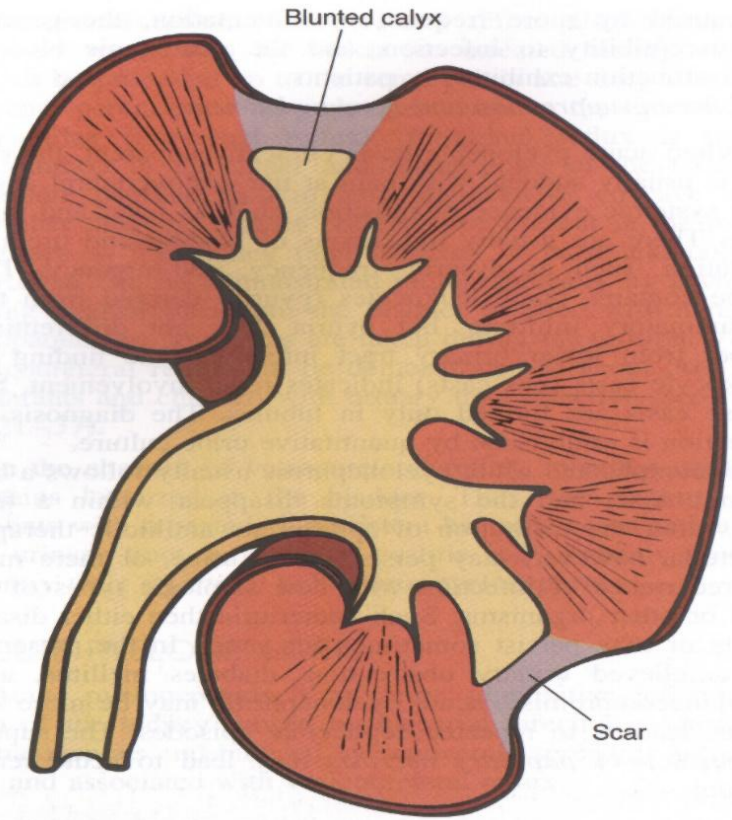
Morphology:

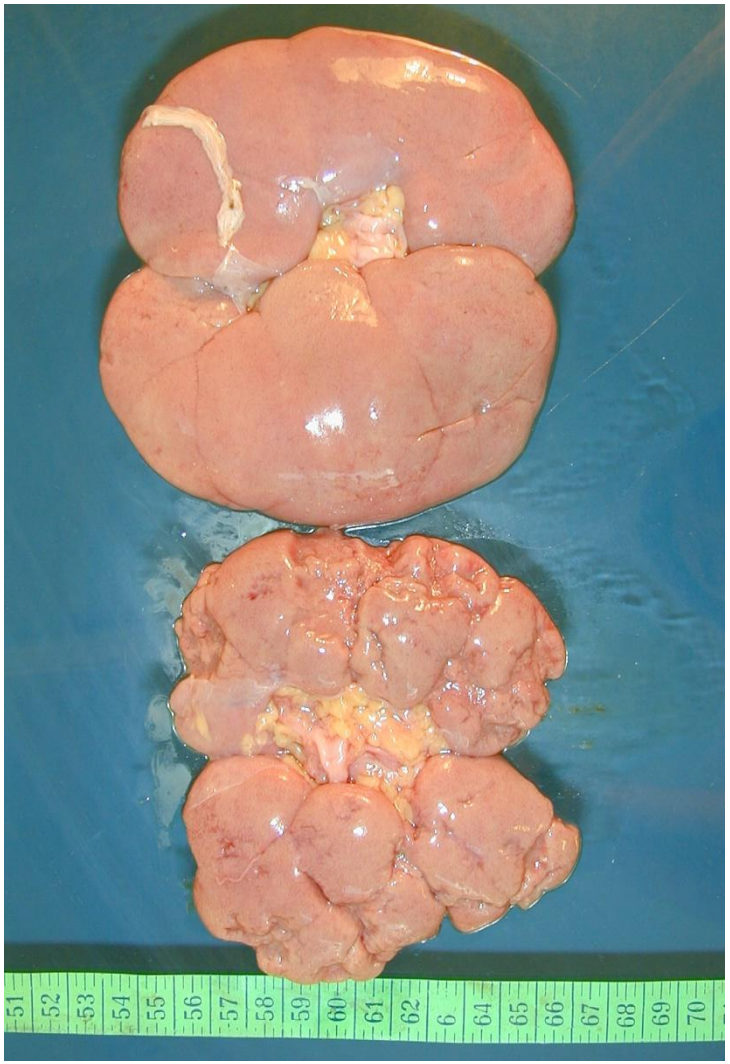
Kidneys are irregularly scarred, corticomedullary scars overlying dilated calyces, flattening of the papillae

The calyces are dilated and their mucosa is thickened

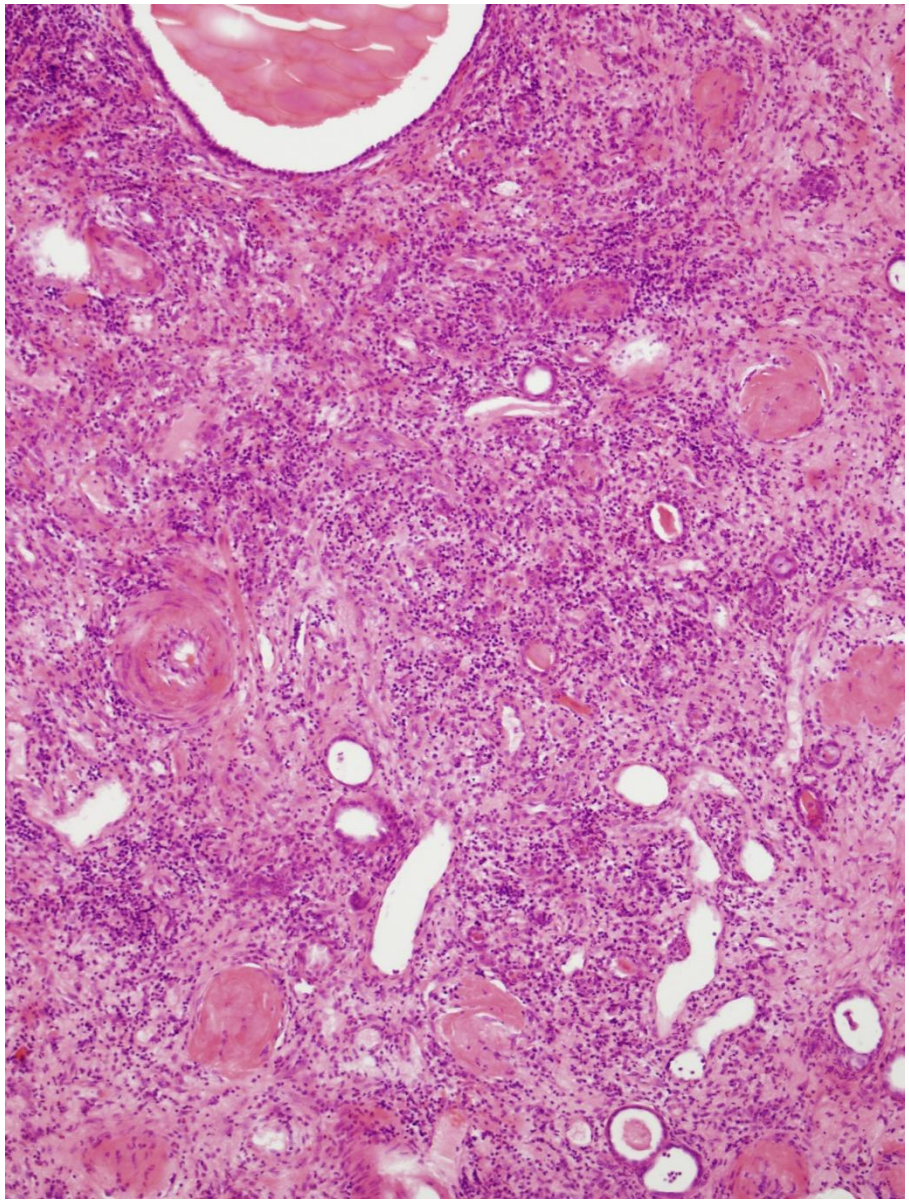
Focal interstitial fibrosis, atrophic tubules, tubular casts (thyroidization), lymphoid infiltration

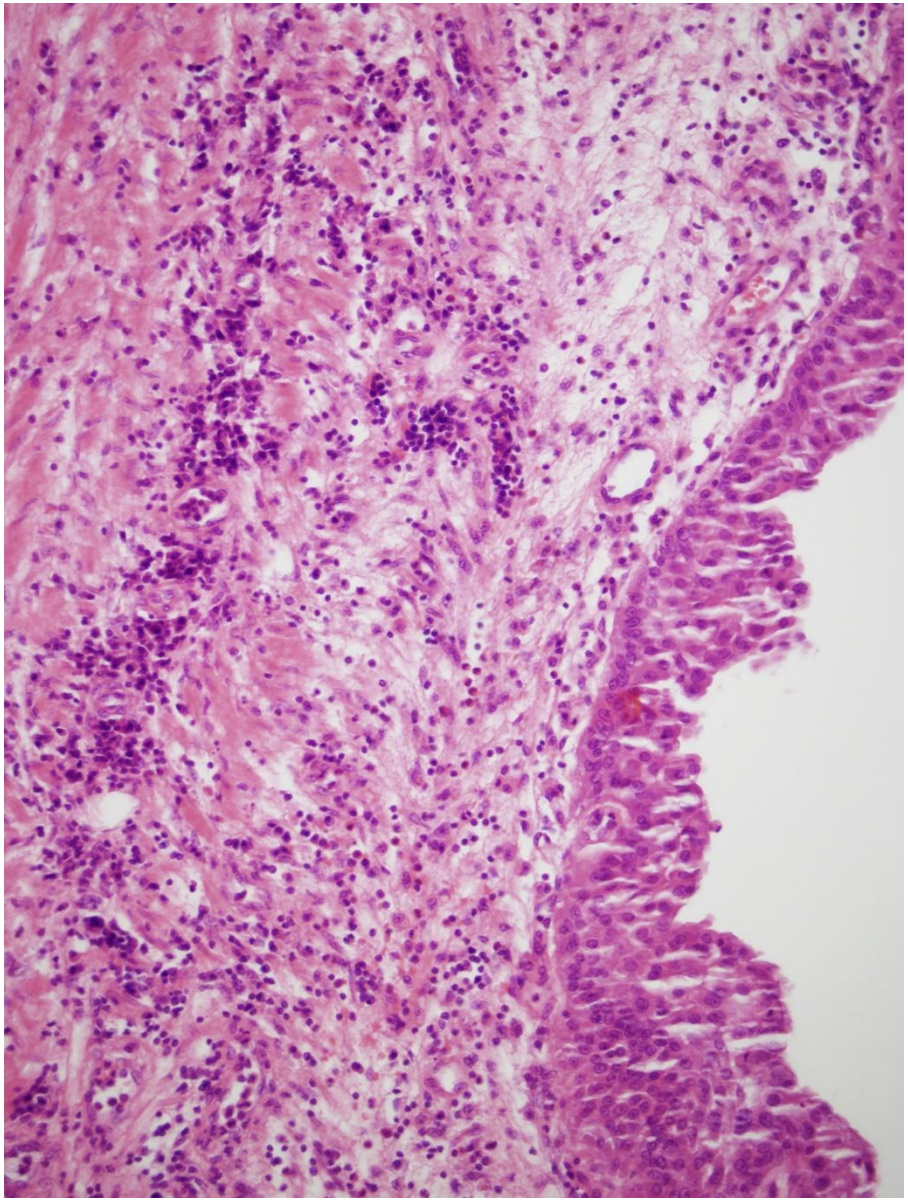
The mucosa of the calyces and pelvis is fibrotic and contains cronic inflammation





Chronic pyelonephritis





Chronic pyelonephritis

V. Pyelonephritis

2. Chronic pyelonephritis

Clinical features:

Uni- or bilateral

Episodes of acute pyelonephritis, or silent clinical course leading to destruction

Bilateral chronic pyelonephritis can result in hypertension and renal insufficiency

10% of patients on dialysis therapy have chronic pyelonephritis

V. Pyelonephritis

3. Xanthogranulomatous pyelonephritis

Middle-aged women with diabetes

Usually unilateral

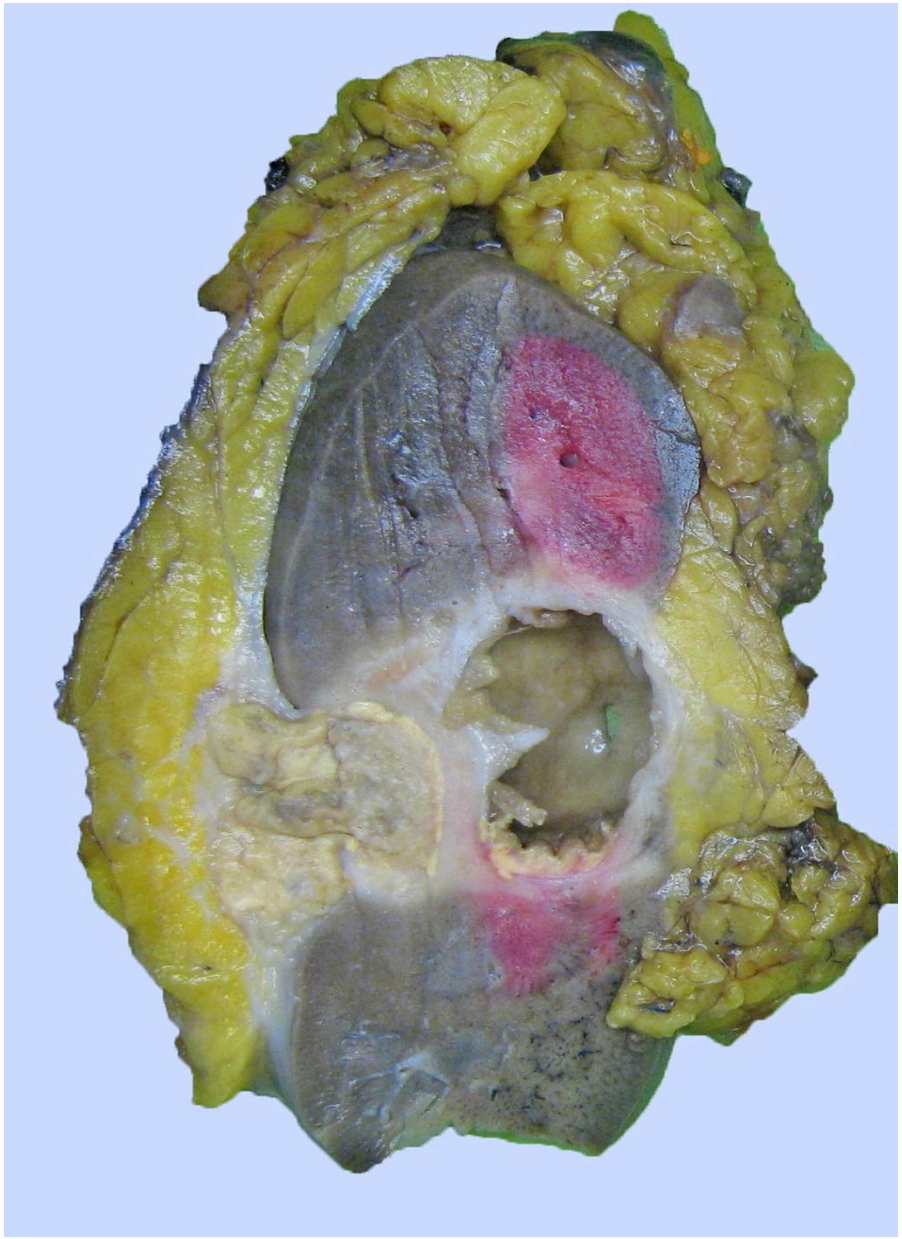
Proteus mirabilis infection

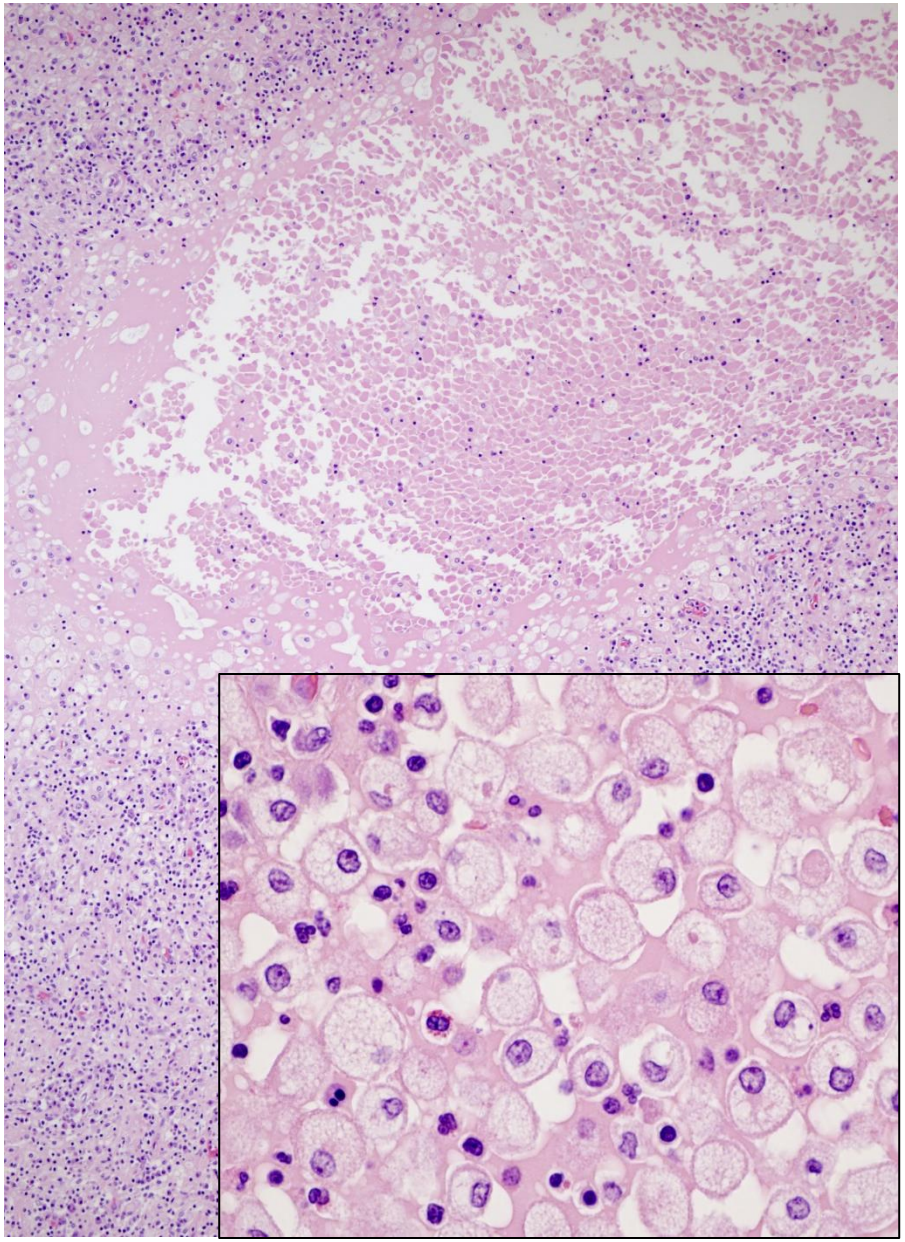
Tumor-like lesion

Yellowish areas, extracapsular spread, infiltrative pattern

Foamy histiocytes, giant cells, lymphocytes, plasma cells, neutrophils

Indicates nephrectomy





Xanthogranulomatous pyelonephritis

VI. Tumors of the kidney

Tumor types

- Benign tumors
- Malignant tumors
- Pediatric tumors

Genetic background

Prognostic factors

Clinical features

WHO classification of tumours of the kidney

Renal cell tumours	
Clear cell renal cell carcinoma	8310/3
Multilocular cystic renal neoplasm of low malignant potential	8316/1*
Papillary renal cell carcinoma	8260/3
Hereditary leiomyomatosis and renal cell carcinoma–associated renal cell carcinoma	8311/3*
Chromophobe renal cell carcinoma	8317/3
Collecting duct carcinoma	8319/3
Renal medullary carcinoma	8510/3*
MiT family translocation renal cell carcinomas	8311/3*
Succinate dehydrogenase–deficient renal carcinoma	8311/3
Mucinous tubular and spindle cell carcinoma	8480/3*
Tubulocystic renal cell carcinoma	8316/3*
Acquired cystic disease–associated renal cell carcinoma	8316/3
Clear cell papillary renal cell carcinoma	8323/1
Renal cell carcinoma, unclassified	8312/3
Papillary adenoma	8260/0
Oncocytoma	8290/0
Metanephric tumours	
Metanephric adenoma	8325/0
Metanephric adenofibroma	9013/0
Metanephric stromal tumour	8935/1
Nephroblastic and cystic tumours occurring mainly in children	
Nephrogenic rests	
Nephroblastoma	8960/3
Cystic partially differentiated nephroblastoma	8959/1
Paediatric cystic nephroma	8959/0
Mesenchymal tumours	
Mesenchymal tumours occurring mainly in children	
Clear cell sarcoma	8964/3
Rhabdoid tumour	8963/3
Congenital mesoblastic nephroma	8960/1
Ossifying renal tumour of infancy	8967/0
Mesenchymal tumours occurring mainly in adults	
Leiomyosarcoma	8890/3
Angiosarcoma	9120/3
Rhabdomyosarcoma	8900/3
Osteosarcoma	9180/3
Synovial sarcoma	9040/3
Ewing sarcoma	9364/3
Angiomyolipoma	8860/0
Epithelioid angiomyolipoma	8860/1*
Leiomyoma	8890/0
Haemangioma	9120/0
Lymphangioma	9170/0
Haemangioblastoma	9161/1
Juxtaglomerular cell tumour	8361/0
Renomedullary interstitial cell tumour	8966/0
Schwannoma	9560/0
Solitary fibrous tumour	8815/1
Mixed epithelial and stromal tumour family	
Cystic nephroma	8959/0
Mixed epithelial and stromal tumour	8959/0
Neuroendocrine tumours	
Well-differentiated neuroendocrine tumour	8240/3
Large cell neuroendocrine carcinoma	8013/3
Small cell neuroendocrine carcinoma	8041/3
Phaeochromocytoma	8700/0
Miscellaneous tumours	
Renal haematopoietic neoplasms	
Germ cell tumours	
Metastatic tumours	

The morphology codes are from the International Classification of Diseases for Oncology (ICD-O) {917A}. Behaviour is coded /0 for benign tumours; /1 for unspecified, borderline, or uncertain behaviour; /2 for carcinoma in situ and grade III intraepithelial neoplasia; and /3 for malignant tumours. The classification is modified from the previous WHO classification {756A}, taking into account changes in our understanding of these lesions.
*New code approved by the IARC/WHO Committee for ICD-O.

VI. Tumors of the kidney

Histogenesis of renal tumors

Tubular epithelium

Papillary adenoma

Oncocytoma

Clear cell renal cell carcinoma

(renal cell carcinoma: RCC)

Multilocular cystic neoplasm

Papillary RCC

Chromophobe RCC

Clear cell papillary RCC

Mesenchyme

Angiomyolipoma

Metanephrogenic elements

Metanephric adenoma

Nephroblastoma (Wilms tumor)

VI. Tumors of the kidney

Benign tumors

1. Papillary adenoma

Papillary tumor with low-grade tumors cells, ≤ 15 mm

Grey-white, round nodule, can be multifocal

Commonly incidental finding

Cuboidal, monomorphic tumor cells, papillary architecture, psammoma bodies

VI. Tumors of the kidney

Benign tumors

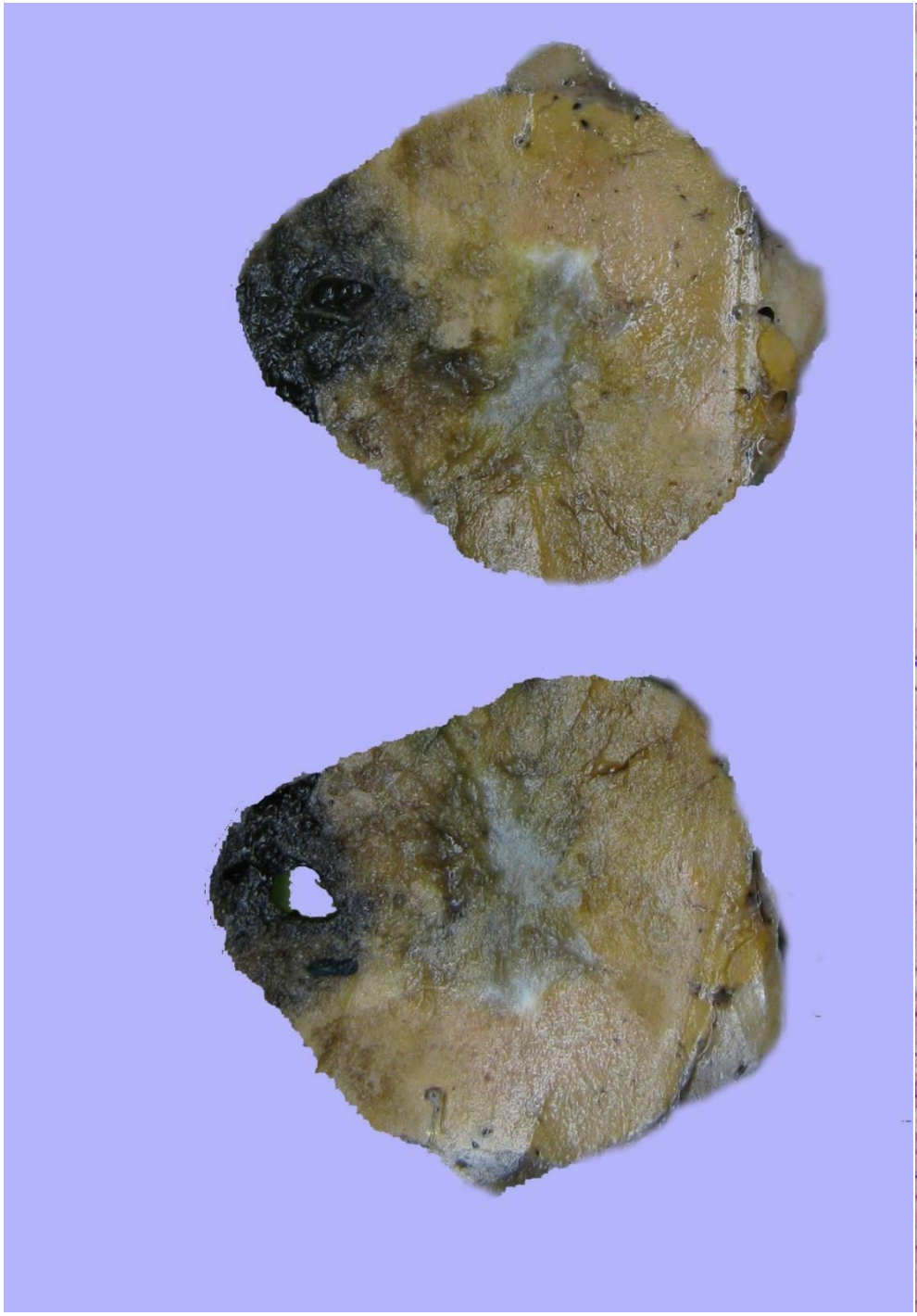
2. Oncocytoma

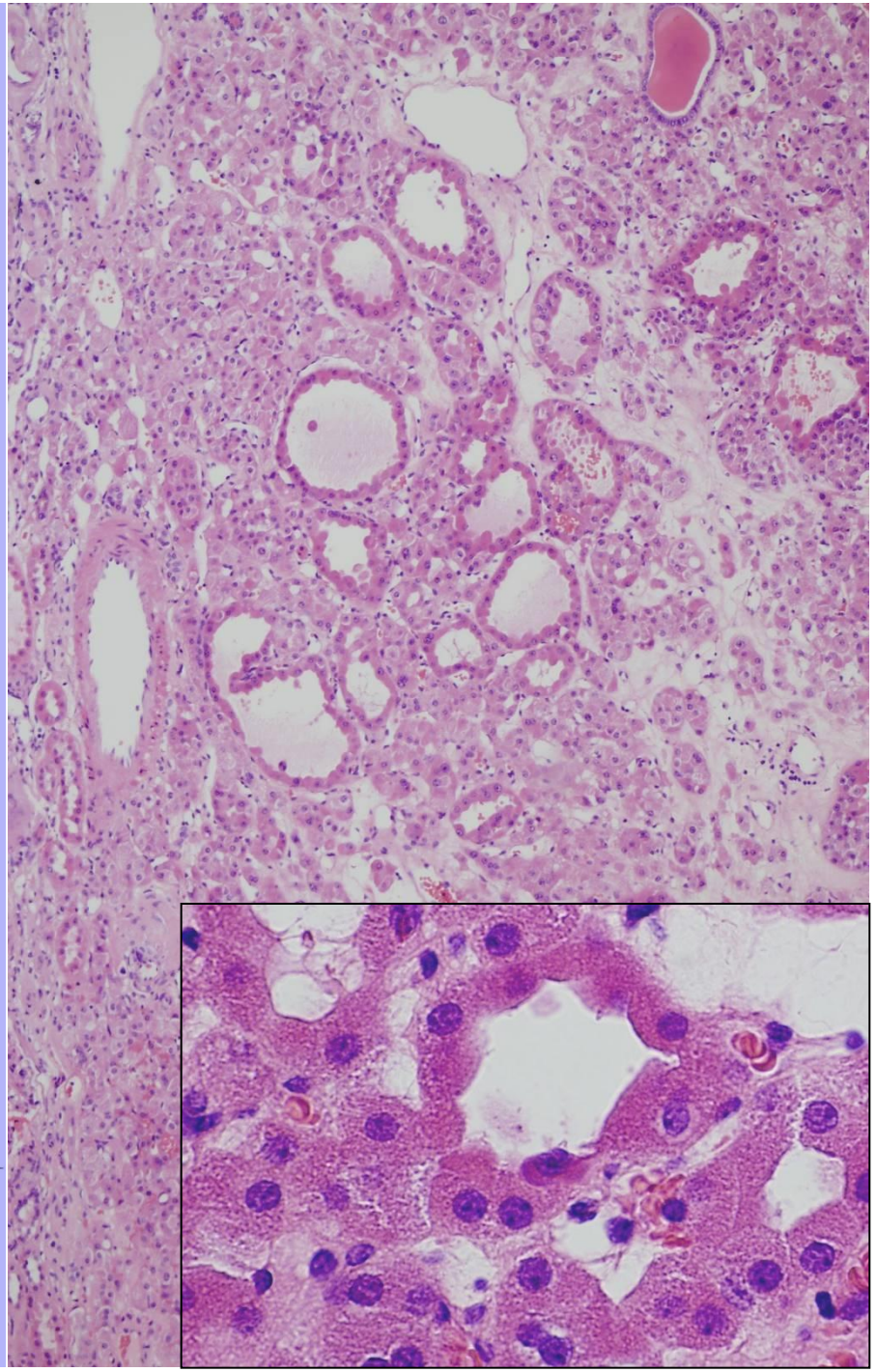
5% of renal tumors

Mahogany brown, characteristic central scar

Nested, trabecular architecture, degenerative signs

Oncocytic, bland looking cells (large, granular eosinophilic cytoplasm), however, bizarre nuclei, extracapsular infiltration, vascular invasion might be encountered





VI. Tumors of the kidney

Benign tumors

3. Angiomyolipoma

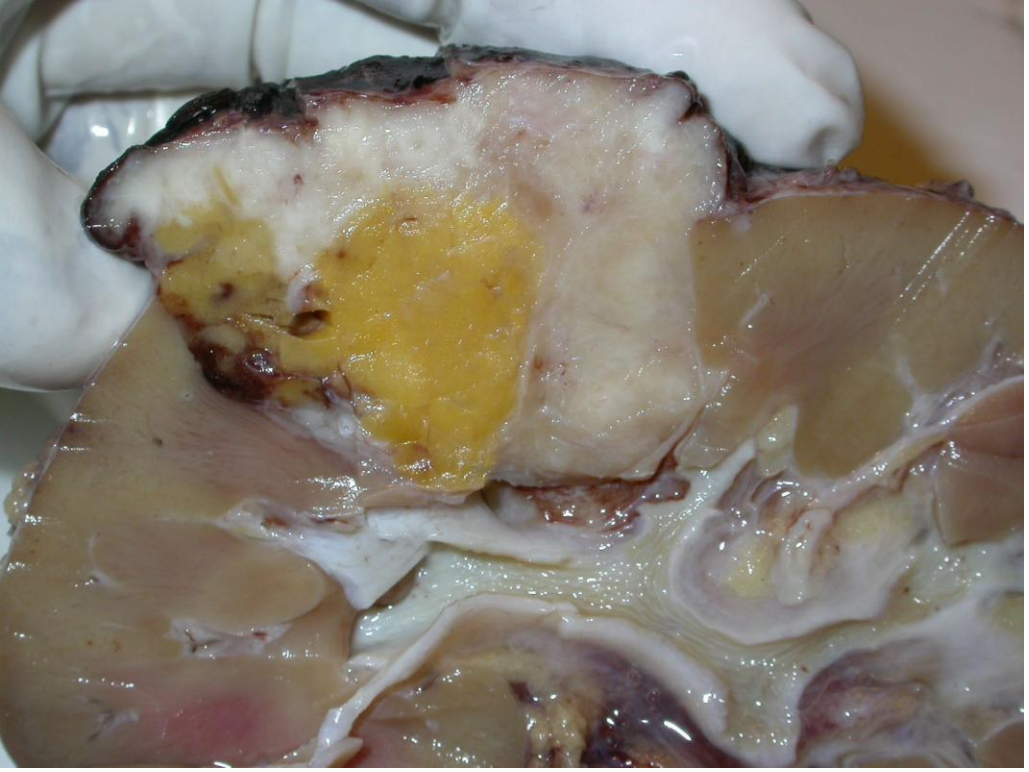
PEComa: *perivascular epithelioid cell tumor*

1% of the resected renal tumors, but it is more common (by US detected tumors that are not operated)

Well-circumscribed, usually fatty appearance

Adipose tissue, thick-walled vessels, smooth muscle

HMB45+, Melan A+ (melanocytic markers!!)



VI. Tumors of the kidney

Benign tumors

4. Metanephric adenoma

More common in females

Average size is 5 cm

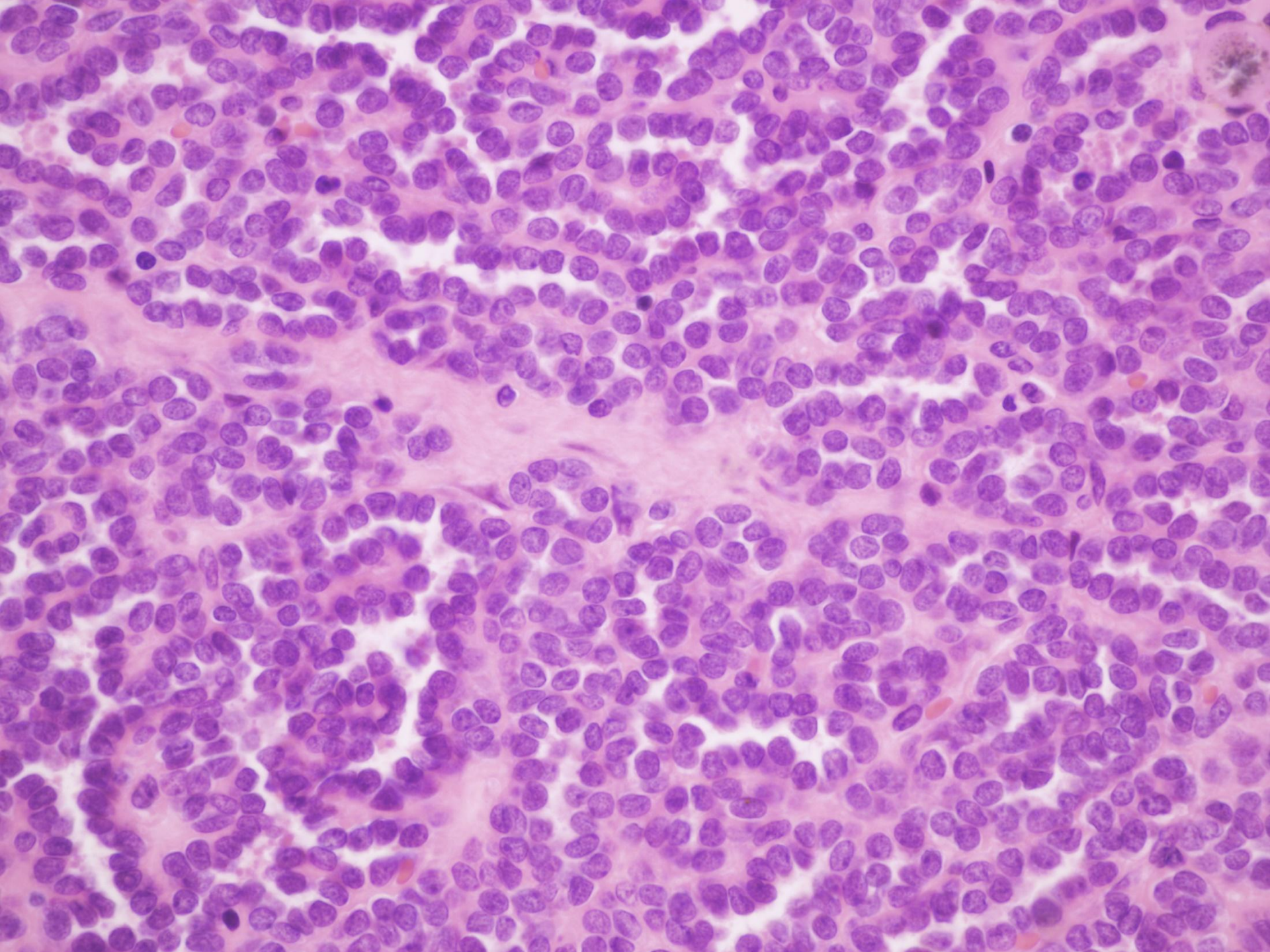
Grey-brown, solid, cystic degeneration may be present

Well-circumscribed but unencapsulated

Tubulary, solid, or papillary architecture

No mitoses

WT1+, CD57+, CK7-, EMA-



VI. Tumors of the kidney

Malignant tumors

1. Clear cell RCC

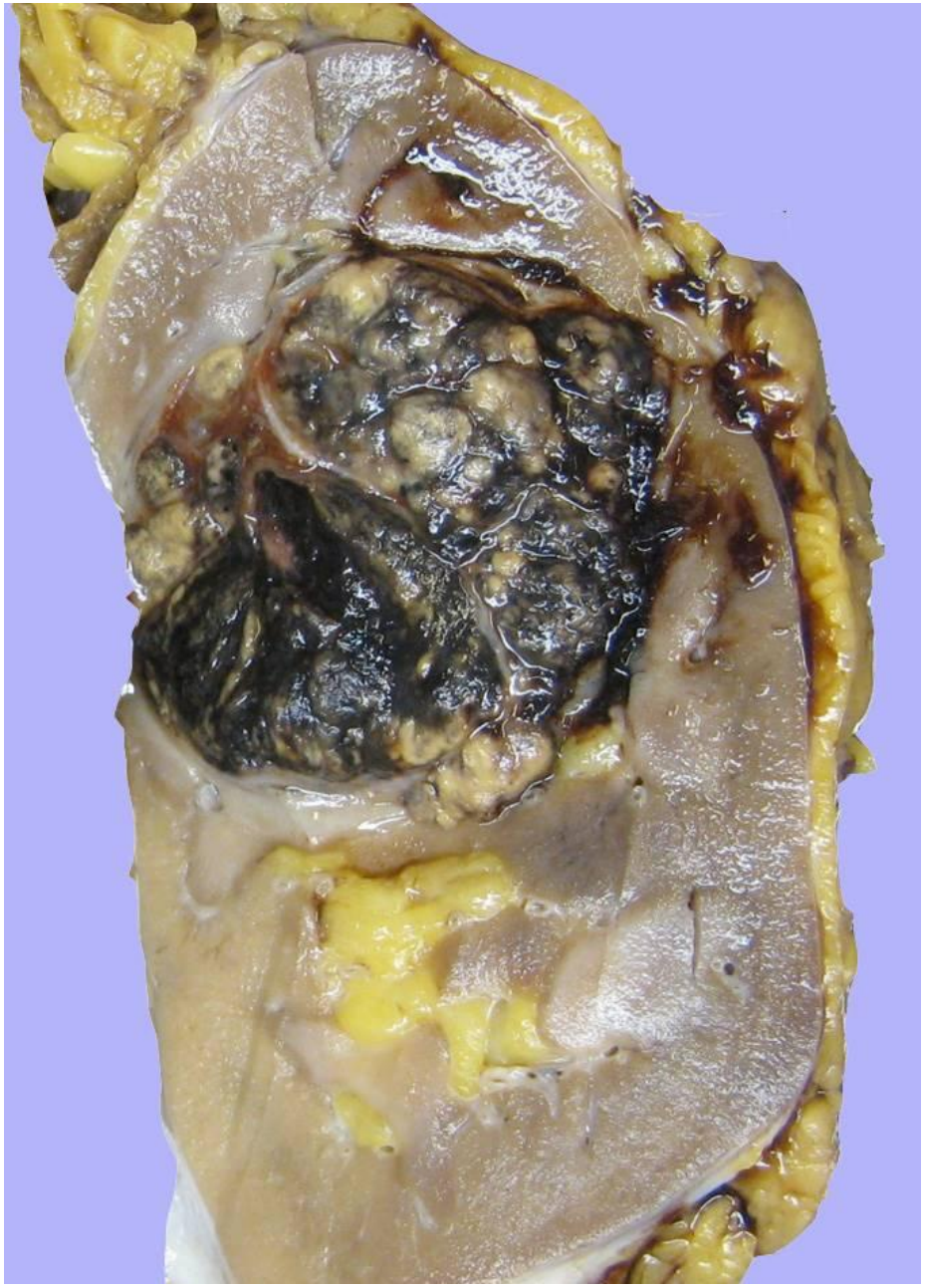
Most common type (approx. 80%)

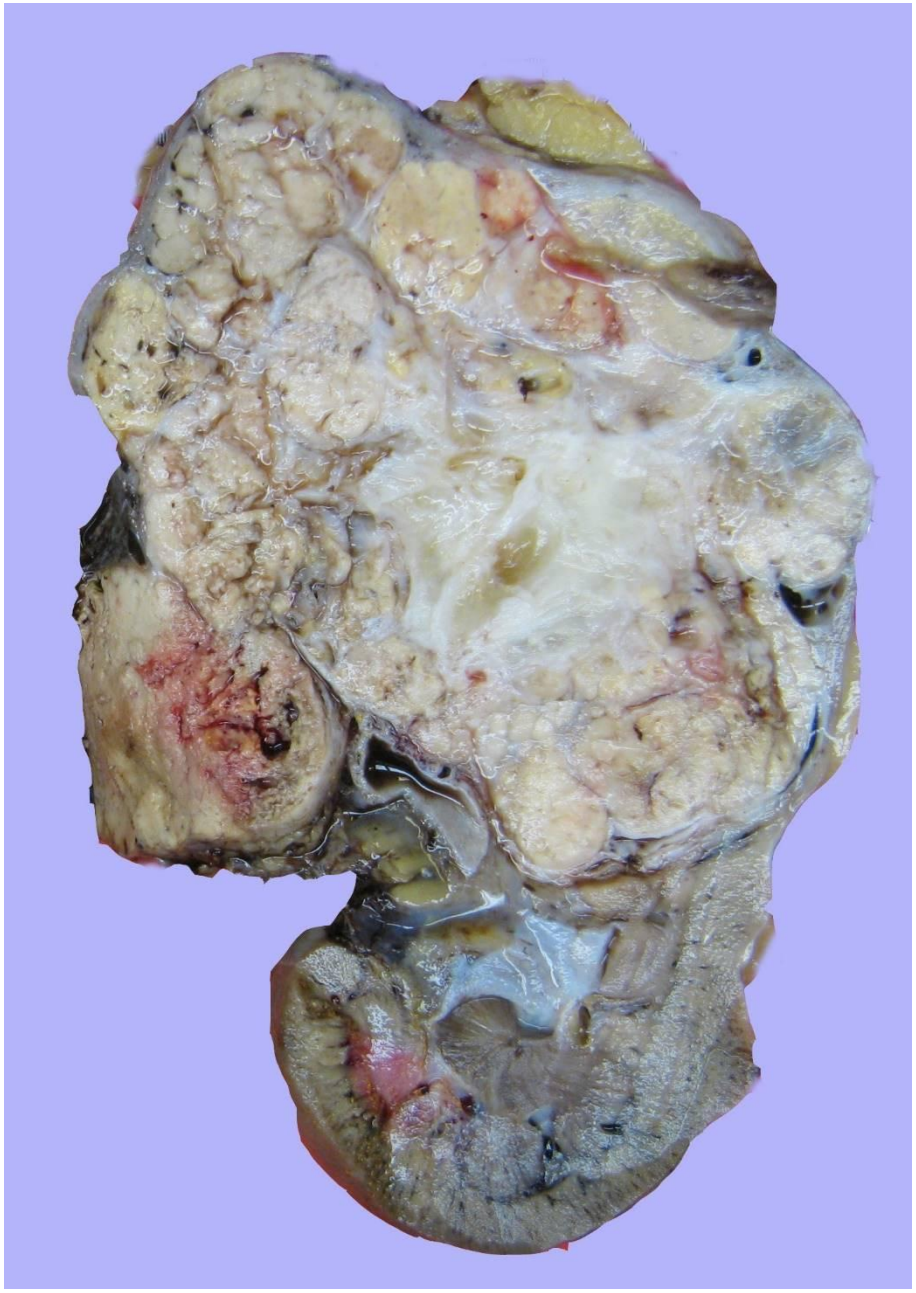
Characteristic golden yellow color

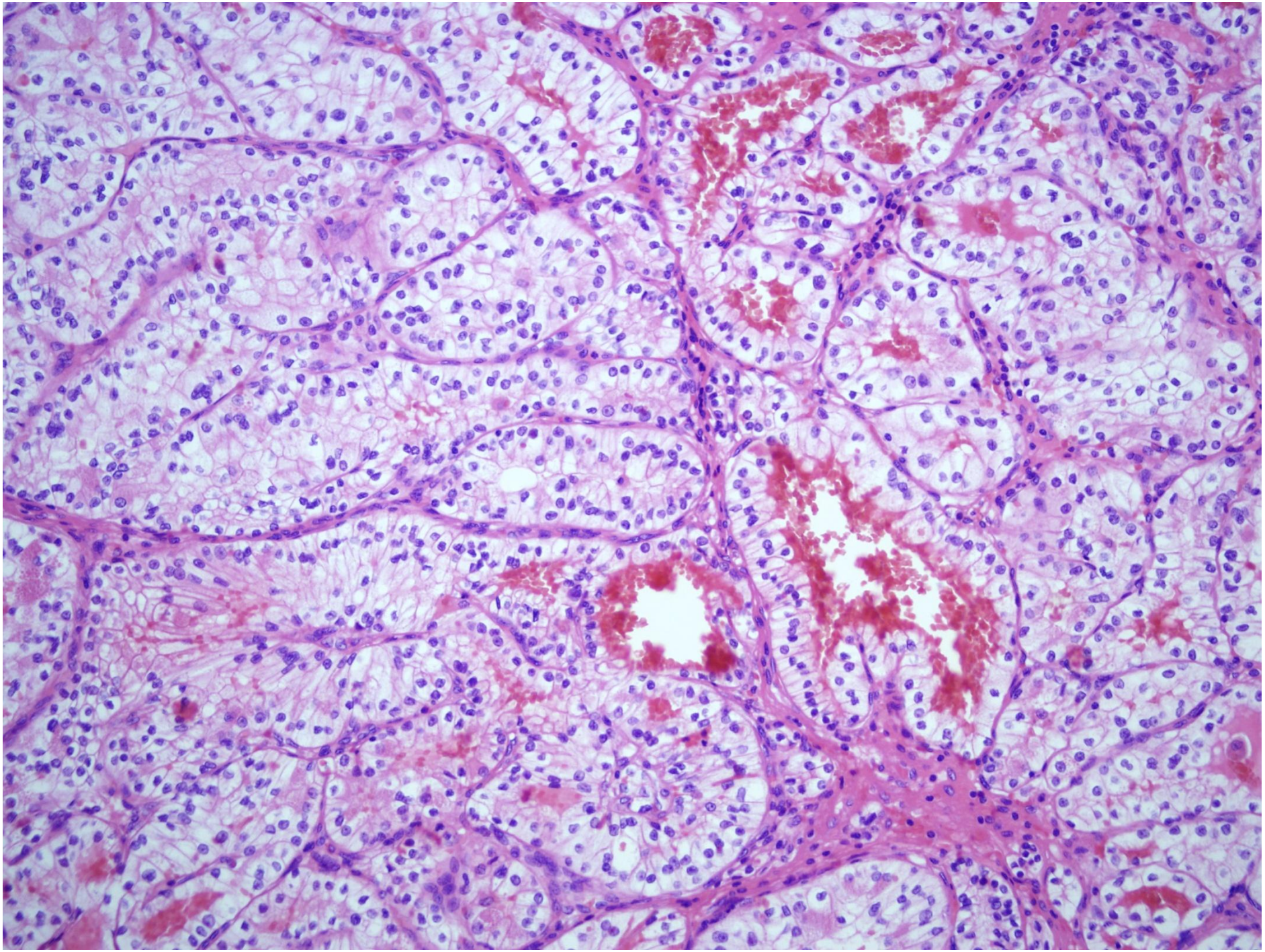
Variable architecture: solid, tubular, papillary, microcystic, cystic

Haemorrhages and necroses are usual

Genetic/epigenetic alteration: 3p deletion, VHL mutation, VHL hypermetilation







VI. Tumors of the kidney

Malignant tumors

2. Multilocular cystic renal neoplasm of low malignant potential

2-3% of RCCs

Middle-aged patients, usually incidentally detected

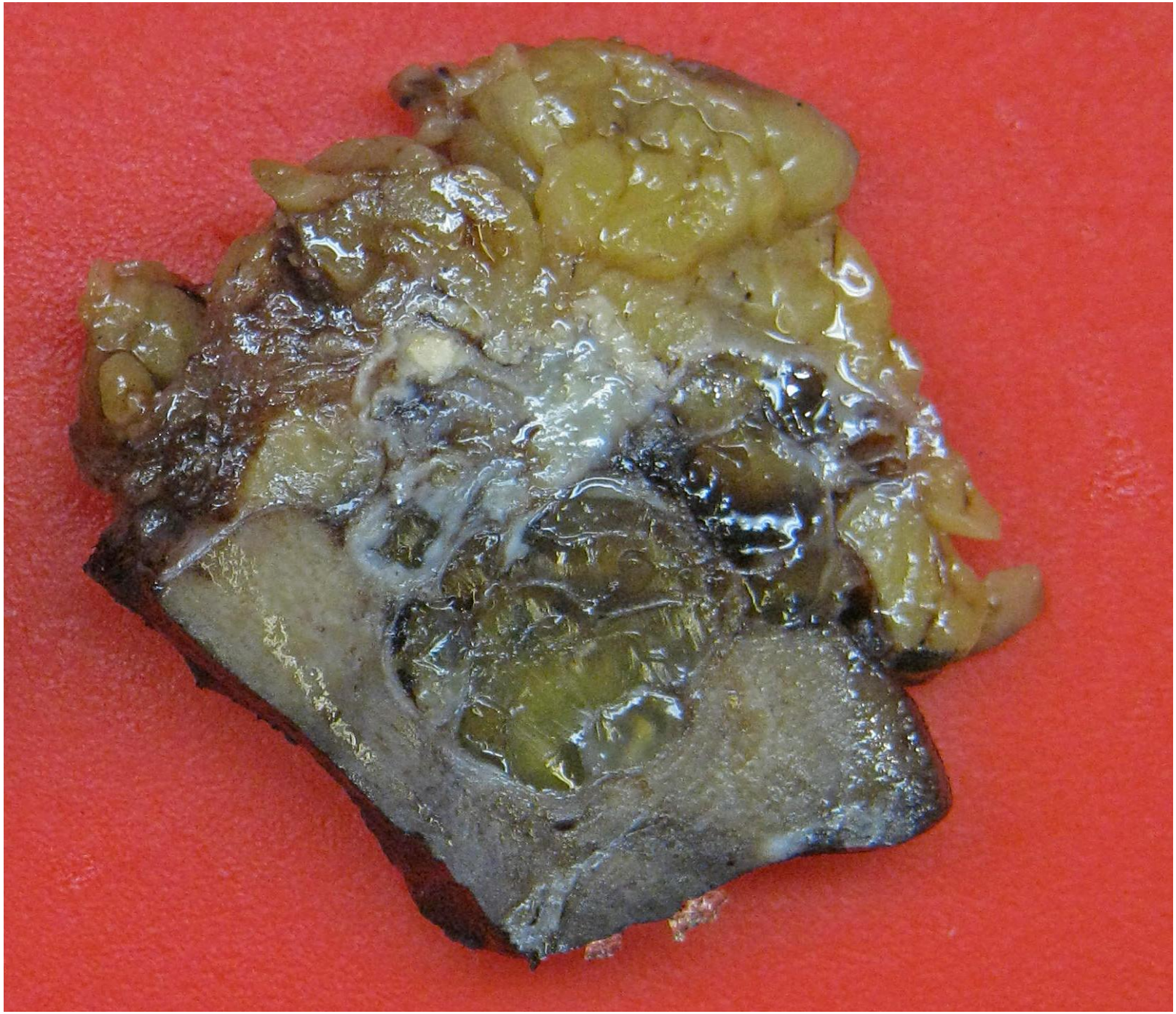
Complex cystic lesion by radiological examination

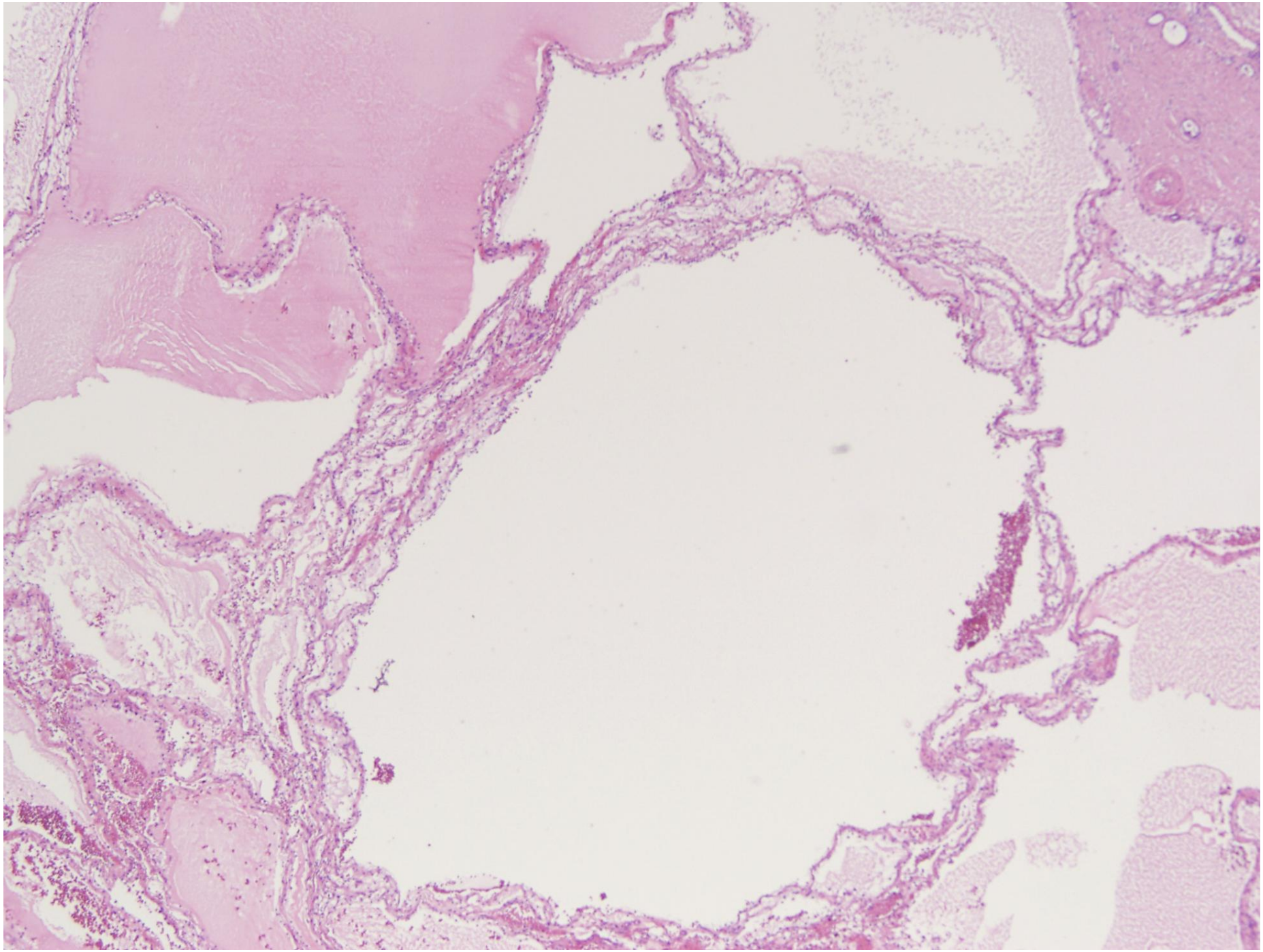
Composed exclusively of thin-walled cysts

Clear cyst content

Low-grade tumor cells: internal surface of cysts, small groups in the septums

Excellent prognosis





VI. Tumors of the kidney

Malignant tumors

3. Papillary RCC

Second most common (approx. 12-15%)

More commonly multifocal

Type 1

Grey-white, well-circumscribed, encapsulated, haemorrhages

Papillary, tubular, or solid architecture

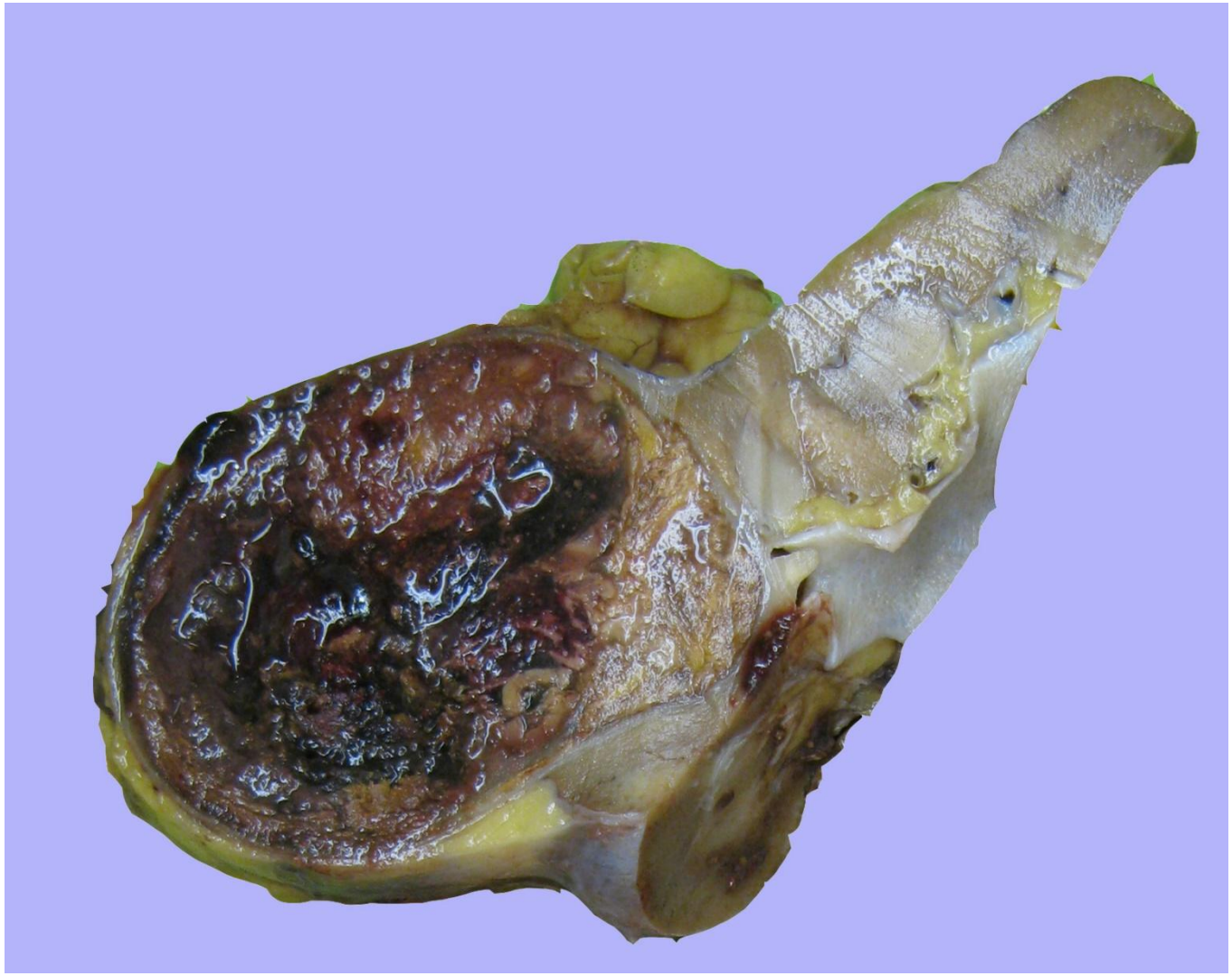
Cuboidal cells, foamy macrophages, psammoma bodies

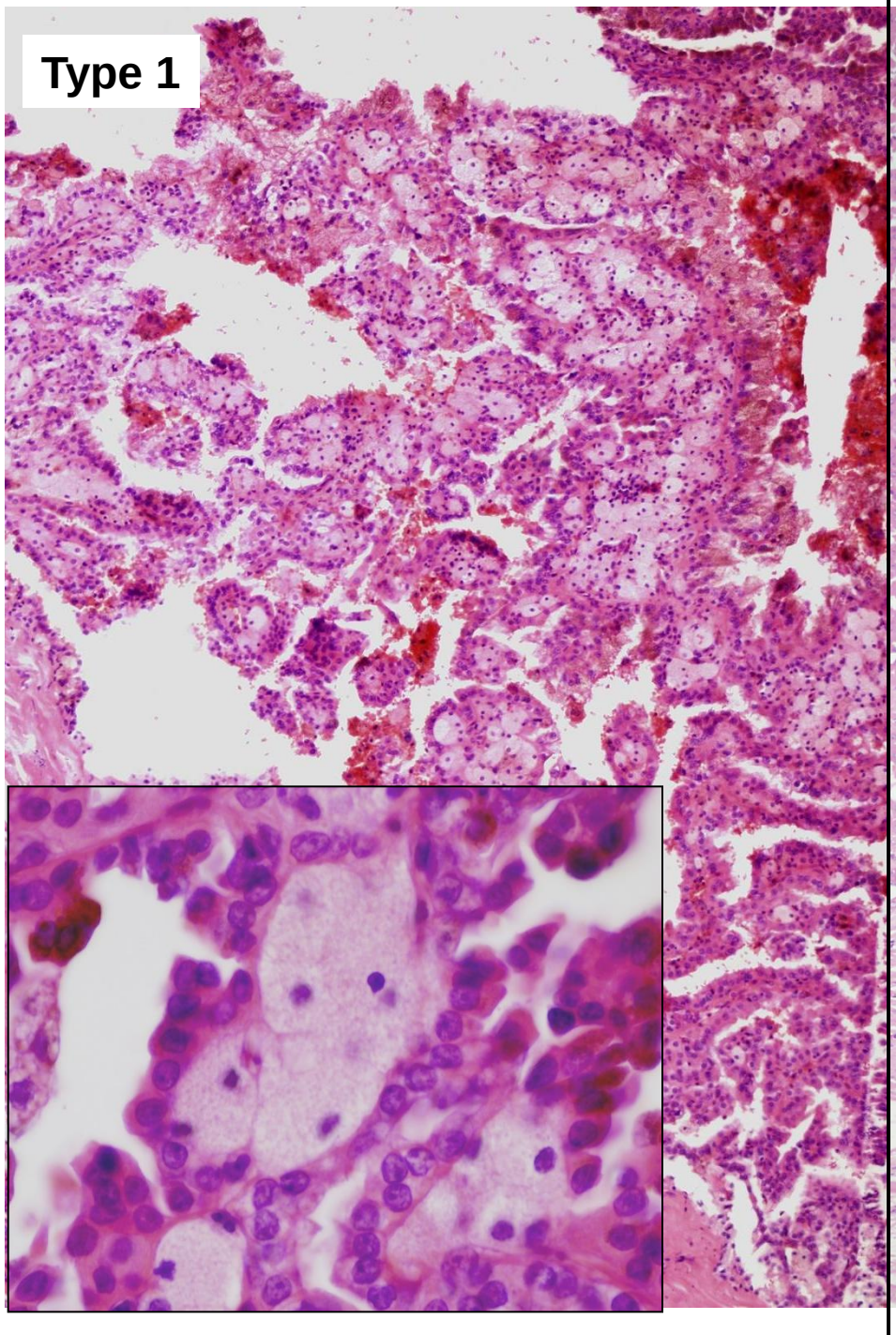
Type 2

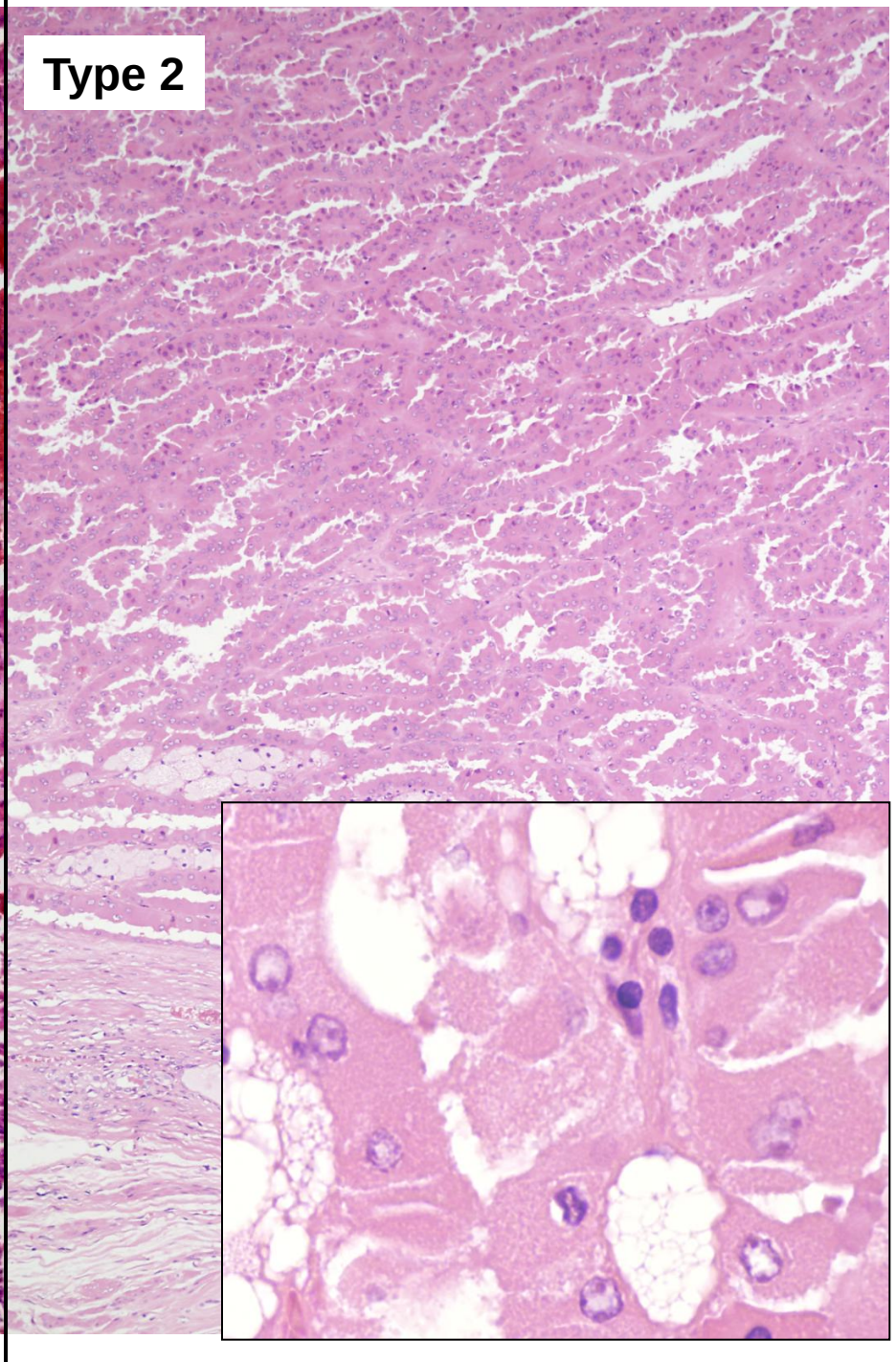
Variable appearance, necroses, haemorrhages

Larger cells, higher grade

Characteristic genetic alteration: trisomies (**7, 17**, 12, 16 20), loss of Y, c-Met mutation




Type 1


Type 2

VI. Tumors of the kidney

Malignant tumors

4. Chromophobe RCC

Approx. 4-5%

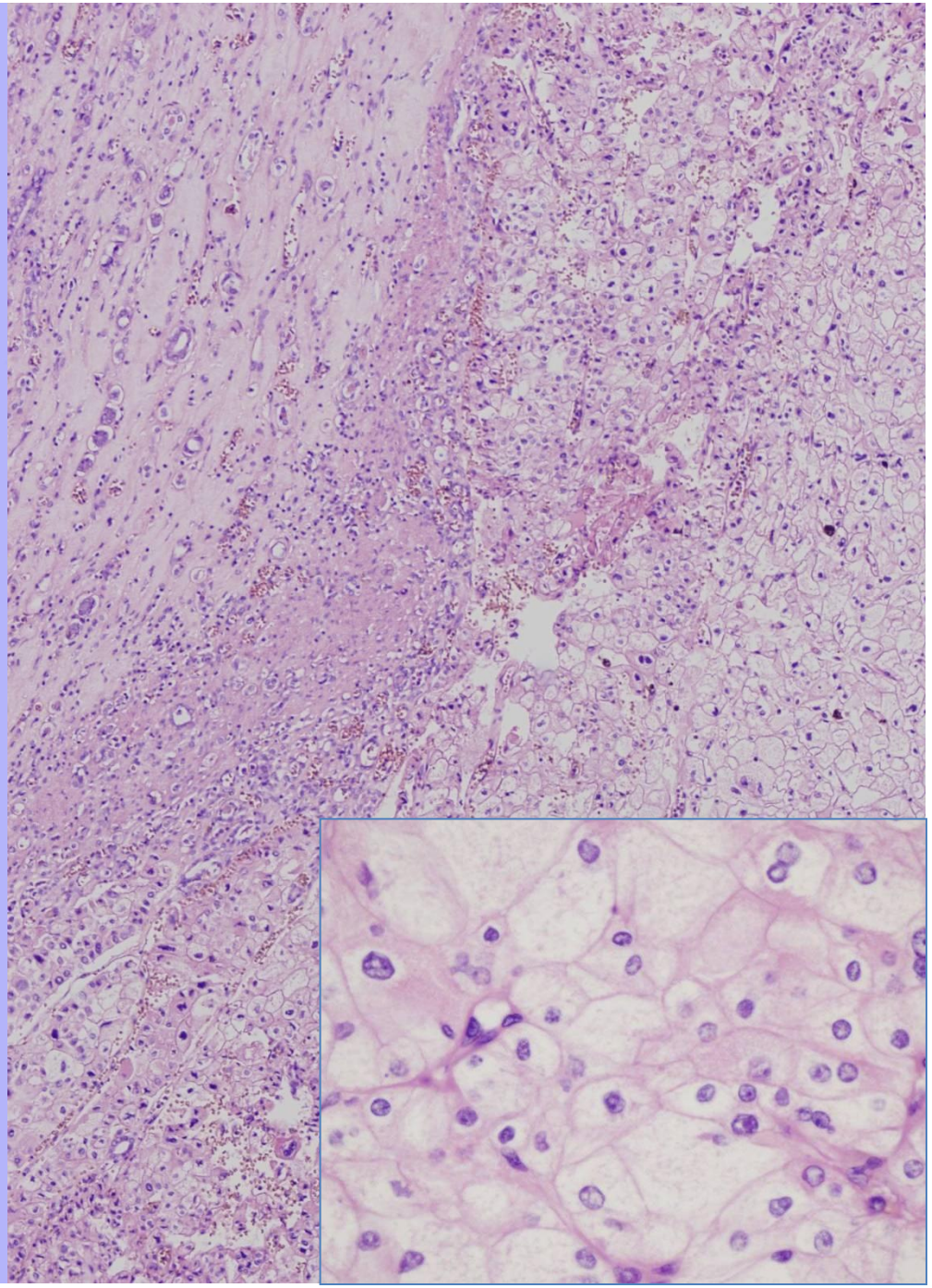
Well-circumscribed, grey-white

Clear or eosinophilic cytoplasm, distinct cell borders, binucleated figures, rasinoid nuclei, perinuclear halo

Widespread chromosomal losses

Better prognosis

DD: oncocytoma



VI. Tumors of the kidney

Malignant tumors

5. Clear cell papillary RCC

Originally descriped being associated with end-stage kidney disease

1-1,5% of renal cell tumors

Well-circumscribed, encapsulated, grey-brown

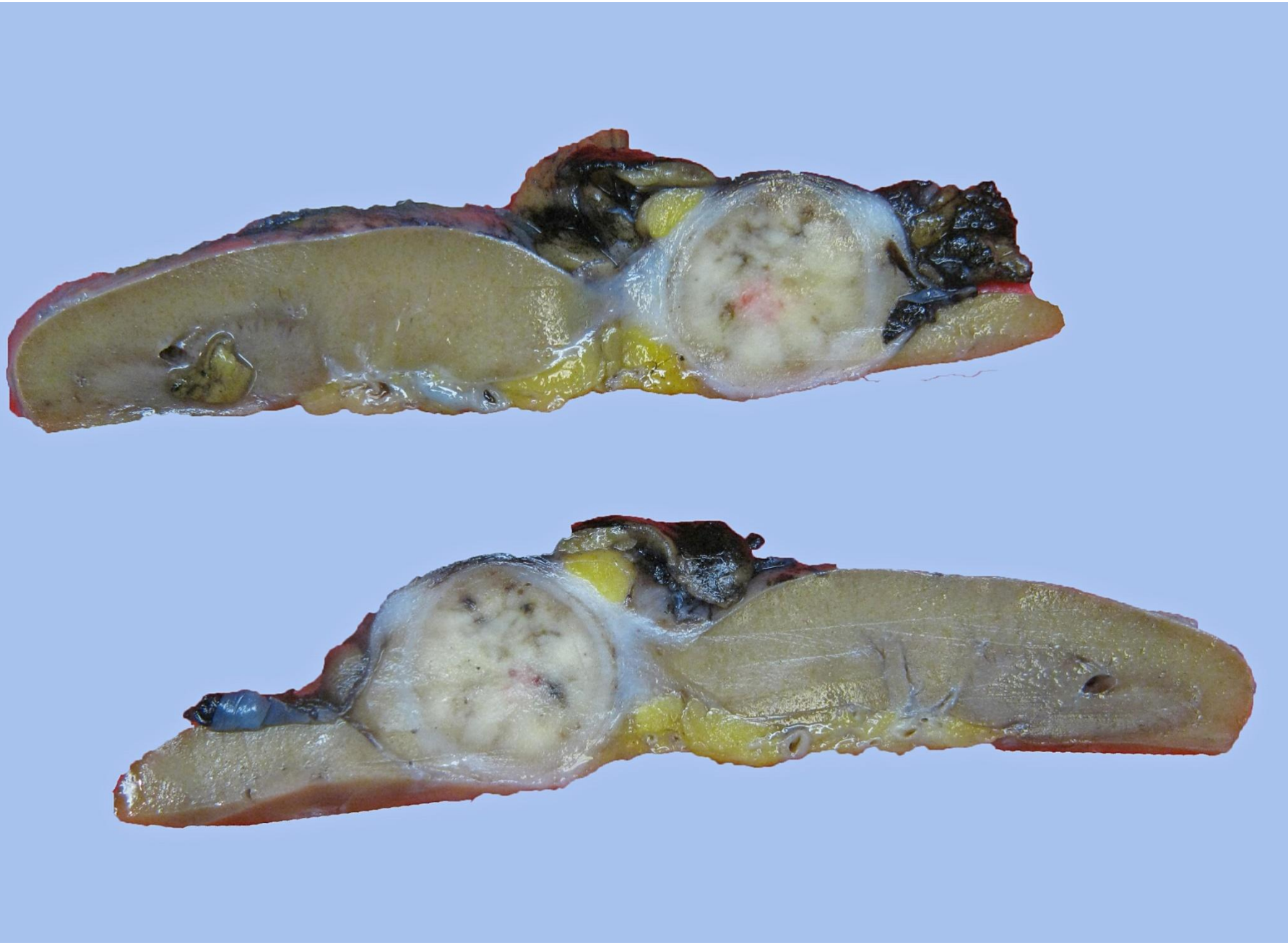
Solid and cystic areas

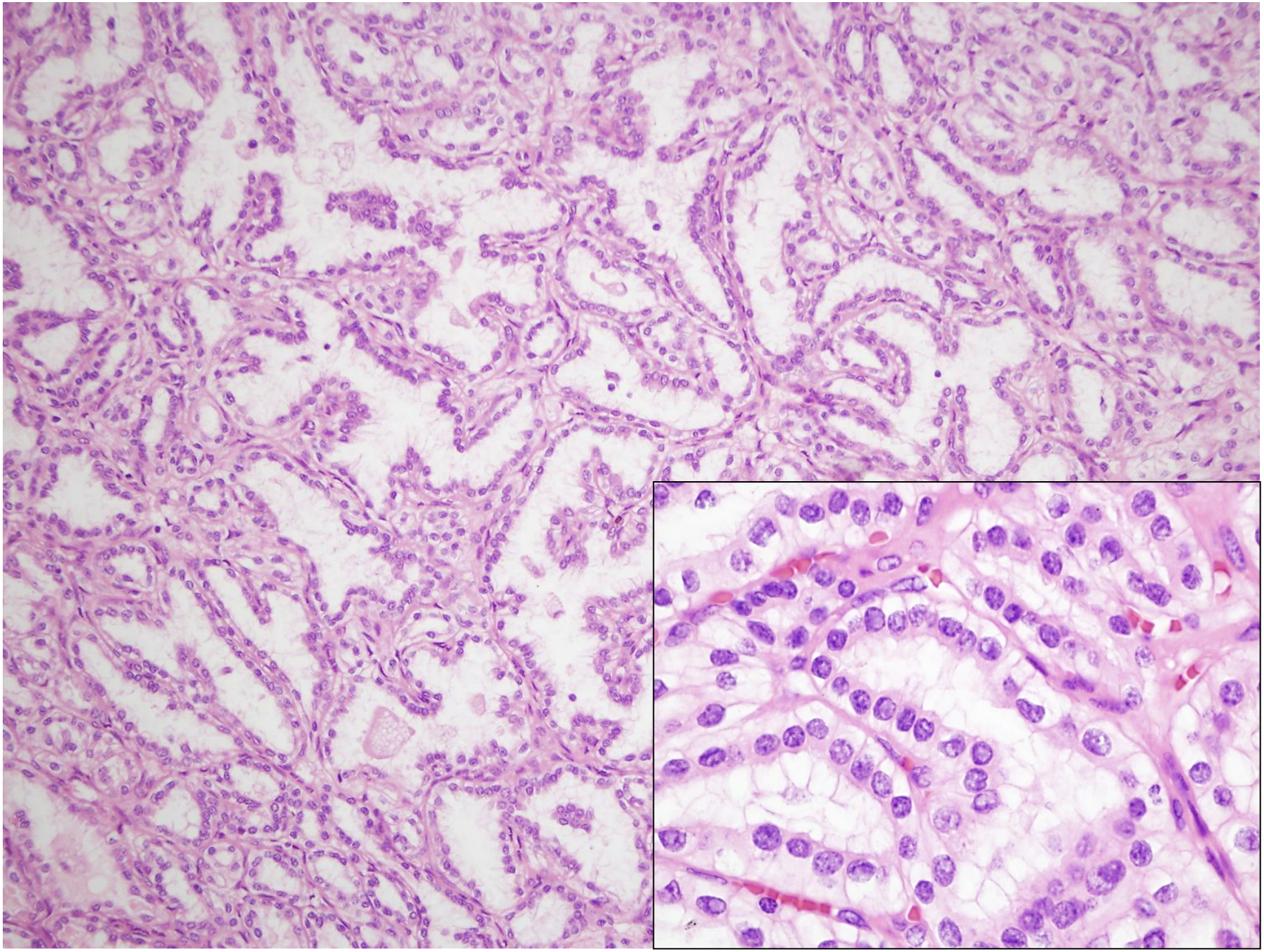
Mostly branching tubular, less commonly papillary architecture

Clear cells with low-grade morphology

Subnuclear vacuolization

Indolent behavior (no metastatic case has been published to date)





VI. Tumors of the kidney

Malignant tumors

Rare types

Collecting duct (Bellini) carcinoma

Hereditary leiomyomatosis and renal cell carcinoma-associated RCC

MiT gene family translocation RCC

Succinate dehydrogenase-deficient RCC

Tubulocystic RCC

Acquired cystic disease-associated RCC

Mucinous tubular and spindle cell RCC

Medullary RCC

VI. Tumors of the kidney

Pediatric tumors

1. Nephroblastoma (Wilms tumor)

Malignant tumor that derives from nephrogenic blastema cells

10% associated with congenital malformations (e.g. WAGR)

98% diagnosed prior to age 10 years, very rarely detected in adults

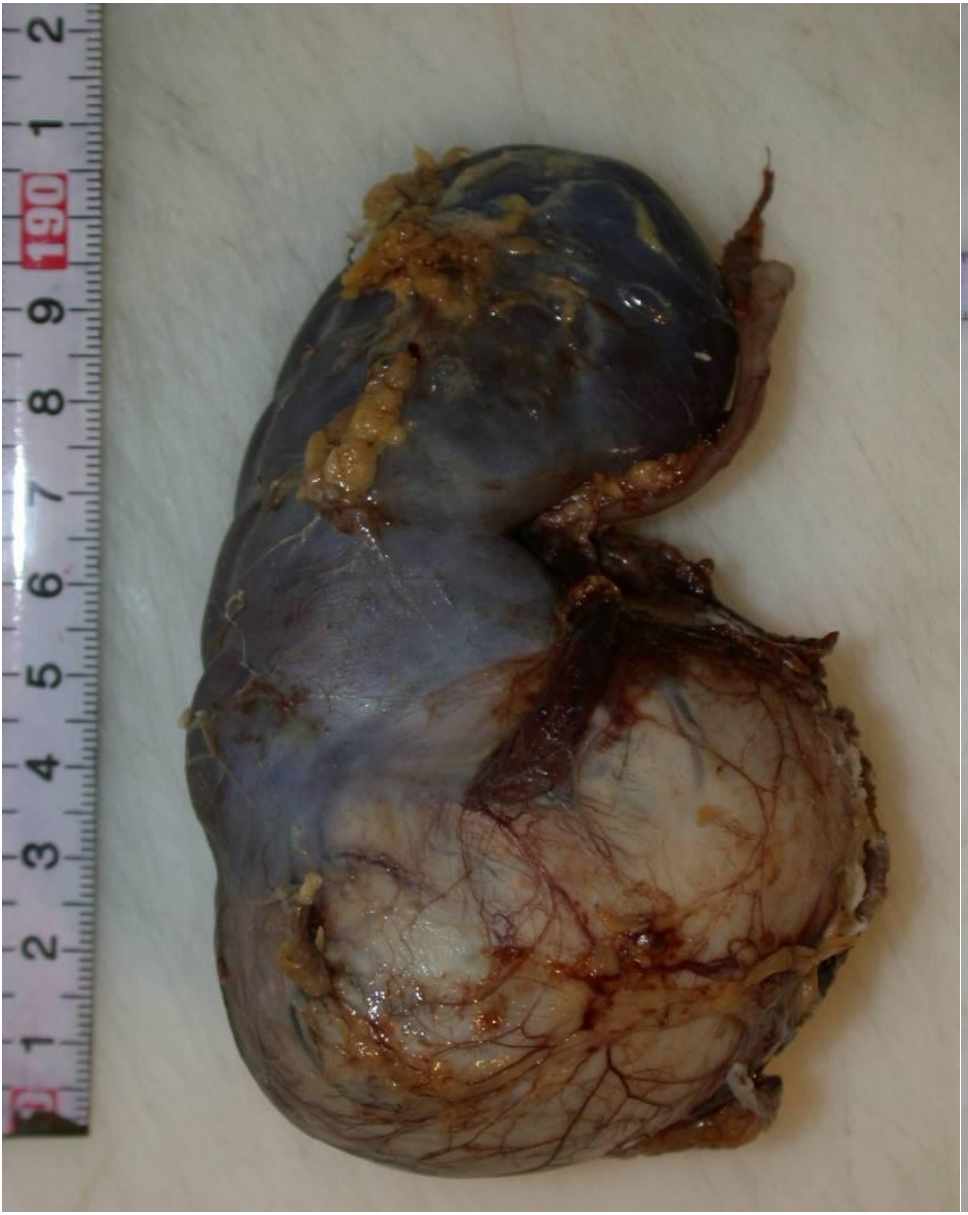
Palpable abdominal mass, abdominal pain, haematuria

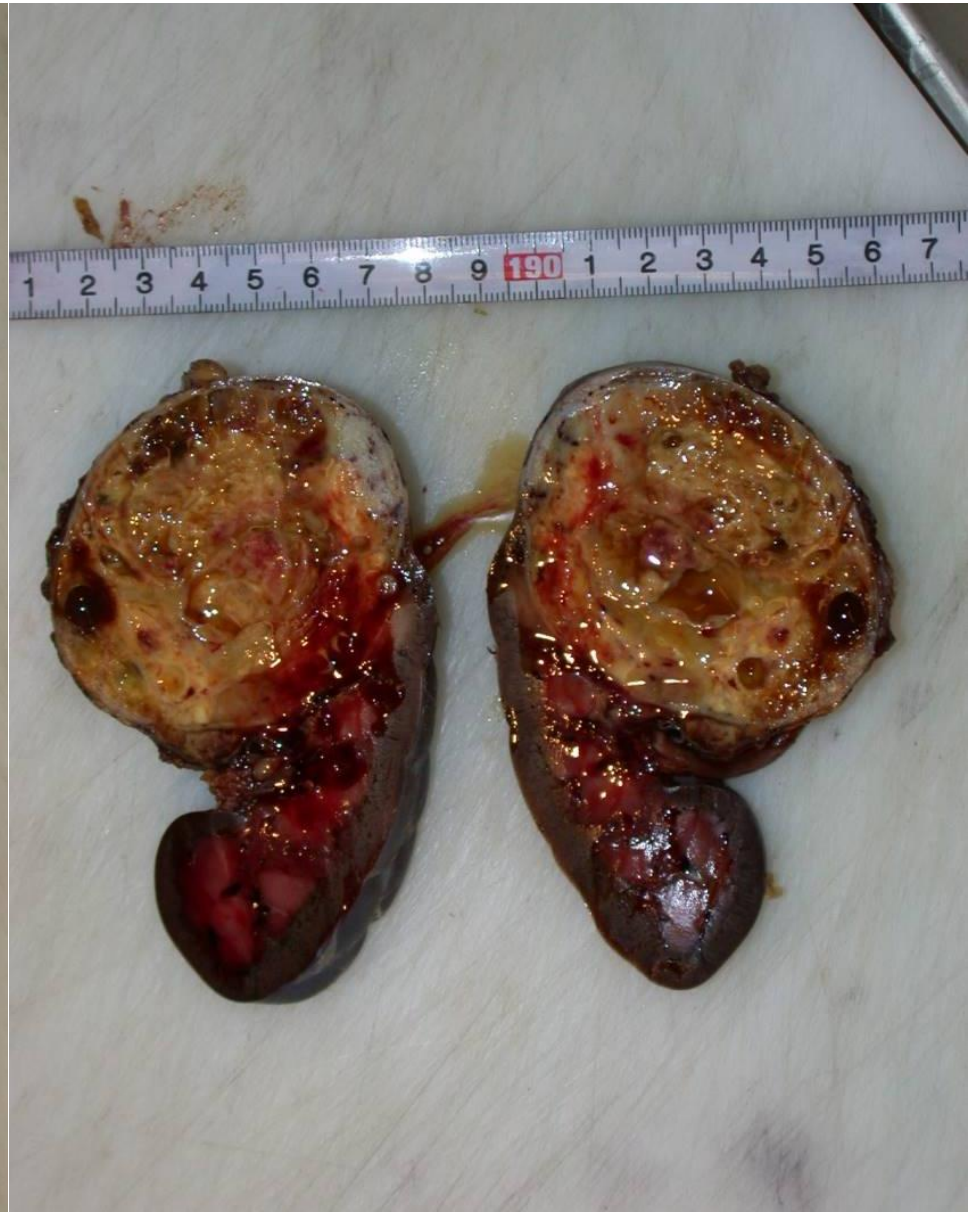
10% bilateral, greyish tumor, cystic areas

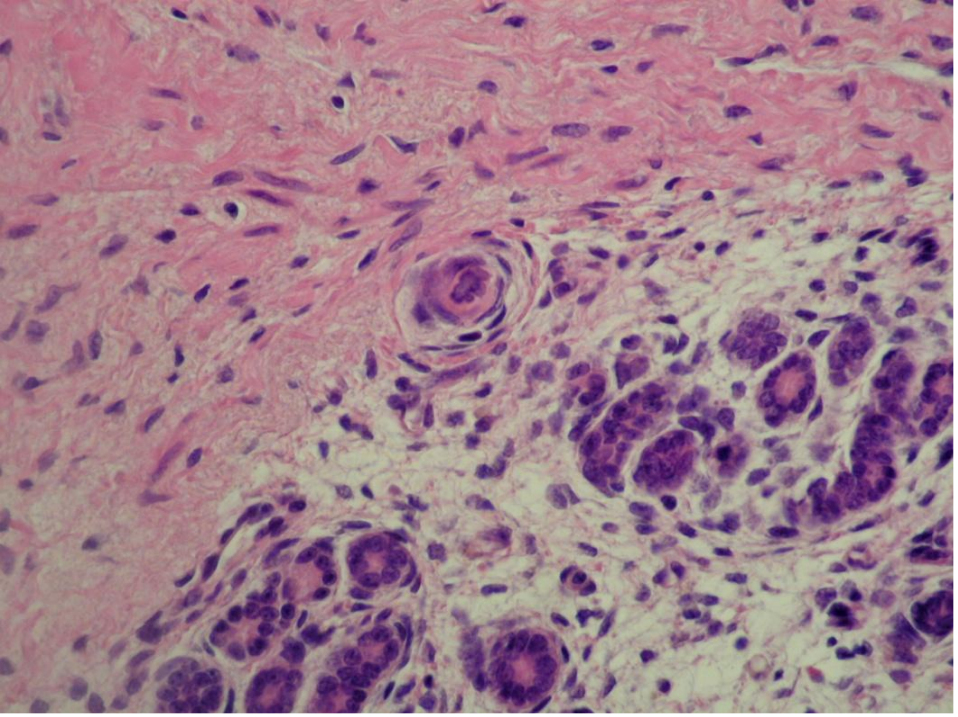
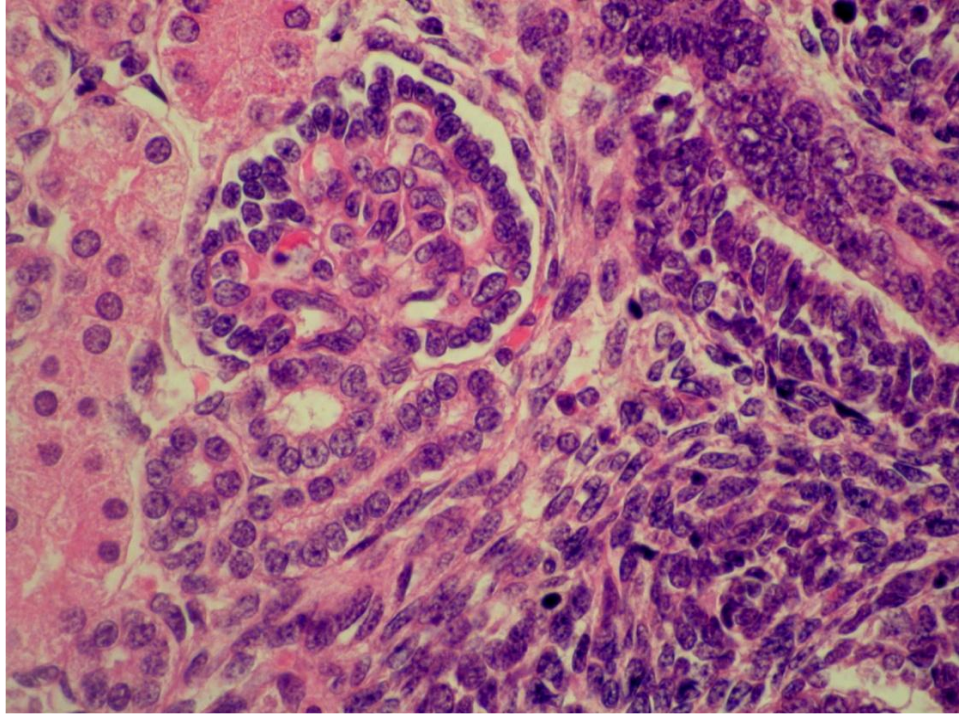
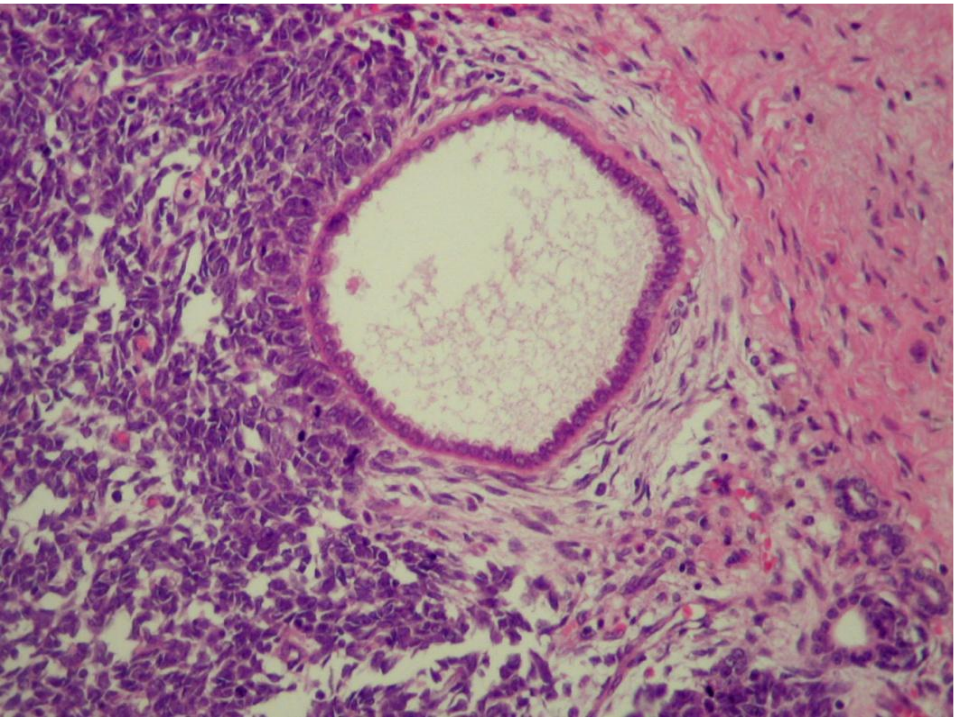
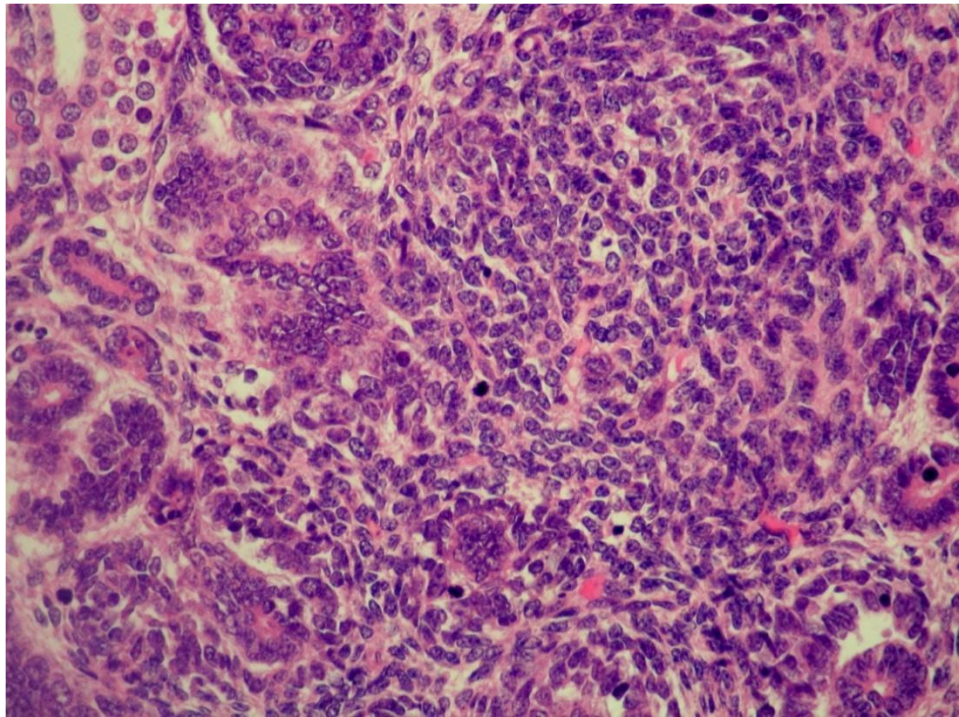
Triphasic appearance: blastema cells, epithelial elements, stroma

WT1 deletion in 1/3, as well as WT1 mutation in 1/10 of sporadic cases

Usually good prognosis





VI. Tumors of the kidney

Pediatric tumors

2. Mesoblastic nephroma

Derives from nephrogenic mesenchyme

Congenital tumor

Indolent behavior

3. Clear cell sarcoma of the kidney

Derives from nephrogenic mesenchyme

Mean age of presentation is 2 years

Bone metastases

Poor outcome

4. Rhabdoid tumor of the kidney

Large eosinophilic cytoplasma, excentric nuclei

Prior to age 2 years

Poor prognosis

VI. Tumors of the kidney

Genetic background of RCCs

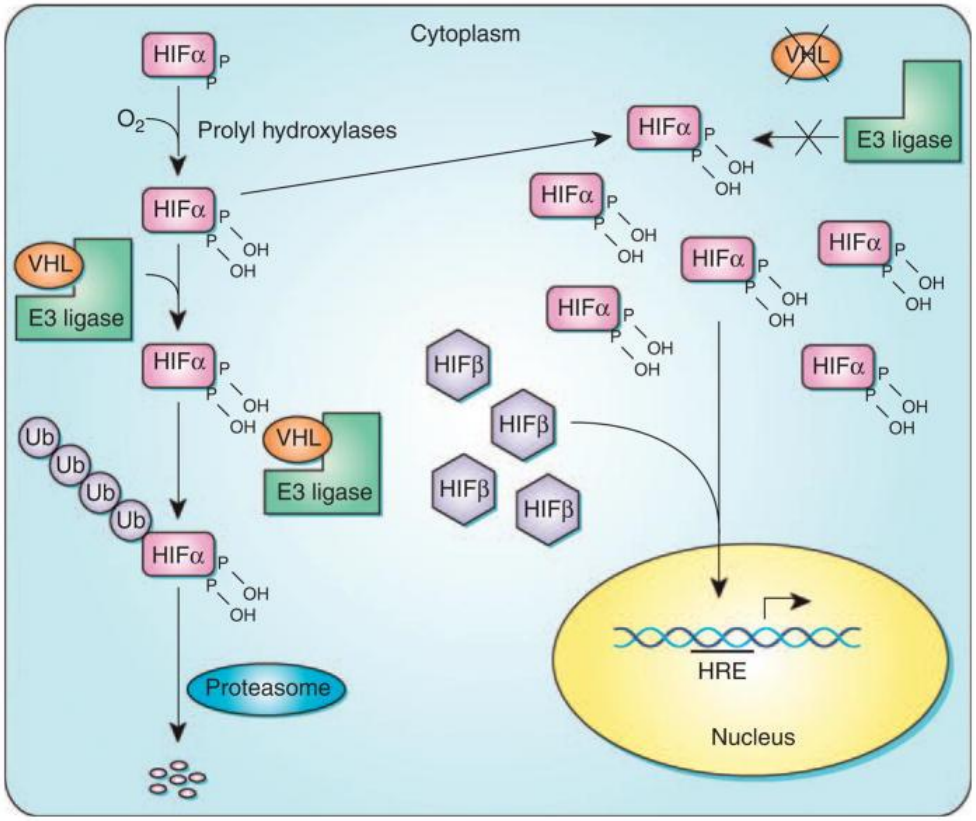
VHL gene

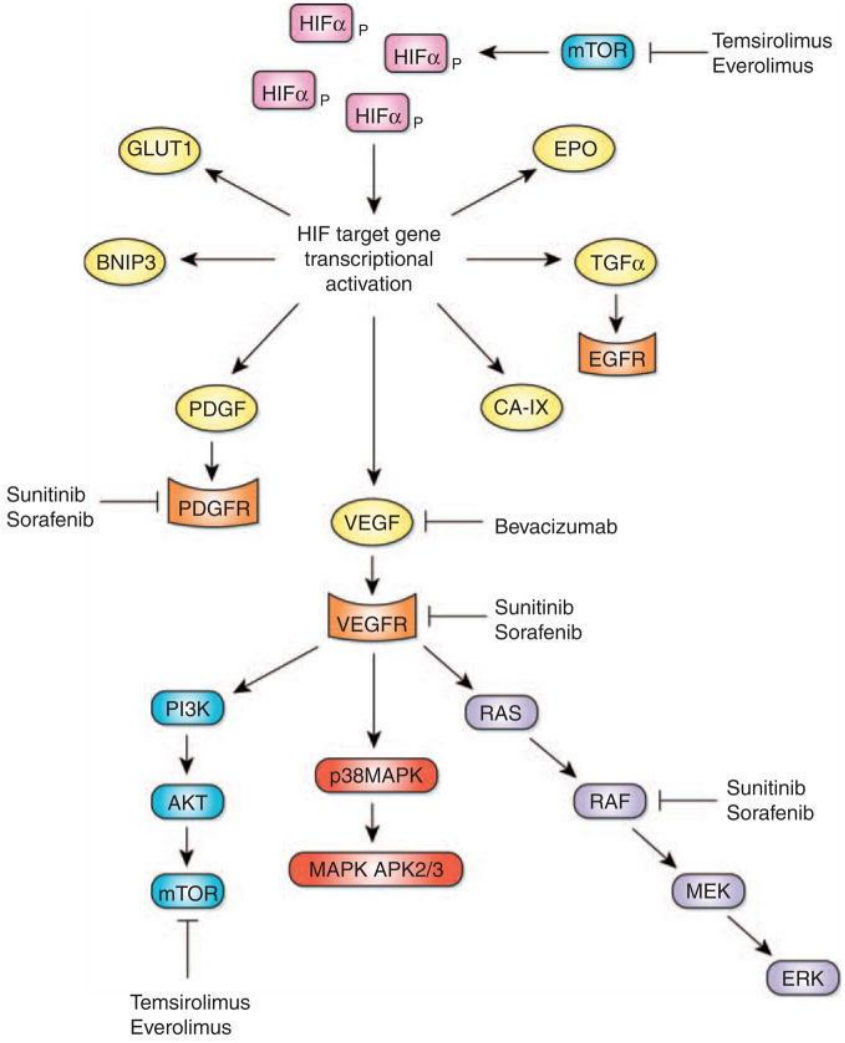
von Hippel-Lindau syndrome

sporadic clear cell RCCs

Degradation of HIF1 (hypoxia-inducible factor, HIF1α, HIF2 α)

HIF target genes: MAPK pathway, mTOR pathway, c-Myc





Kidney Int. 2009 Nov; 76(9): 939–945.

VI. Tumors of the kidney

Genetic background of RCCs

MET gene

Product: c-Met/HGF receptor

Hereditary papillary RCC

Mutation of MET can be detected in a subset of type 1 papillary RCCs

c-Met inhibitor: foretinib

TSC1/TSC2

Tuberous sclerosis complex

Renal manifestation of tuberous sclerosis: angiomyolipoma, clear cell RCC

mTOR pathway

VI. Tumors of the kidney

Genetic background of RCCs

Folliculin

Birt-Hogg-Dubé syndrome

Fumarate hydratase

Hereditary leiomyomatosis and renal cell carcinoma

HIF1 accumulation

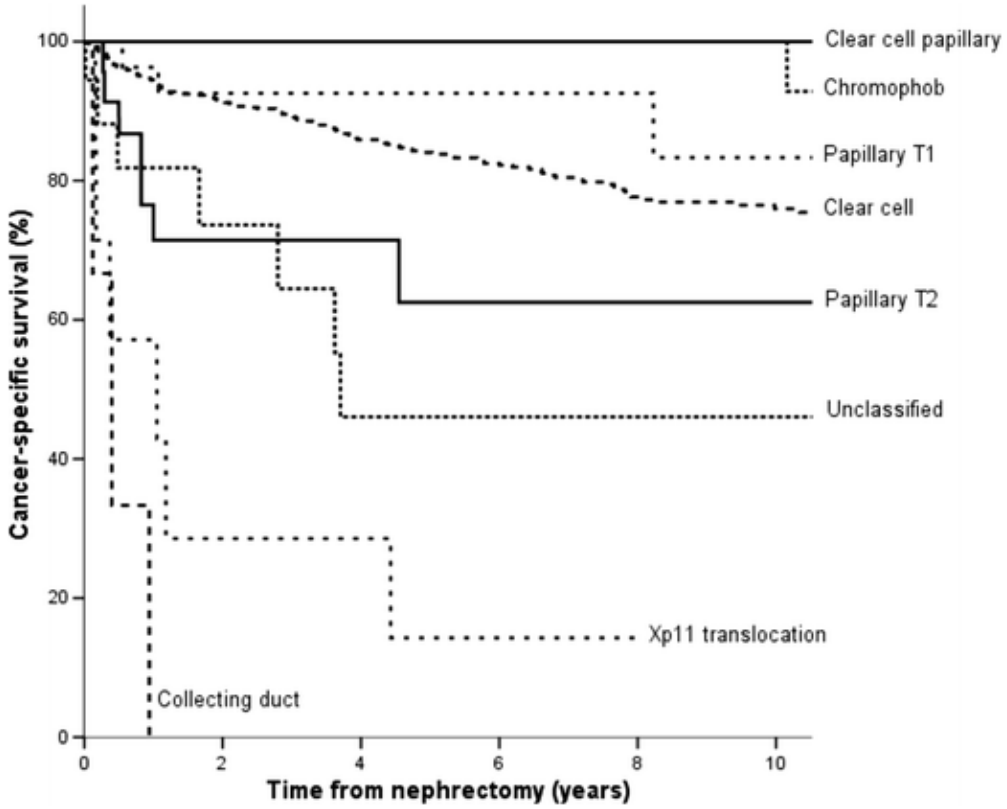
Succinate dehydrogenase

Paraganglioma, pheochromocytoma, RCC

VI. Tumors of the kidney

Prognostic factors

Tumor type



Kuthi L et al. Pathol Oncol Res. 2017 Jul;23(3):689-698.

VI. Tumors of the kidney

Prognostic factors

Stage

pT:

pT1 – tumor ≤7 cm in greatest dimension, limited to the kidney (pT1a ≤4 cm, pT1b >4 cm)

pT2 – tumor >7 cm in greatest dimension, limited to the kidney (pT2a ≤10 cm, pT2b >10 cm)

pT3 – tumor extends into major veins (renal vein, VCI) or perinephric tissues (ERE) (pT3a renal vein invasion and/or ERE, pT3b VCI invasion below diaphragm, pT3c VCI invasion above diaphragm)

pT4 – tumor invades beyond the Gerota fascia (including contiguous extension into the ipsilateral adrenal gland)

VI. Tumors of the kidney

Prognostic factors

Grade:

Fuhrman grade/ISUP grade

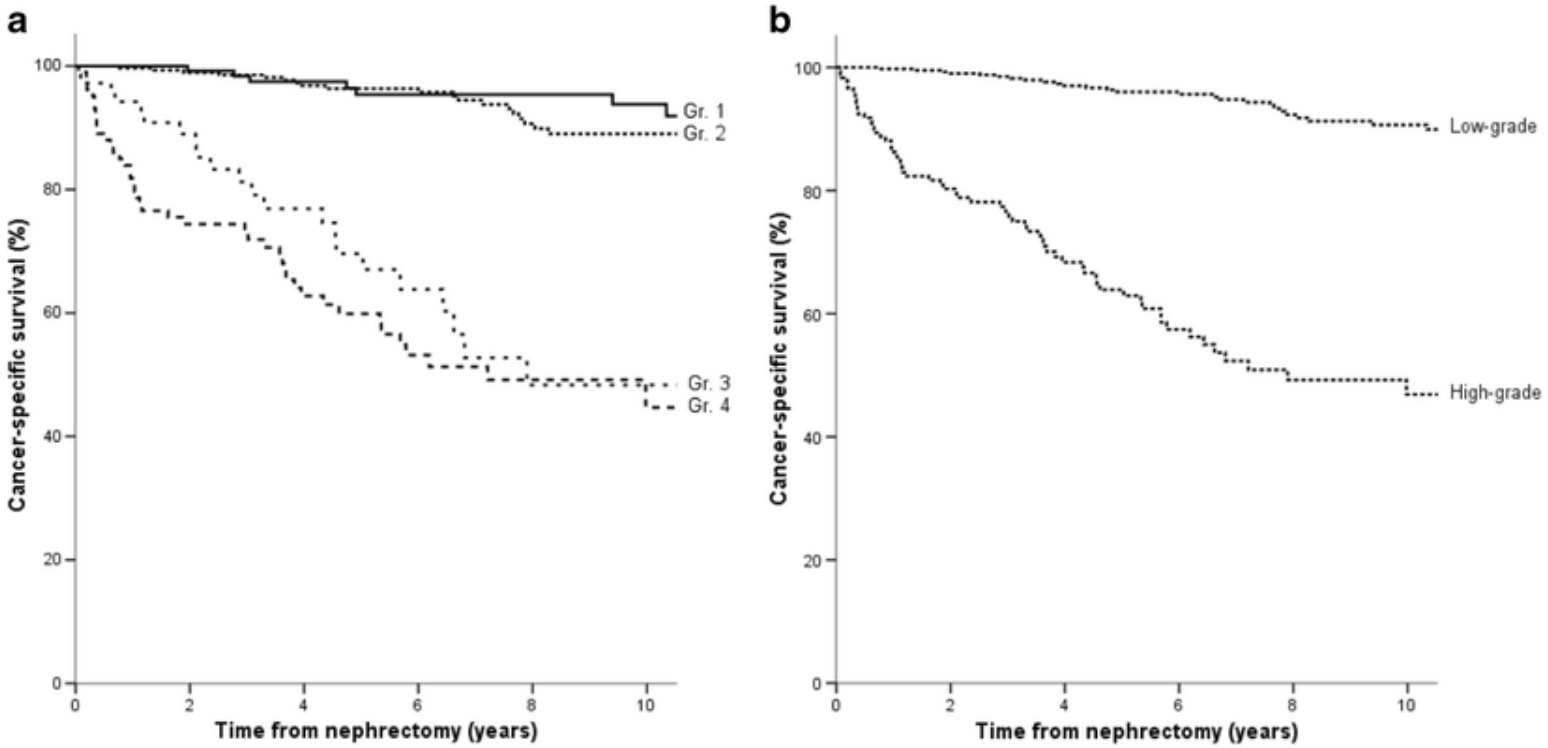
Clear cell RCC, papillary RCC

VI. Tumors of the kidney

Prognostic factors

Grade:

Fuhrman grade/ISUP grade



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VI. Tumors of the kidney

Prognostic factors

Table 2 Cox regression analysis for cancer-specific survival rates in non-metastatic clear cell RCC

Characteristic	Hazard ratio	CI 95%	*p* value
Univariate			
ISUP grade	7.50	5.01–11.21	<0.001
TNM stage	2.54	2.04–3.15	<0.001
Surgical margin status	2.95	1.57–5.53	<0.001
Microscopic tumor necrosis	6.74	4.53–10.07	<0.001
Rhabdoid/sarcomatoid change	5.14	3.39–7.78	<0.001
Giant tumor cells	3.93	2.51–6.15	<0.001
Multivariate			
ISUP grade	4.33	2.36–7.95	<0.001
TNM stage	1.86	1.49–2.33	<0.001
Surgical margin status	2.61	1.39–5.2	0.003
Microscopic tumor necrosis	1.69	0.93–3.05	0.081
Rhabdoid/sarcomatoid change	0.96	0.57–1.61	0.896
Giant tumor cells	0.67	0.4–1.13	0.139

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VI. Tumors of the kidney

Clinical features

1. Symptomes

Costovertebral pain

Hematuria

Palpable mass

Fever (FUO)

Weight loss

Malaise

Paraneoplastic syndromes (polycythemia, hypercalcemia, hypertension, hepatic dysfunction, feminization, masculinization, Cushing syndrome, eosinophilia, leukemoid reaction, amyloidosis)

Symptomes of metastases (any organ can be affected)

VI. Tumors of the kidney

Clinical features

2. Diagnostics

Majority of renal tumors are discovered incidentally by abdominal imaging

US, CT, MR

Preoperative diagnostics: FNAB, core biopsy (US- or CT-guided)

VI. Tumors of the kidney

Clinical features

3. Treatment

Partial (pT1 tumors) or radical nephrectomy (open or laparoscopic surgery)

Targeted therapy (metastatic cases): sunitinib,

Acknowledgement

Eszter Székely

For a subset of the pictures