RENAL TUMORS

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RENAL TUMORS

- Benign neoplasms such as small cortical papillary adenomas (<0.5 cm in diameter) are found in up to 40% of adults in autopsies.
- The most common malignant neoplasm of the kidney is renal cell carcinoma.
- Nephroblastoma (Wilms tumor) is the second most common type of tumors.

ONCOCYTOMA

- A benign neoplasm that arises from the intercalated cells of collecting ducts.
- It represents about 10% of renal neoplasms.
- It is associated with loss of chromosomes 1 and Y—that is characteristic.

- **Oncocytomas are characterized by a plethora of mitochondria causing tan color and finely granular eosinophilic cytoplasm seen histologically.**
- **A central stellate scar is a characteristic feature of oncocytomas seen on imaging studies.**

RENAL CELL CARCINOMA

- It is derived from the renal tubular epithelium
- Located predominantly in the cortex.
- Represents 80-85% of all primary malignant neoplasms of the kidney and 2- 3% of all cancers in adults.
- Most common from the 6^{th} -7^{th}
- M:F 2:1

- **Risk factors:**

1. **Smoking**
2. **Hypertension**
3. **Obesity**
4. **Occupational exposure to cadmium**
5. **Acquired polycystic renal disease (30X increase)**
6. **Genetic**

Classification

The three most common forms are:

1. Clear cell carcinoma
2. Papillary renal cell carcinoma
3. Chromophobe renalcarcinoma

CLEAR CELL CARCINOMA

- It is the most common type
- 65% of renal cell cancers
- Mostly are sporadic but also occur in familial forms or in association with von Hippel-Lindau (VHL) disease
- Histologically they are composed of cells with clear cytoplasm.

- **VHL disease is inherited as an autosomal dominant trait**
- **It is characterized by:**

1. Predisposition to a variety of neoplasms but particularly to hemangioblastomas of the cerebellum and retina

2. Bilateral renal cysts and bilateral multiple clear cell carcinomas (in 40-60% of affected individuals

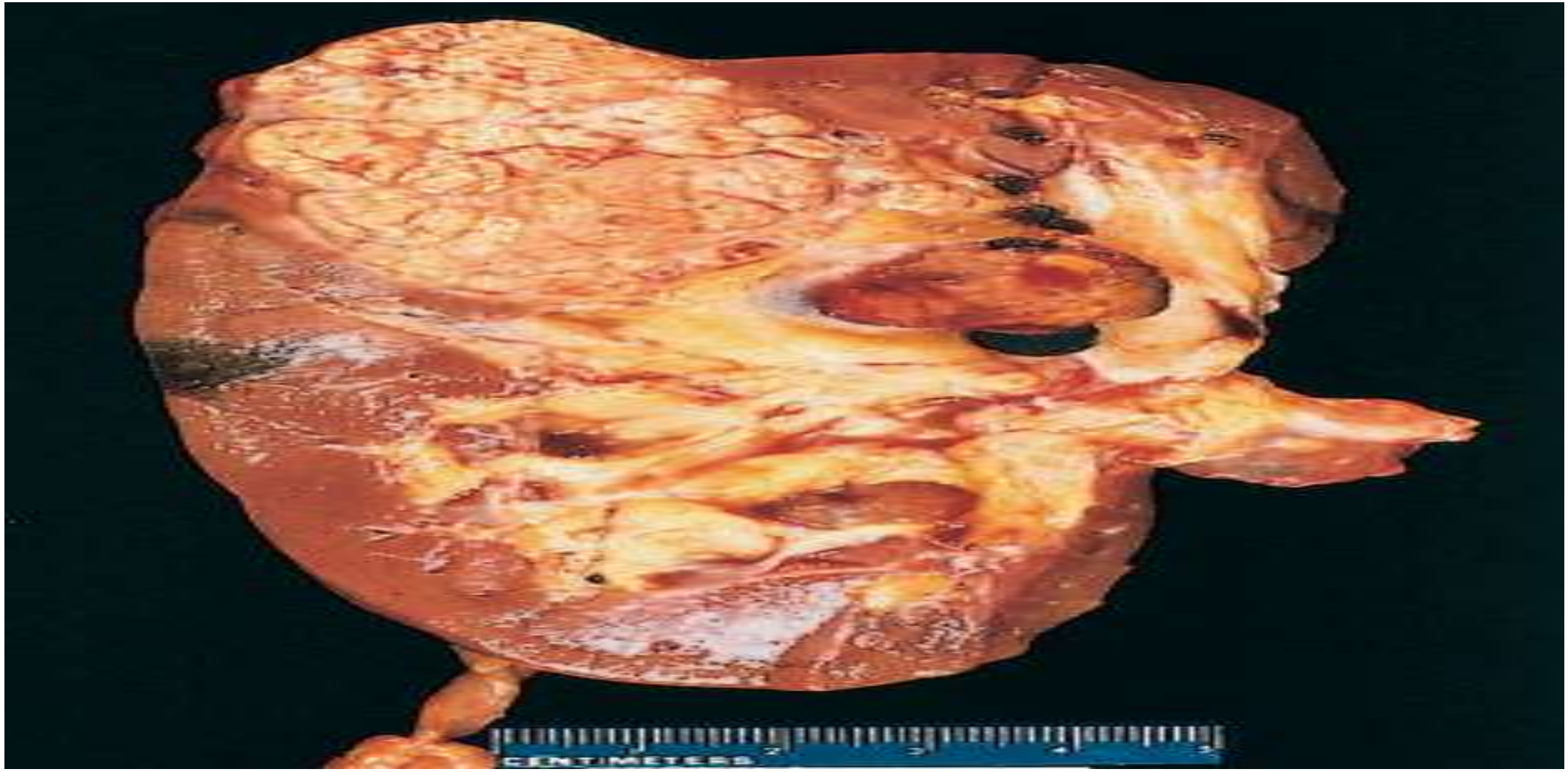
- **Those with VHL disease inherit a germline mutation of the *VHL* gene on chromosomal band 3p25 and lose the second allele by somatic mutation**
- **The *VHL* gene also is involved in the majority of sporadic clear cell carcinomas**
- **Loss of a segment on chromosome 3p that harbors the *VHL* gene are often seen in sporadic renal cell cancers**
- **The second, nondeleted allele is inactivated by a somatic mutation or hypermethylation in 60% of sporadic cases**

- **The VHL protein causes the degradation of hypoxia-induced factors (HIFs)**
- **HIFs are transcription factors that contribute to carcinogenesis by stimulating the expression of vascular endothelial growth factor (VEGF) as well as a number of other genes that drive tumor cell growth**

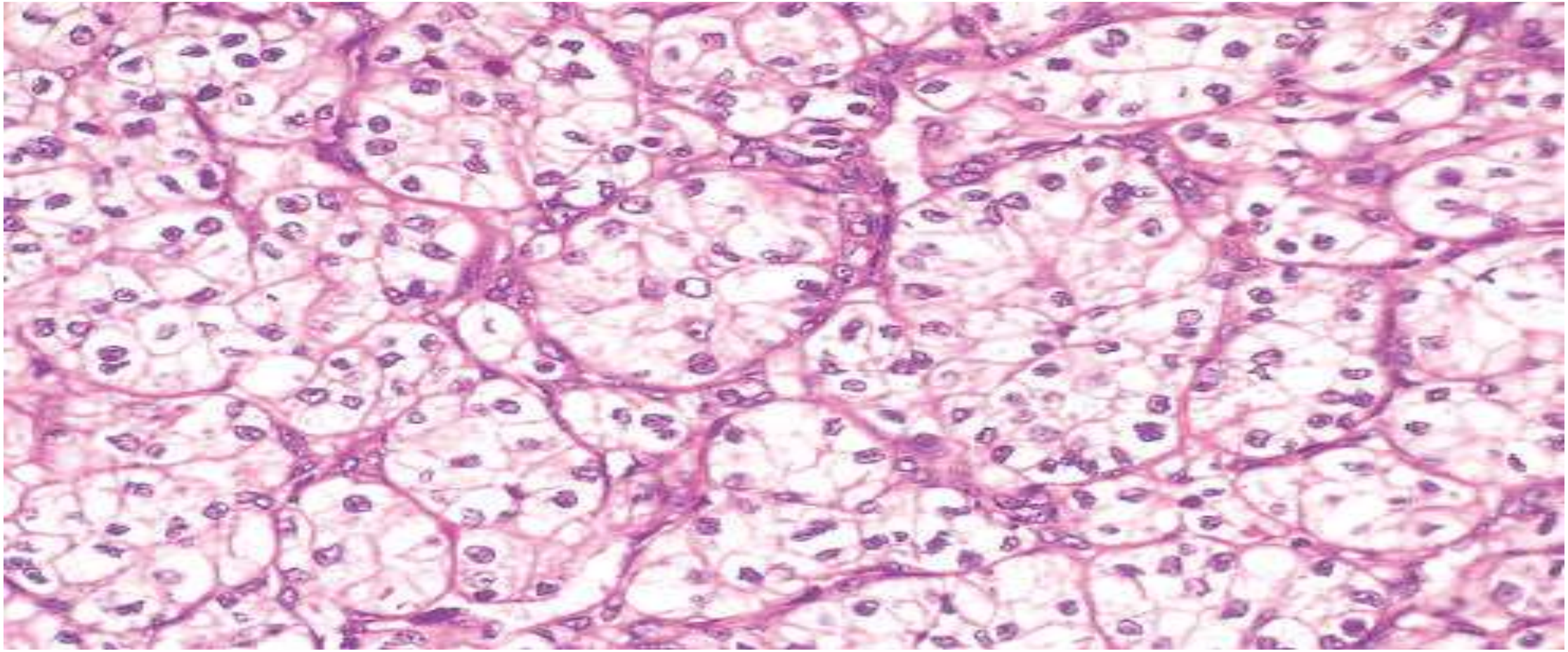
- **An uncommon familial form of clear cell carcinoma unrelated to VHL disease also is associated with cytogenetic abnormalities involving the short arm of chromosome 3 (3p).**

- **Usually are solitary and large**
- **They may arise anywhere in the cortex.**
- **The cut surface of clear cell renal cell carcinomas is yellow to orange to gray-white, with prominent areas of cystic softening or of hemorrhage**

Clear cell renal carcinoma



Clear cell renal carcinoma



- **The margins of the tumor are well defined initially but local invasion is present with tumor progression**
- **The tumor invades the renal vein and grows as a solid column within the vessel sometimes extending in serpentine fashion as far as the inferior vena cava and even into the right side of the heart Occasionally, direct invasion into the perinephric fat and adrenal gland may be seen**

- **Depending on the amounts of lipid and glycogen present the neoplastic cells of clear cell renal cell carcinoma may appear almost vacuolated or may be solid**
- **The classic vacuolated (lipid-laden) cells or clear cells are demarcated only by their cell membranes**
- **The nuclei are usually small and round**

- **The tumor cells can be granular cells resembling the tubular epithelium with small, round, regular nuclei and granular pink cytoplasm**
- **Highly anaplastic tumors show numerous mitotic figures and markedly enlarged, hyperchromatic, pleomorphic nuclei**
- **The stroma is usually scant but highly vascularized**

- **Clear cell cancers usually are solitary and large when symptomatic**
- **Spherical masses 3-15 cm in diameter**
- **They may arise anywhere in the cortex.**
- **The cut surface of is yellow to orange to gray-white, with prominent areas of cystic softening or of hemorrhage**
- **The margins of the tumor are well defined**.

- **The tumor invades the renal vein and grows as a solid column within this vessel**
- **It can extend in serpentine fashion as far as the inferior vena cava and even into the right side of the heart**
- **Some neoplasms are highly anaplastic**

PAPILLARY RENAL CELL CARCINOMAS

- It accounts for 10-15% of all renal cancers
- It is defined in part by their papillary growth pattern
- Frequently multifocal and bilateral
- Appears as early-stage tumors
- It occurs in familial and sporadic forms
- It arises from the proximal tubular epithelial cell

- **Papillary renal carcinoma is not associated with abnormalities of chromosome 3**
- **Characterised by mutation of the *MET* proto-oncogene, located on chromosome 7q**
- ***The MET* gene encodes a tyrosine kinase receptor for hepatocyte growth factor.**

- **The tumor exhibits various degrees of papillary formation with fibrovascular cores**
- **They tend to be bilateral and multiple**
- **They also may show gross evidence of necrosis, hemorrhage, and cystic degeneration**
- **The tumor cells are less vibrantly orange-yellow because of their lower lipid content**
- **The cells may have a clear or, more commonly, pink cytoplasm.**

CHROMOPHOBE RENAL CARCINOMA

- Are the least common form representing 5% of all renal cell carcinomas.
- It arises from intercalated cells of collecting ducts
- Tumor cells stain more darkly (i.e, they are less clear) than cells in clear cell carcinoma
- Characterized by having multiple losses of entire chromosomes leading to extreme hypoploidy

- **The tumor appears grossly tan-brown**
- **The cells usually have clear flocculent cytoplasm with very prominent distinct cell membranes**
- **The nuclei are surrounded by halos of clear cytoplasm. Ultrastructurally large numbers of characteristic macrovesicles are seen**

- **Chromophobe renal cancers have a favorable prognosis**

CLINICAL FEATURES

- The most frequent presenting manifestation is hematuria occurring in more than 50% of cases.
- Macroscopic hematuria tends to be intermittent and fleeting, superimposed on a steady microscopic hematuria
- Less commonly flank pain and a palpable mass

- **Extrarenal effects are *fever* and *polycythemia***
- **Polycythemia affects 5-10% of affected individuals and results from production of erythropoietin by the cancer cells**
- **Paraneoplastic syndrome due to tumor production of other hormone-like substances resulting in hypercalcemia, hypertension, Cushing syndrome, or feminization or masculinization.**

Urinary bladder

- **Bladder cancer accounts for approximately 5% of cancers**
- **3 types:**

1. The vast majority of bladder cancers is urothelial carcinomas.

2. Squamous cell carcinoma represents about 3-7%

3. Adenocarcinomas of the bladder are rare.

- **M>F**
- **About 80% of patients are between 50-80 years of age.**

Risk factors

1. **Cigarette smoking**
2. **Occupational carcinogens**
3. **Cyclophosphamide or radiation therapy.**
4. **A family history of bladder cancer**
5. **Squamous cell carcinoma is related to Schistosoma haematobium infections in areas where it is endemic**
6. **Acquired genetic mutations**

- **Two distinct precursor lesions of invasive urothelial carcinoma:**

1. The most common is a noninvasive papillary tumor

2. Carcinoma in situ (CIS)

- **The most important prognostic factor in noninvasive papillary urothelial neoplasms is their grade.**
- **The grade is based on both architectural and cytologic features**.

- **Grading system subclassifies tumors as follows:**

(1)Papilloma

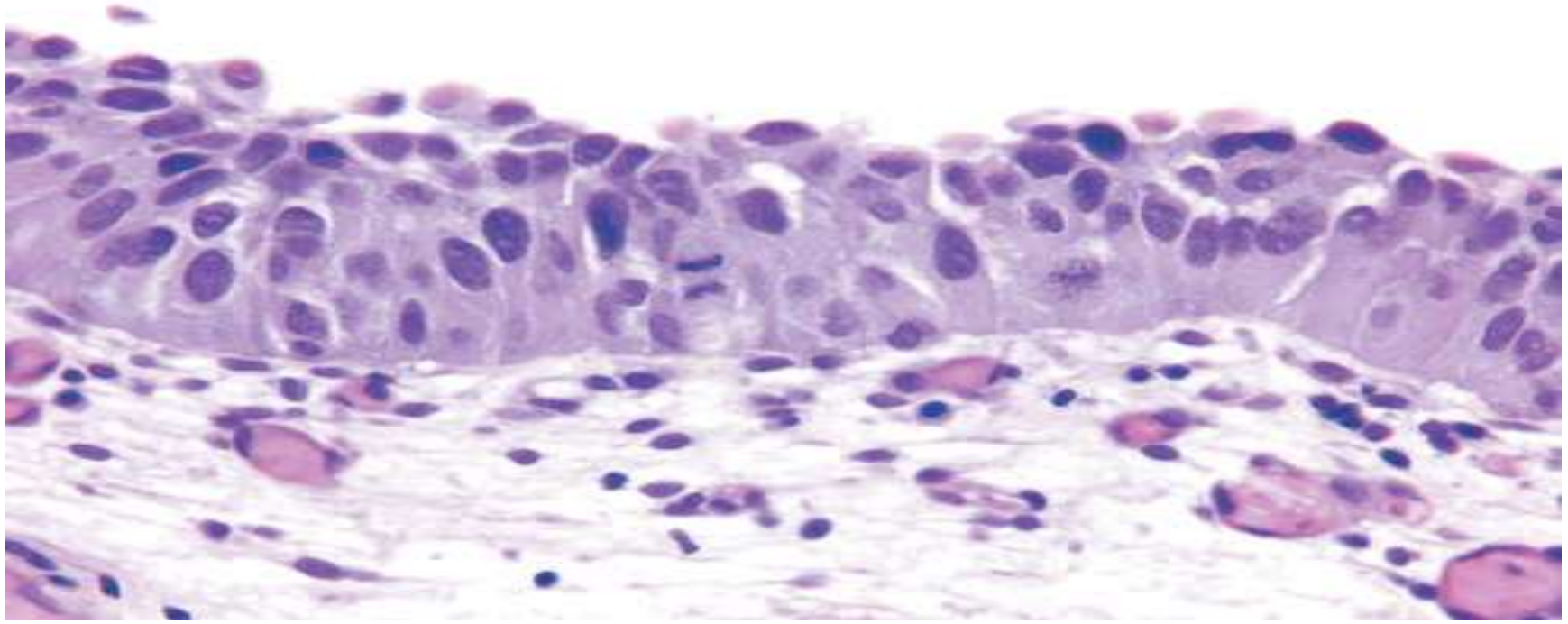
(2) Papillary urothelial neoplasm of low malignant potential (PUNLMP)

(3) Low-grade papillary urothelial carcinoma

(4) High-grade papillary urothelial carcinoma

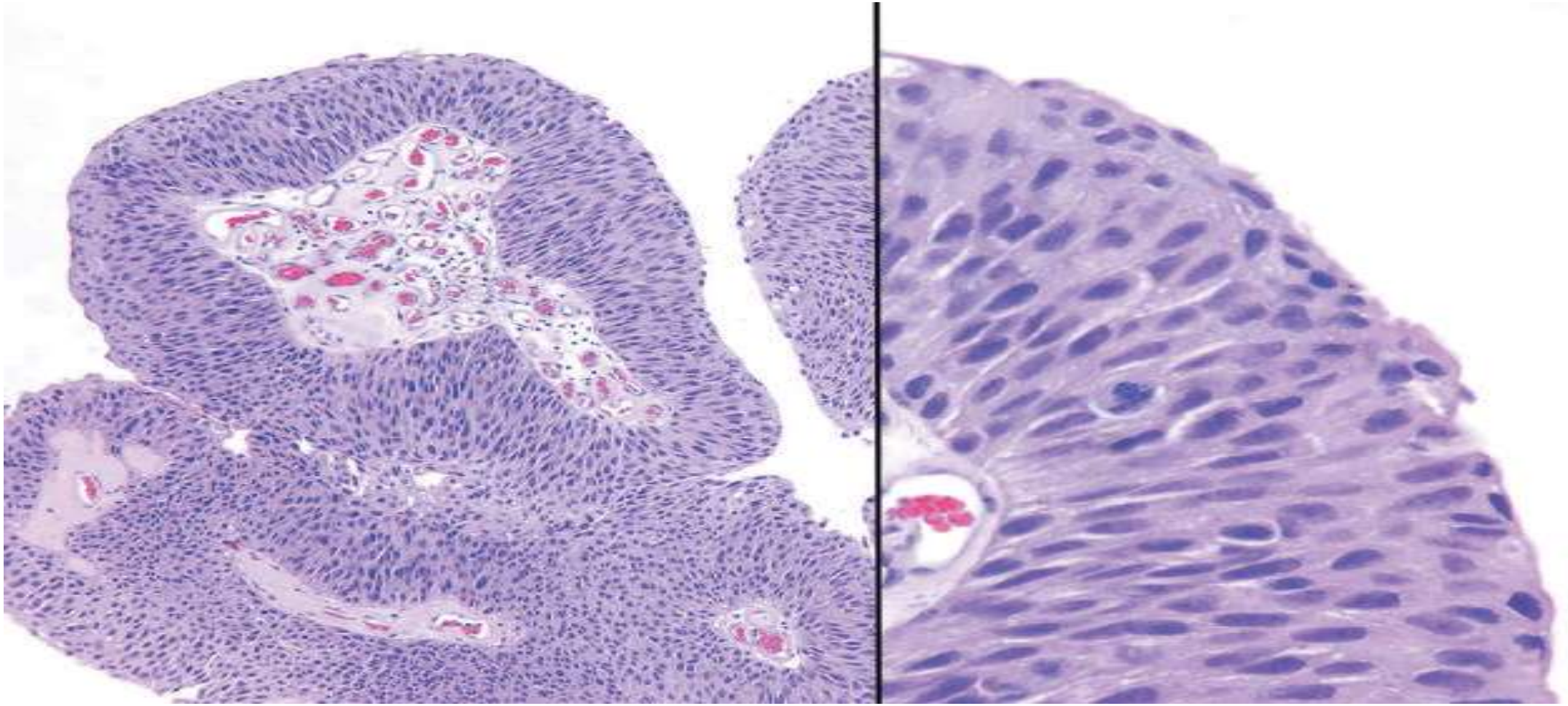
- **CIS is defined by the presence of overtly malignant appearing cells within a flat urothelium**
- **CIS commonly is multifocal and sometimes involves most of the bladder surface or extends into the ureters and urethra**
- **Without treatment 50-75% of CIS cases progress to invasive cancer**

Carcinoma in situ (CIS) with enlarged hyperchromatic nuclei and a mitotic figure



- **Invasive urothelial cancer associated with papillary urothelial cancer (usually of high grade) or CIS may superficially invade the lamina propria or extend more deeply into underlying muscle.**
- **The extent of invasion and spread (staging) at the time of initial diagnosis is the most important prognostic factor**
- **Almost all infiltrating urothelial carcinomas are high grade**.

Noninvasive low-grade papillary urothelial carcinoma.
Higher magnification *(right)* shows slightly irregular nuclei with scattered mitotic figures



Clinical Features

- **Painless hematuria.**
- **The risk for recurrence is related to several factors:**

1. Tumor size

2. Stage

3. Grade

4. Multifocality

5. Mitotic index

6. Associated dysplasia

7. CIS in the surrounding mucosa.