RENAL CELL CARCINOMA (clear cell type)

1) Clinical features (Triad)

- Costovertebral or flank pain
- Palpable abdominal mass
- Hematuria (most reliable)

2) Etiology (Risk factors)

1) Age and gender

- More common in males (M:F → 2:1)
- M/c in 6th – 7th decades

2) Tobacco (M. imp aquired factor)

- Tobacco carcinogens are filtered and concentrated in renal tubules → produce DNA mutations in tubular epi cells.

3) Obesity (imp in females)

- ↑ed estrogen, hyperinsulinemia → chronic inflammation + cell proliferation

4) Hypertension

- chronic renal ischemia → DNA injury

5) Occupational exposure

- Exposure to: Asbestos, petroleum products, cadmium, heavy metals

6) Chronic kidney disease

7) Genetic predisdeposition (4-5%) are hereditary

- Most imp s/d → Von Hippel-Lindau s/d

3) Pathogenesis

Von-Hippel Lindau

Hallmark event → Inactivation of VHL tumor suppressor gene.

- Locn: chromosome 3p
- 90% of speradic and 100% of hereditary CCRCC show VHL abnormalities.

Normal mechanism of VHL

- The VHL protein normally binds and degrades Hypoxia-Inducible Factor (HIF) under normal oxygen levels.
- This prevents unnecessary activation of genes involved in angiogenesis and cell proliferation.

Deletions of VHL

mut

↓

loss of pVHL → HIF not degraded and accumulates even in normal oxygen (pseudo hypoxia)

↓

HIF enters nucleus and activates transcription of several growth-promoting genes :-

- VEGF → Angiogenesis
- PDGF → cell proliferation
- TGF-α → tumor cell growth

- GLUT-1 → increased glucose uptake
- Erythropoietin → May cause polycythemia (paraneoplastic s/d)

4) Microscopic variants of RCC

	Clear (M/C) cell cancer	Papillary cancer (chromophilic)	chromophobe cancer	Collecting duct carcinoma (L/C)
1)	Deletion of VHL (of chromo 3 short arm)	Two types → Sporadic: • Trisomy 7, 16, 17; Familial: • Trisomy 7	Hypoploidy. Best prognosis	Bellini duct carcinoma. Worst prognosis
2)	Clear or granular cytoplasm	papillary pattern. plasmoma bodies	eosinophilic cyto + perinuclear halo	Prominent fibrotic stroma
3)	PCT	DCT	Collecting duct (intercalated cell)	Collecting duct (Medulla)

5) Morphology

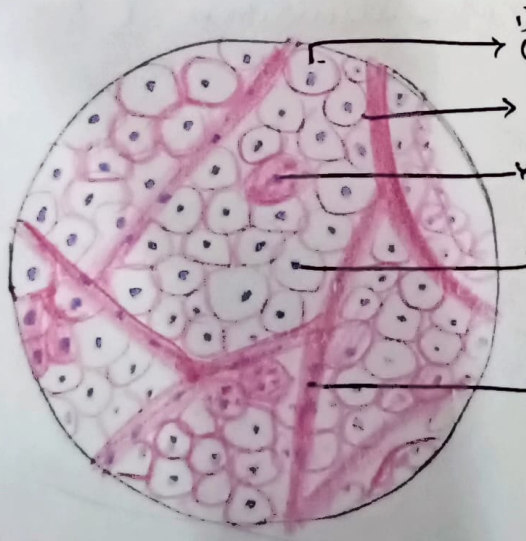
Gross

- May arise in any part — M/C upper pole
- Usually solitary & unilateral lesions
- Outer surface — Bosselated

- C/S - large, circumscribed, spherical masses with well-demarcated margins
  - Bright golden yellow tumour → lipid content
  - with areas of necrosis, haemorrhage, cystic change
    → Variegated appearance
- Venous invasion (Renal vein)

Microscopy

- Arrangement - Trabecular (cord-like), nests or tubular
- Tumour Cells
  - clear / granular cytoplasm → due to glycogen & lipids removed during processing of tissue
  - non-papillary
  - Round / polygonal in shape
  - Nucleus centrally located & small (masks the malig. of tumour)
- Stroma - Branching vasculature



BCC
(clear cell type)
→ no papillae

6) Spread

1) Hematogenous route (M/c)

- C/ site → lungs (Cannon ball deposits and pleating secondaries)
- bone, liver, adrenal

2) local spread → invades perinephric fat and renal sinus

3) lymphatic spread → hilar, aortic, caval lymph nodes

7) Paraneoplastic s/d

- Polycythemia (due to Erythropoietin)
- Hypercalcemia (PTHrp protein)
- Hypertension (Renin)
- Feminization / Masculinization (Sex hormo)