Questions. ① RCC - etiopathogenesis ✓
morphology ✓
paraneoplastic syndromes ✓

② manifestations of nephritic syndrome ✓
• light m/c findings in post streptococcal GN + role of IF findings ✓

③ PSGN - etiology / pathogenesis ✓
kidney morphology ✓

④ Classify Tumours of kidney ✓
Gross, c/f mx of mc renal tumor in adults.

Renal cell Carcinoma

aka: adenocarcinoma of the kidney, hypernephroma, Grawitz tumor.

ETIOLOGY - Risk factors

- Tobacco - cigarette smoker (2x) : mortality
- Obesity (common).
- Hypertension.
- unopposed estrogen therapy
- asbestos, petroleum products, heavy metal exposure
- chronic kidney disease.
- acquired cystic disease.
- tuberous sclerosis.

Genetic factors

- Von Hippel Lindau gene mutation chromosome 3p - clear cell RCC
- familial RCC syndromes.
- MET - proto oncogene mutations.
- BHD - Birt - Hogg - Dube gene mutation.

PATHOGENESIS - FIGURE Ramdas

• Clear cell RCC

- solitary & unilateral lesion.
- most common (70-80%).
- arises from Proximal tubular epithelium.
- VHL gene inactivation.
↓
↑ HIF-1α (hypoxia inducible factor-1) is not degraded
↓
VEGF, PDGF activation & ↑ production of TGF-α, TGFβ } pro angiogenic factors.
↓
tumor angiogenesis

10-15% Papillary RCC

- multifocal, can be bilateral.
- arises from DCT.
- MET proto - oncogene mutation, (Chromosome 7) (continuation).

5% Chromophobe RCC

- arises from intercalated cells of CD
- multiple chromosome losses

<1% Collecting duct carcinoma

- loss of tumour suppressor (eg: SMARCB1, FH).
- origin: medullary collecting duct, aggressive.

Xp11 translocation RCC

TFE3 gene translocation.
- TFE3 overexpression.
- TFE3 gene is located at Xp 11.2.

MORPHOLOGY

RCC

general features) o RCC.

GROSS

① arise in any part → m/c → poles
↓
upper poles

② cut surface → solid (lipid)
bright yellow - grey - white.
variegated appearance ← hemorrhage, necrosis, cystic changes.

③ tendency to invade renal vein.

- Circumscribed, spherical mass, capsulated some shows breach in capsule.

MICROSCOPY

① Clear cell Carcinoma - PCT
• solitary, unilateral

* growth pattern : solid
tubular
tubular.

cytoplasm

* Tumour cells : abundant clear or granular cytoplasm
↓
glycogen + lipids.

• round, polygonal shaped
• sharply outlined cell membrane
- vesicular cell.

Nucleus → centrally located, small.

Special stains

✓ PAS → glycogen
✓ Oil Red O → fat.

Papillary tumours • PCT
• multifocal, bila

growth pattern - papillary growth pattern.

• cuboidal / low columnar cells arranged in papillary formation.
• Interstitial foam cells are seen core of papillary projection.

cytoplasm : eosinophilic.

• psammoma bodies may be seen

✗ Stroma: Scanty, highly vascularized.

Intercalated cells of CD
③ chromophobe RCC
pale stain - cytoplasm blue.

→ cells are arranged in solid sheets.
→ cells → pale eosinophilic cytoplasm.
→ perinuclear halo.
→ greatest concentration of cells are around blood vessels

Medullary CD
④ Collecting duct Carcinoma

• nests of malignant cells separated by prominent fibrotic stroma.
• Irregular channels lined by highly atypical epithelial cells with a tubular pattern.

Clinical features

- Classical diagnostic triad (seen in only 10% cases) are:
  - Costovertebral / flank pain.
  - palpable abdominal mass
  - Hematuria. (most reliable)

Paraneoplastic Syndromes produced by renal cell carcinoma:

RCC is known to produce various PNS due to.

↓

ectopic production of hormones.

① hypercalcemia.

due to (ep) of PTHrp (related peptide).

② Cushing's syndrome

(ep) of ACTH.

③ polycythemia

due to (ep) → erythropoietin.

④ Stauffer syndrome

⑤ hypertension → due to renin.

⑥ hepatic dysfunction due to IL-6 leads to ↑ ALP, PT, bilirubin.

⑦ feminization or masculinization.

Spread

- local → perinephric fat.
- lymphatic → Regional L.N.
- Hematogenous →

Lungs → cannon ball deposits & pulsating secondaries.

bones → liver → adrenal → brain.

+ Classification of Tumours box — just read

NEPHRITIC SYNDROME

Manifestations

① Hematuria - red blood cells & red cell casts in urine.

② oliguria.

③ Hypertension

④ Azotemia - elevated BUN & creatinine levels

⑤ Proteinuria - mild <1g / 24 hour sample.

→ Acute proliferative glomerulonephritis.

→ PSGN.
→ RPGN
→ goodpasture.
→ Non streptococcal GN.

Nephroblastoma.
(Wilms tumour)

It is a highly malignant primary embryonal tumour. derived from nephrogenic blastemal cells that replicate the histology of developing kidneys and often shows divergent patterns of differentiation

- most common renal tumor in childhood.
- 2-5 years.

Pathogenesis & Genetics

Molecular anomalies in congenital.

- mutations in tumour suppressor genes

WT1, WT2
↓
Chromosome 11 p 13.

- Congenital malformations associated with increase risk:

(WAGR, DDS, BWS)

- WAGR - wilms tumor
  ↓
  11p 13.
  WT1 gene
  aniridia
  genital anomalies.
  mental retardation.
- DDS - Denys - Drash syndrome
- Beckwith - Wiedemann syndrome
  BWS.

molecular abnormalities in Non syndromic (sporadic)

① β-catenin gene: gain of function mutation.

② mutations in genes encoding proteins in micro RNA processing
→ DROSHA
DGCR8
CICER1

③ TP53 mutations.

④ associated with other malignancy
→ osteosarcoma.
→ rhinoblastoma.
→ HCC

Morphology

GROSS.

- large, single, round, well circumscribed uni, bi, multicentric
- cut S: soft, homogenous, tan-grey
  - hemorrhage, necrosis foci

Microscopy - triphasic combination

① Blastemal Component (undiff.)
small, round, undifferentiated blue cell, high N:C ratio.
- mitotic figures
immature.

② Epithelial component
- abortive tubules & glomeruli.

③ immature stromal component
- fibrocytic or myxoid tissue.
- heterologous diff → smooth muscle, skeletal muscle etc.