Renal Pathology 1: Glomerulus

With many thanks to Elizabeth Angus PhD for EM photographs
Anatomy of the Kidney

- Calyces
- Renal Pelvis
- Renal Artery
- Medulla
- Renal Vein
- Cortex
- Ureter

http://www.yalemedicalgroup.org/stw/Page.asp?PageID=STW028980
The Nephron

The Renal Corpuscle

- Afferent arteriole
- Vascular pole
- Efferent arteriole
- Lobule
- Urinary pole
- Bowman's capsule
- Bowman's space
- Basement membrane of
- Glomerulus
- Proximal convoluted tubule

Wheater’s Functional Histology A Text & Colour Atlas, 2009
Needle Biopsy

Cortex

Glomerulus

Medulla
Top and Tail for EM
Top and Tail for EM

![Image of renal tissue with annotations]

- Top image: x2 magnification
- Bottom image: x20 magnification
SEM – Glomerulus

Freeze, fractured rodent glomerulus

Courtesy of Anton Page
Part of a human glomerulus x 1,000

Courtesy of Anton Page
EM – Capillary loop
EM basement membrane

Foot process

Podocyte

Bowman’s capsule

Glomerulus

2000 nm
EM basement membrane

Original E.M. magnification x3,300

Foot process

Podocyte

Podocyte

Courtesy of Sue Cox
EM - mesangium
Basement Membrane

Normal basement membrane thickness (250-350nm) x 5,000

Thin basement membrane thickness (≤ 200nm)

Thick basement membrane thickness (≥400nm)

Courtesy of Sue Cox
Foot Processes
Mesangial Hypercellularity

The glomerular mesangium contains increased matrix and four nuclei (M). The capillary is normal. There is loss of epithelial cell foot processes. Original E.M. magnification x3,300

Courtesy of Sue Cox
Electron Dense Deposits
Electron Dense Deposits
Amyloid
Glomerulonephritis (GN) patterns

- “Primary”
- (minimal change disease)
- Mesangial proliferative GN
- Focal segmental glomerulosclerosis
- Membranous GN
- Post infectious GN
- Crescentic GN
- Membranoproliferative GN

- “Secondary” lupus diabetes, amyloid, light chain disease, cryoglobulinemia,
terms

• Diffuse: involves whole glomerulus (vs focal)
• Global: involves whole glomerulus (vs segmental)
Nephrotic vs nephritic

- Nephrotic
  - minimal change disease, mesangial proliferative (eg. IgA disease/HSP), focal and segmental, membranous
- Nephritic
  - Post-infectious (eg post-Streptococcal), membranoproliferative
Clinical Stories

• 1-month history of malaise. renal failure, weight loss, fevers, ?cause.
• additional information: creat 300s, MCV 60
• Complement C3 and C4 within normal range
• Perinuclear ANCA (IgG) Weak positive
• Cytoplasmic ANCA (IgG) Negative
• Connective tissue ANA screen Borderline
Crescentic glomerulonephritis

- Glomeruli: There are 22 glomeruli, all of which are abnormal showing varying degrees of sclerosis and active proliferative changes. At least 9 glomeruli are globally sclerosed. Numerous fresh crescents are identified with proliferating epithelial cells seen in the urinary space. There are neutrophils present. There is periglomerular fibrosis around several glomeruli.

- Tubules / interstitium: focal tubular atrophy around damaged glomeruli.
- mixed inflammatory infiltrate: occ eosinophils, plasma cells, lymphocytes
- Vessels: no vasculitis.

- Immunohistochemistry: IgA, IgG, IgM, C1q and C3 stains are negative.

- EM: No electron dense deposits are identified.

- Comment: the crescentic glomerulonephritis, negative immunohistochemistry and absence of electron dense deposits are highly suggestive of pauci immune glomerulonephritis.

- Ddx=pauci-immune GN, postinfectious GN
seronegative pauci immune crescentic GN

- Working diagnosis is seronegative pauci immune crescentic GN. Her creatinine has significantly dropped from approx 450 to 100 (following steroids, plasma exchange, cyclophosphamide). Plan is to recheck ANCA in 3 months
Nephrotic syndrome

- 11-year old boy
- Nephrotic syndrome, partial response to steroids
- 40 glomeruli are present, none of which are globally sclerosed. Some of the glomeruli show mesangial cell hypercellularity with an increase in mesangial matrix and lobularity. There are focal, segmental sclerotic lesions. No crescents are present.
- working histological diagnosis=primary FSGS