Kidney pathology

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Review of histology
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Needle biopsy
1. Light histology, stainings:

- routine
  - hematoxylin and eosin
- for extracellular material
  - periodic acid-Schiff (PAS)
  - periodic acid-methenamine silver
  - Masson’s trichrome
- for fibrin
  - Martius, Scarlet and Blue (MSB)
2. Immunohistology

- Immunofluorescence (fluorescein-labeled antibodies)
- Immunohistochemistry (enzyme-labeled antibodies)
- Immunoglobulines (IgG, IgA, IgM)
- Complement components (C1q, C3, C4d)
- Collagen IV chains
Examination of Renal Tissue

3. Electron microscopy
Patterns

1. Hypercellularity
   - Infiltration (leukocytes, monocytes)
   - Proliferation (endothelial and mesangial cells)
   - Endocapillary (in capillary tuft)
   - Extracapillary (in Bowman space)
Patterns

2. Increase of extracellular matrix
   - mesangial matrix
   - GBM thickening
   - sclerosis
   - hyalinosis
Patterns

3. Other changes
   - fibrin precipitation
   - deposition of substances (e.g. amyloid)
   - thrombosis
Patterns of glomerular damage

- **Focal or Diffuse**
- **Segmental or Global**

glomeruli
Patterns of glomerular damage

- Focal or Diffuse
- Segmental or Global
Terms

- **Azotemia**: ↑ BUN, creatinine
- **Uremia**: azotemia with clinical symptoms
  - gastroenteritis, dermatitis, metabolic acidosis, pericarditis, peripheral neuropathy, hyperkalemia

- **Acute renal failure**: sudden onset of azotemia with oliguria (or anuria)
- **Chronic renal failure**: prolonged uremia
Terms

- **Nephritic syndrome** (from “nephritis”)
  - Hematuria
  - Proteinuria
  - Hypoalalbuminemia
  - Oliguria (↓ GFR, ↑ Cr, ↑ BUN)
  - Edema (salt and water retention)
  - Hypertension

- Immunologically-mediated
- Characterized by proliferative changes and inflammation
Terms

- **Nephrotic syndrome** (from “nephrosis”)
  - Proteinuria ("nephrotic range" >3.5g/24h)
  - Hypoalbumimienia
  - Edema
  - Hyperlipidemia
  - Lipiduria
Glomerular Diseases

- Primary
  - kidney is the primary organ involved

- Secondary
  - kidney is one of multiple organs involved by a systemic disease process (SLE, Diabetes mellitus, Amyloidosis)
Acute Diffuse Proliferative Glomerulonephritis

- aka. Acute post-streptococcal glomerulonephritis (APGN)

- produces the **nephritic syndrome**

- in two weeks after a respiratory or skin infection with a “nephritogenic strain” of group A, beta-hemolytic streptococci.

- The cause is **deposition of circulating immune complexes which fix complement and attract neutrophils**.
Acute Diffuse Proliferative Glomerulonephritis

- swelling and proliferation of glomerular endothelial cells.
- This chokes off their blood supply, making the glomeruli hypercellular and bloodless.
- This explains the oliguria, edema, and hypertension.

95% patients recover

never leads to any chronic renal disease
Acute Diffuse Proliferative Glomerulonephritis

A glomerulus with endocapillary hypercellularity and closure of the glomerular capillaries. Because of the increased cellularity within each lobule, there is an accentuation of the lobularity. (H&E)
Acute Diffuse Proliferative Glomerulonephritis

Considerable infiltration of the glomerulus by neutrophils. (PAS)
Acute Diffuse Proliferative Glomerulonephritis

Immunofluorescence for IgG – coarsely granular pattern along the capillary walls and less prominent granular mesangial pattern.

IHC with antibody to C3 – coarsely granular large subepithelial deposits
Acute Diffuse Proliferative Glomerulonephritis

Electron micrograph shows a hump on the epithelial side of the glomerular capillary basement membrane. The hump is covered by a dense zone in the epithelial cytoplasm.
Rapidly progressive glomerulonephritis (RPGN)

- aka. Crescentic glomerulonephritis

- 2 to 5% of all cases of glomerulonephritis in adults
- poor prognosis: sudden and progressive decline in renal function
- It can accompany most forms of primary GN in childhood and can be associated with various systemic disorders (e.g., systemic lupus erythematosus) and several forms of systemic vasculitis
Rapidly progressive glomerulonephritis (RPGN)

- acute nephritis presentation (*nephritic syndrome*) with proteinuria, hematuria, volume overload, hypertension, and renal impairment
- may evolve quickly and initially give the impression of a postinfectious glomerulonephritis but can be associated with a more protracted clinical course
Rapidly progressive glomerulonephritis (RPGN)

- Type I RPGN (approximately 20% cases), injury is caused by antibodies directed against the glomerular basement membrane.
  - Goodpasture’s syndrome

- Type II RPGN (25% cases and) is characterized by the deposition of immune complexes in the glomerulus.
  - SLE, other vasculites

- Type III RPGN features antibodies directed against neutrophils (anti-neutrophil cytoplasmic antibodies, ANCA).
  - ANCA nephritis, Wegener granulomatosis
Rapidly progressive glomerulonephritis (RPGN)

Cells accumulate in Bowman’s space, form crescents
Rapidly progressive glomerulonephritis (RPGN)

Global linear staining for IgG indicative of diffuse binding of anti-GBM antibodies to type 4 collagen in glomerular basement membranes. (Goodpasture's syndrome)
Rapidly progressive glomerulonephritis (RPGN)

Large mottled kidney: dark dots on the surface that correspond mainly to blood in tubular lumens and in Bowman's spaces
Membranoproliferative Glomerulonephritis (MPGN)

- thickening of the glomerular capillary wall (*membrano-*)
- increase in the number of cells in the glomerular tuft (*proliferative*)
- various clinical characteristics (nephritic or a nephrotic syndrome or both, asymptomatic microhematuria and proteinuria)
Membranoproliferative Glomerulonephritis (MPGN)

Increased lobulation, intracapillary hypercellularity (including neutrophil infiltration), and thickening of the capillary walls. (H&E)
Membranoproliferative Glomerulonephritis (MPGN)

Positive IF to IgA, IgM, IgG, C1q, C3, C4 (different combinations) with granular or linear pattern
Membranoproliferative Glomerulonephritis (MPGN)

Tram-tracking or reduplication of GBM (JMS and PAS)
Membranoproliferative Glomerulonephritis (MPGN)

The mesangial cell has interposed itself between the endothelium and the basement membrane and has also produced an inner “mesangial matrix/basement membrane”-like material.
Membranoproliferative Glomerulonephritis (MPGN)

- Type I (with subendothelial deposits, classic type), aka. Mesangiocapillary glomerulonephritis

Numerous large electron-dense subendothelial deposits and scattered mesangial deposits
Membranoproliferative Glomerulonephritis (MPGN)

- Type II (Dense Deposit Disease, DDD)

Characteristic ultrastructural appearance of the glomerular intramembranous deposits
Membranoproliferative Glomerulonephritis (MPGN)

Type III

Large intramembranous and subepithelial deposits and spikes of GBM-like material.
Let’s Take a Break...back in 10 minutes

- Manneken Pis
  - (literally “Little Man Pee”, also known in French as “le Petit Julien”)
  - by Jerome Duquesnoy
    - 1388 - original version
    - 1619 - current version
  - Brussels, Belgium
Minimal Change Disease

- aka. Lipoid nephrosis

- the cause is poorly understood (some genes can be involved)

- common in ages 2-6 yrs

- produces the nephrotic syndrome

- > 90% respond to steroids (kids)

- by light & IF – normal

- EM shows fusion of foot processes
Minimal Change Disease

No LM changes in glomeruli. Sometimes minimal mesangial proliferation. (H&E)
Minimal Change Disease

Protein droplets in tubules. (PAS)
Minimal Change Disease

Fusion (effacement) of foot processes.
Minimal Change Disease

Cytoplasm vacuolization and microvillous hyperplasia.
Membranous nephropathy

- aka. Membranous glomerulonephritis
- The most common cause of the nephrotic syndrome in adults
- In about 85% of patients, no associated condition can be identified (idiopathic).

Other cases occur secondary to systemic diseases:

- Drugs (penicillamine, captopril, gold, NSAIDs).
- Underlying malignant tumors, particularly carcinoma of the lung and colon and melanoma.
- SLE.
- Infections (chronic hepatitis B, hepatitis C, syphilis, schistosomiasis, malaria).
- Other autoimmune disorders, such as thyroiditis.
Membranous nephropathy

- Microscopic: uniform, diffuse thickening of the glomerular capillary wall.
- Basement membrane material is laid down between these deposits, appearing as irregular spikes protruding from the GBM.
- These spikes are best seen by silver stains, which color the basement membrane black.
Membranous nephropathy

- Stage I exhibits scattered subepithelial deposits. The outer contour of the basement membrane remains smooth.
- Stage II disease has projections (spikes) of basement membrane material adjacent to the deposits.
- In stage III disease, newly formed basement membrane has surrounded the deposits.
- With stage IV disease, the immune-complex deposits lose their electron density, resulting in an irregularly thickened basement membrane with irregular electron-lucent areas.
Membranous nephropathy
Membranous nephropathy

Advanced MN (stage IV). The glomerulus shows diffuse, marked thickening of the GBM. (H&E)
Membranous nephropathy

MN stage II-III. Newly formed basement membrane has partly surrounded the deposits.
Membranous nephropathy

MN stage II. Every capillary in this field has small spikes projecting from the epithelial side of the GBM. Stage III shows thickening of GBM and numerous “holes” and “splits”. (JMS)
Membranous nephropathy

Diffuse, intense granular deposits of IgG are seen along the GBM. Mesangial areas are free of deposits.
Focal Segmental Glomerulosclerosis (FSGS)

- Usually produces **nephrotic syndrome**
- Poor prognosis
- Unknown pathogenesis
Focal Segmental Glomerulosclerosis (FSGS)

- **Podocyte injury, unknown cause**
  - Primary FSGS

- **Podocyte injury, defined cause**
  - Viral (HIV, Parvovirus B19), Drugs (Interferon, Pamidronate, Lithium)

- **Secondary to structural and/or functional adaptations**
  - Unilateral renal agenesis, Renal dysplasia, Polycystic kidney disease, (adult type), Reflux nephropathy, Chronic interstitial nephritis and pyelonephritis, Partial cortical necrosis, Sickle cell disease

- **Primary glomerulopathies**
  - Nephrectomy and more extensive surgical ablation, Morbid obesity, Cyanotic congenital heart disease, Diabetic nephropathy, Glycogen storage diseases, Secondary to genetic diseases

- **Other associations**
  - C1q nephropathy, Renal tubular acidosis, Sarcoidosis, Kaposi's sarcoma, Behcet syndrome, Prader-Willi syndrome, Turner Syndrome, Non-Hodgkin lymphoma, Systemic lupus erythematosus, Loa loa filariasis, Schistosomiasis mansoni, Pre-eclampsia, Renal transplantation, Heroin
Focal Segmental Glomerulosclerosis (FSGS)
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Acute Pyelonephritis

- **Causes:**
  - ascending infection - vesicoureteral reflux into the renal pelvis and papillae; E. coli, Proteus, Enterobacter.
  - hematogenous seeding - due to septicemia or endocarditis; Staphlococcus and E. coli.

- **Common in patients with:**
  - incompetent ureteral valves.
  - diabetes.
  - immunocompromise

- **Clinical signs:**
  - Flank pain, fever, dysuria, pyuria and bacteriuria.
Acute Pyelonephritis

- Patchy suppurative inflammation, tubular necrosis, neutrophilic casts.
- Abscesses and papillitis more common in diabetics.
Acute Pyelonephritis
Acute Pyelonephritis
Chronic Pyelonephritis

- Chronic tubulointerstitial inflammation with renal scarring.
- Clinical: recurrent infections, tubular dysfunction, hypertension, chronic renal failure.
- Two forms:
  - reflux-associated: common, congenital vesicourterehral reflux or intrarenal reflux.
  - obstructive: posterior urethral valves, ureteral calculi or abnormalities.
Characteristic morphologic features are seen on gross examination:

- irregular scarring.
- coarse, discrete, corticomedullary scar overlying a dilated and deformed calyx.
- most in upper and lower poles consistent with the frequency of reflux in these sites.
Chronic Pyelonephritis
Chronic Pyelonephritis

- Microscopic:
  - changes involve predominantly tubules and interstitium.
  - tubules show atrophy in some areas and hypertrophy in others.
  - thyroidization: dilated tubules may be filled with colloid casts.
  - varying degrees of chronic inflammation and fibrosis.
  - a variety of glomerular changes may be present.
Chronic Pyelonephritis
Ivan Klasnić

Croatian international footballer. After kidney failure in late 2006, he underwent an unsuccessful transplant in January 2007, followed by a successful one from his father two months later. He returned to action with Werder Bremen in November, and played at Euro 2008, becoming the first kidney transplant patient to play in a major football finals.