Overview of glomerular diseases

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Endothelial cells are fenestrated...each fenestra: 70-100nm in diameter

Glomerular basement membrane (GBM) is mainly composed of:
- Collagen IV
- Laminin
- Proteoglycans...polyanionic
- Fibronectin...etc

= filtration slit (20-30nm wide)
...bridged by thin slit diaphragm...mainly composed of: nephrin from adjacent foot processes

Nephrin & its partner proteins (e.g., podocin) are very important in the selective permeability of the filtration barrier

GBM: lamina densa inside & lamina rara on each side (interna & externa)
Glomerular diseases

- Most 1ry & many 2ry glomerular diseases are immune-mediated
  - circulating Ag-Ab complexes that deposit in the glomerulus
  - in situ deposition of antibodies
    - Fixed antigens
    - Planted antigens
    - anti-GBM antibody-mediated GN

These are called in general: glomerulonephritis (GN)...because they are immune-mediated glomerular injury
The immune-mediated glomerular diseases (= Glomerulonephritis (GN))

(1) GN caused by circulating immune complexes
...the antigen is not intrinsic in glomerulus
...the antigen may be *endogenous* or *exogenous*
...the antigen is often unknown

...these complexes will cause injury
...mainly through activating complement
...recruitment/activation of WBCs (through complement or directly through the interaction between antibodies & Fc receptors on leukocytes)

- lupus nephritis
- Membranoproliferative GN (MPGN)
- bacterial infection (streptococcal)
- viral (hepatitis B)
- parasites (*Plasmodium falciparum*)
- spirochetal (*Treponema pallidum*)
GN caused by circulating immune complexes, cont’d

...on light microscopy:

• leukocytic infiltration (exudation) into glomeruli

• variable proliferation of  
  - endothelial cells
  - mesangial cells
  - parietal epithelial cells

• 3 possible sites of immune complex deposition:
  - mesangium
  - between endothelium & BM (subendothelial)
  - between podocytes & BM (subepithelial)

Deposits may be located at more than one site in a given case
The immune-mediated glomerular diseases (= Glomerulonephritis (GN)), cont’d

(2) GN caused by in situ immune complexes

...fixed or planted (nonglomerular) antigens

Membranous nephropathy

*also in: -SLE
  -group A streptococci...endostroptosin

*may be the circulating immune complexes themselves when deposit in the glomerulus
  ...by exposing additional targets for antibody deposition

...on light microscopy:
  • leukocytic infiltration (exudation) into glomeruli
  • variable proliferation of
    -endothelial cells
    -mesangial cells
    -parietal epithelial cells

...3 possible sites of immune complex deposition:
  -mesangium
  -between endothelium & BM (subendothelial)...more associated with leukocyte infiltration
  -between podocytes & BM (subepithelial)...less associated with leukocyte infiltration
The immune-mediated glomerular diseases (= Glomerulonephritis (GN)), cont’d

(3) Anti-glomerular basement membrane antibody–mediated glomerulonephritis

...α3 chain of the type IV collagen of the GBM is the target here

...Sometimes the anti-GBM antibodies cross-react with basement membranes of lung alveoli, resulting in simultaneous lung and kidney lesions
   ...this is called???

...less than 1% of GN cases but:
Many instances are characterized by very severe glomerular damage with necrosis and crescents and the development of the clinical syndrome of rapidly progressive GN
Immunofluorescence (IF)

• When the nephrologist or pediatrician takes a kidney biopsy, he takes 3 samples (one fresh for IF, one in formalin for light microscopy, and one in glutaraldehyde for electron microscopy)

• We take frozen sections of the kidney sample that was fresh and put them on slides

• We use antibodies labelled by fluorochrome

• The targets of these antibodies are IgG, IgA, IgM, C3, C4...etc.
  ...for example: in one slide we direct anti-IgG to the tissue, in another one we direct anti-C3...and so on
  ...if a disease for example is characterized by IgG deposition, the slide that we directed labelled anti-IgG to it will show positivity in the fluorescence microscope
IF, cont’d

• Now the positivity is as the following:

- Capillary(BM) VS Mesangial

- Granular VS Linear
Granular VS Linear IF patterns

Immune complex-mediated GN

Anti-GBM GN
Important notes to mention

• In the inflammatory process that occurs, sometimes there are roles of thrombin and platelets (as partners of the inflammatory process) inducing more WBC recruitment and mediator release

• Any renal disease (glomerular or nonglomerular) that destroys sufficient nephrons to reduce the GFR to 30-50% of normal...adaptive responses in the remaining renal tissue occur and this may be complicated by FSGS and global sclerosis entering a vicious cycle of nephron loss and maladaptation causing progressive glomerulosclerosis
Major renal clinical syndromes (some are specific for glomerular disease)

- **Nephritic syndrome:**
  - due to glomerular injury
  - acute onset
  - usually grossly visible hematuria (RBCs & RBC casts)
  - proteinuria of mild to moderate degree
  - azotemia
  - edema
  - hypertension
Major renal clinical syndromes (some are specific for glomerular disease), cont’d

- Nephrotic syndrome:
  ...also a glomerular syndrome
  ...heavy proteinuria...>3.5gm/day
  ...hypoalbuminemia
  ...severe edema
  ...hyperlipidemia
  ...lipiduria
Major renal clinical syndromes (some are specific for glomerular disease), cont’d

• Asymptomatic hematuria, nonnephrotic proteinuria, or both:  
  ...mild glomerular abnormalities

• Rapidly progressive glomerulonephritis:  
  ...severe glomerular injury  
  ...loss of renal function in a few days or weeks  
  ...manifested by:  
    - microscopic hematuria  
    - dysmorphic RBCs & RBC casts  
    - mild to moderate proteinuria
Major renal clinical syndromes (some are specific for glomerular disease), cont’d

• Acute kidney injury:
  ...dominated by oliguria or anuria
  ...recent onset of azotemia
  ...can result from any acute condition affecting any part of the nephron

• Chronic kidney disease:
  ...prolonged symptoms and signs of uremia
  ...the result of progressive scarring in the kidney from any cause
  ...may culminate in end-stage kidney disease
Major renal clinical syndromes (some are specific for glomerular disease), cont’d

- Urinary tract infection is characterized by bacteriuria and pyuria (bacteria and leukocytes in the urine). The infection may be symptomatic or asymptomatic, and it may affect the kidney (pyelonephritis) or the bladder (cystitis) only.

- Nephrolithiasis (renal stones) is manifested by renal colic, hematuria (without red cell casts), and recurrent stone formation.
Thank You