Glomerular pathology-2
Nephritic syndrome

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The Nephritic Syndrome

- **Pathogenesis:** inflammation
- **proliferation of the cells in glomeruli & leukocytic infiltrate →**
- **Injured capillary walls → escape of RBCs into urine →↓ GFR →**
- **oliguria, fluid retention, and azotemia.**
- **Hypertension** (a result of both the fluid retention and some augmented renin release from kidneys).
Nephritic Syndrome: Presentation

- **PHAROH**
- **Proteinuria**
  - <3.5g/1.73m2/day
- **Hematuria**
  - Abrupt onset
- **Azotemia**
  - Increased creatinine and urea
- **RBC Casts**
- **Oliguria**
- **HTN**

Peripheral Edema/Puffy Eyes

“Smoky Urine”
Glomerular diseases mostly presenting with Nephritic syndrome
1- Membranoproliferative Glomerulonephritis (MPGN)

- Abnormal proliferation of glomerular cells
- Usually nephritic syndrome; others have a combined nephrotic-nephritic picture.

Types of MPGN:

1-type I (80% of cases) → immune complex disease (The inciting antigen is not known)

2-type II → excessive complement activation
Type I MPGN

- circulating immune complexes
- Many associations: hepatitis B and C; SLE; infected A-V shunts.
Type II MPGN (*dense-deposit disease*)

- **Cause:** *excessive complement activation*

- autoantibody against C3 convertase called *C3 nephritic factor* (it stabilizes the enzyme and lead to uncontrolled cleavage of C3 and activation of the alternative complement pathway).

- **Result:** Hypocomplementemia
• **Morphology**

• **LM**

• both types of MPGN are similar by LM.

• glomeruli are large with accentuated **lobular appearance** and show **proliferation of mesangial and endothelial cells** as well as infiltrating leukocytes

• **GBM is thickened** (double contour or "tram track")

• The **tram track** appearance is caused by "splitting" of the GBM
silver stain -**double contour** of the basement membranes("**tram-track**" ) that is characteristic of (MPGN)(arrows).
• **IF**
  
• Type I MPGN → subendothelial electron-dense deposits (IgG and complement C1q and C4)
  
• Type II MPGN → C3 alone in GBM
EM- dense deposits in the basement membrane of MPGN type II in a ribbon-like mass (arrows)
• **Clinical Course**
• prognosis poor.
• No remission.
• 40% progress to end-stage renal failure.
• 30% had variable degrees of renal insufficiency.
• **Dense-deposit disease (type II) has a worse prognosis.**
• It tends to recur in renal transplant recipients
2- Acute Postinfectious (Poststreptococcal) Glomerulonephritis (PSGN)

- deposition of **immune complexes** + proliferation of glomerular cells and leukocytes (neutrophils).
- **Not** direct infection of the kidney

- **Causes:** infection of pharynx or skin
- poststreptococcal GN (most common).
- Infections by other organisms as pneumococci and staphylococci
Poststreptococcal GN

• 1-4 wks after recovery from a group A streptococcal infection (pharynx or skin).

• A few strains (3%) of β-hemolytic streptococci are capable of this

• **Mechanism**: binding of immune complexes or antibodies to bacterial antigens “planted” in the GBM
• **LM**
  - proliferation of endothelial and mesangial cells and neutrophilic infiltrate.

• **IF**
  - deposits of IgG and complement within the capillary walls

• **EM**
  - immune complexes “subepithelial "humps" in GBM.”
PSGN: increased epithelial, endothelial, and mesangial cells as well as neutrophils in and around the capillary loops (arrows)
Subepithelial “humps”

Epithelial cell

“hump”-like deposit

GBM
PSGN- Clinical Course

- acute onset.
- fever, nausea, and nephritic syndrome.
- gross hematuria.
- Mild proteinuria.
- Serum complement levels are low during the active phase of the disease.
- ↑serum anti-streptolysin O antibody titers.
- Recovery occurs in most children.
3- IgA Nephropathy

• one of the most common causes of recurrent microscopic or gross hematuria

• children and young adults.

• hematuria 1 or 2 days after nonspecific upper respiratory tract infection.

• hematuria lasts several days and then subsides and recur every few months.
**Pathogenesis**

- abnormality in IgA production and clearance.

- **LM:** variable

- **IF:** mesangial deposition of IgA with C3

- **EM:** deposits in the mesangium
IF : IgA mesangial staining.
Rapidly Progressive (Crescentic) Glomerulonephritis
Rapidly Progressive (Crescentic) Glomerulonephritis

• characterized by the presence of crescents (crescentic GN).

• proliferation of the parietal epithelial cells of Bowman's capsule in response to injury and infiltration of monocytes and macrophages.

• nephritic syndrome rapidly progresses to oliguria and azotemia.
Crescentic GN (PAS stain).
the collapsed glomerular tufts and the **crescent-shaped** mass of proliferating cells and leukocytes internal to Bowman's capsule.
Hereditary Nephritis

• a group of hereditary glomerular diseases caused by mutations in GBM proteins (most common X-linked).

• *Most important type: Alport syndrome*
• **Alport syndrome**
  nephritis + nerve deafness + eye disorders (lens dislocation, posterior cataracts, corneal dystrophy).

• **Pathogenesis:**
  • Mutation of any one of the \( \alpha \) chains of type IV collagen
  • renal failure occurs between 20-50 yrs of age

• **EM**
  • GBM thin and attenuated
  • GBM later develops splitting and lamination "basket-weave" appearance
Basket weave GBM in Alport syndrome
<table>
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<tr>
<th>Disease</th>
<th>Presentation</th>
<th>Age</th>
<th>LM</th>
<th>IF</th>
<th>EM</th>
<th>Prognosis</th>
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<tr>
<td>MCD</td>
<td>nephrotic</td>
<td>Children</td>
<td>none</td>
<td>negative</td>
<td>Effaced foot processes</td>
<td>good</td>
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<tr>
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<td>adults</td>
<td>Segmental sclerosis</td>
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<td>Effaced foot processes</td>
<td>Poor?</td>
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<tr>
<td>MNP</td>
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<td>adults</td>
<td>Thickened GBM</td>
<td>IgG+  C3+</td>
<td>Sub-epithelial spikes and domes</td>
<td>Poor?</td>
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<tr>
<td>MPGN-type1</td>
<td>Nephritic/ nephrotic</td>
<td>adults</td>
<td>Tram track</td>
<td>Ig s</td>
<td>Subendothelial deposits</td>
<td>poor</td>
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<tr>
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<td>Nephritic/ nephrotic</td>
<td>adults</td>
<td>Tram track</td>
<td>C3+</td>
<td>Dense deposits</td>
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<td>IgG+  C3+</td>
<td>Subepithelial deposits (humps)</td>
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<tr>
<td>Alport syndrome</td>
<td>hematuria, hearing loss</td>
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<td>variable</td>
<td>negative</td>
<td>Basket weave GBM</td>
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