Nephritic syndrome

We will discuss:
1) Nephritic syndrome:
   - Acute postinfectious (poststreptococcal) GN
   - IgA nephropathy
   - Hereditary nephritis
2) Rapidly progressive GN (RPGN)

Ali Al Khader, M.D.
Faculty of Medicine
Al-Balqa’ Applied University
Email: ali.alkhader@bau.edu.jo
A clinical syndrome, composed mainly of:

(1) hematuria
   ...with dysmorphic red cells and red cell casts in the urine

(2) some degree of oliguria and azotemia

(3) hypertension

Proteinuria & edema may also be present but less severe than nephrotic syndrome
Acute postinfectious/poststreptococcal glomerulonephritis

- Deposition of immune complexes

- Proliferation of different types of cells including WBCs & especially neutrophils

- Typically: poststreptococcal, but may be: pneumococci, staphylococci...etc.
  
  ...as well as several common viral diseases such as mumps, measles, chickenpox, and hepatitis B and C

- Lupus nephritis (endogenous antigen) may present with proliferative pattern...but more commonly to present with secondary membranous nephropathy
Poststreptococcal GN, cont’d

• Typically: a child 1-4 weeks after recovery from group A streptococcal infection
  ...only certain “nephritogenic” strains
  ...mostly pharyngeal or cutaneous

Streptococcal exotoxin B (Spe B) and streptococcal GAPDH are the main streptococcal antigens

- circulating immune complexes...and may also be planted
- complement classical & alternative pathway activation
- hypocomplementemia
- granular deposits of IgG & complement...mainly capillary (but mesangially also present to a lesser degree)

Alternative more than classical pathway...so mainly C3 is decreased in serum and it is the main complement that is deposited (C4 & C2 to a lesser extent)
Poststreptococcal GN, morphology

- **LM:** -the most characteristic: increased glomerular cellularity...diffusely
  -sometimes: necrosis in glomerulus
  -in a few cases: crescents...due to severe inflammatory injury

- **EM:** the deposits are seen:
  -subendothelially
  -intramembranous
  -most prominent: subepithelial humps
  -occasionally mesangial

Caused by proliferation and swelling of endothelial and mesangial cells and by infiltrating neutrophils and monocytes.
Poststreptococcal GN, IF

• IgG & complement
  ...granular
  ...capillary (mainly) & some mesangial areas

• These deposits usually are cleared over a period of about 2 months
Poststreptococcal GN, clinical course

- Abrupt onset, starting by malaise, nausea, and slight fever

- Nephritic syndrome...in general here: mild to moderate

- May occasionally present as nephrotic syndrome!!

- Recovery in most children in epidemic cases

- Some: rapidly progressive GN or progression to scarring and chronic kidney disease

- Sporadic (nonepidemic) cases:
  - in adults: 15% to 50% of affected persons develop end-stage renal disease over the ensuing few years or 1 to 2 decades
  - much lower incidence of developing chronic kidney disease in children sporadic cases

Serum complement levels are low during the active phase of the disease, and serum anti-streptolysin O antibody titers are elevated in poststreptococcal cases
IgA nephropathy

- One of the most common causes of recurrent microscopic or gross hematuria and is the most common glomerular disease revealed by renal biopsy worldwide

- Usually children and young adults

- Begins as an episode of gross hematuria that occurs within 1 or 2 days of a nonspecific upper respiratory tract infection

- Typically, the hematuria lasts several days and then subsides, only to recur every few months
IgA nephropathy, cont’d

• The hallmark of the disease is: the deposition of IgA & IgA-containing complexes in the mesangium

• Henoch-Schonlein purpura is a systemic syndrome involving the skin (purpuric rash), gastrointestinal tract (abdominal pain), joints (arthritis), and kidneys (in the form of mesangial IgA deposition)

• Increased IgA I production and decreased IgA I clearance (due to abnormal glycosylation)...suggested pathogenesis
  ...also antibodies against abnormal IgA I, so: also: IgA-containing immune complexes are also deposited
IgA nephropathy, cont’d

• C1q & C4 are not deposited...the alternative pathway is activated here

• In genetically susceptible individuals, respiratory or gastrointestinal exposure to microbial or other antigens (e.g., viruses, bacteria, food proteins) will induce the increase in IgA

• Secondary IgA nephropathy is seen in celiac and liver disease
IgA nephropathy, morphology

• LM: variable:
  ...normal
  ...or mesangial widening and segmental inflammation confined to some glomeruli (focal proliferative GN)
  ...or diffuse mesangial proliferation (mesangioproliferative GN)
  ...or (rarely) crescentic GN

Electron microscopy: confirms the presence of electron-dense deposits in the mesangium...in a minority of cases: also subendothelial...especially in focal proliferative GN

*IF:*
The characteristic immunofluorescence picture is of mesangial deposition of IgA, often with C3 and properdin and smaller amounts of IgG or IgM
IgA nephropathy, clinical course

• More than half of those with IgA nephropathy present with gross hematuria after an infection of the respiratory or, less commonly, gastrointestinal or urinary tract.

• 30% to 40% have only microscopic hematuria, with or without proteinuria.

• 5% to 10% develop typical acute nephritic syndrome.

• The hematuria typically lasts for several days and then subsides, only to return every few months.

• Many patients maintain normal renal function for decades.

• Slow progression to chronic renal failure occurs in 25% to 50% of cases over a period of 20 years.

Prognosis can be predicted by biopsy: worse if: diffuse mesangial proliferation, segmental sclerosis, endocapillary proliferation, or tubulointerstitial fibrosis.
Hereditary nephritis

• Mutations in genes encoding GBM proteins
• Alport syndrome...the best studied among these entities
  ...nephritis is accompanied by:
    - nerve deafness
    - various eye disorders
  ...most common:
    - x-linked
    - alpha 5 type IV collagen
**Alport syndrome, morphology**

- LM: unremarkable until late in the course...due to secondary sclerosis
  ...In some kidneys, interstitial cells take on a foamy appearance as a result of accumulation of neutral fats and mucopolysaccharides (foam cells) as a reaction to marked proteinuria...is this specific?
  ...With progression:
    - increasing glomerulosclerosis
    - vascular sclerosis
    - tubular atrophy
    - interstitial fibrosis

**EM:** the basement membrane of glomeruli is thin and attenuated early in the course ...
...late:
the GBM develops irregular foci of thickening or attenuation with pronounced splitting and lamination of the lamina densa, yielding a “basketweave” appearance
Alport syndrome, clinical course

- present at age 5 to 20 years:
  - gross or microscopic hematuria and proteinuria
  - overt renal failure occurs between 20 and 50 years of age

Female carriers of X-linked Alport syndrome or carriers of either gender of the autosomal forms usually present with persistent hematuria, which most often is asymptomatic and is associated with a benign clinical course. In these patients, biopsy specimens show only thinning of the GBM.
Rapidly progressive glomerulonephritis (RPGN) ...
... a brief discussion

- Not specific, just a clinical syndrome

- Laboratory findings typical of the nephritic syndrome, and often severe oliguria

- If untreated, it leads to death from renal failure within a period of weeks to months

- The characteristic histologic finding associated with RPGN is the presence of crescents (crescentic GN)
  ...produced predominantly by the proliferation of the parietal epithelial cells lining Bowman capsule and by the infiltration of monocytes and macrophages

- Idiopathic or due to a known cause
RPGN, classification & pathogenesis

- 12% of the patients have anti-GBM antibody–mediated crescentic GN with or without lung involvement

- 44% have immune complex GN with crescents

- The remaining 44% have pauciimmune crescentic GN

linear deposits of IgG and, in many cases, C3 on the GBM

...Anti-GBM antibodies are present in the serum...diagnosis is important to do plasmapheresis which is effective here

Pulmonary hemorrhage

Any type can be complicated by RPGN

defined by the lack of anti-GBM antibodies or of significant immune complex deposition detectable by immunofluorescence and electron microscopy

Thank You