ACUTE GLOMERULONEPHRITIS
OUTLINE

• Definition
• Etiology
• Pathology/pathogenesis
• Risk factors
• Clinical Presentation
• Investigation
• Differential Diagnosis
• Management
• Outcome/Prognosis
• Indication for Renal Biopsy
• Summary
DEFINITION

- Acute Glomerulonephritis (AGN) is characterized by:
  - Abrupt Onset Hematuria
  - Edema
  - Hypertension
  - Oliguria and Renal insufficiency.
ETIOLOGY- NEPHRITIC SYNDROME

• PSGN follows infection of the throat or skin by certain “nephritogenic” strains of group A β-hemolytic streptococci.

• Epidemics of nephritis have been described in association with throat (serotypes M1, M4, M25, M12) and skin (serotype M49) infections.
Glomerular inflammation and injury due to:

• Acute, self limiting, reversible conditions (Acute Glomerulonephritis or AGN):
  • Post-infectious AGN: can occur after streptococcal (most common) or other bacterial infection/ viral or Mycoplasma infection
  • Henoch Schnolein Nephritis

• First presentation of chronic disease:
  • IgA nephropathy
  • Membranoproliferative glomerulonephritis (MPGN)
  • SLE, PAN, WG and other chronic vasculitis
  • Alport’s Syndrome
PATHOLOGY

• Glomeruli appear enlarged
• Diffuse mesangial cell proliferation
• Polymorphonuclear leukocyte infiltration present
• Crescents and interstitial inflammation in severe cases.
• Immunofluorescence microscopy reveals a pattern of “lumpy-bumpy” deposits of immunoglobulin and complement on the glomerular basement membrane and in the mesangium.
• Electron microscopy, electron-dense deposits, or “humps,” are observed on the epithelial side of the glomerular basement membrane
Hypercellular glomerulus with proliferating endothelial and mesangial cells, and neutrophil infiltration.

Granular bumpy pattern of immune deposits on immunofluorescence
Electron micrograph in poststreptococcal glomerulonephritis demonstrating electron-dense deposits (D) on the epithelial cell (Ep) side of the glomerular basement membrane. A polymorphonuclear leukocyte (P) is present within the lumen (L) of the capillary. BS, Bowman space; M, mesangium.
PATHOGENESIS

THEORIES
1. Trapping of circulating immune complexes in glomeruli
2. Molecular mimicry between strep antigens and renal antigens (glomer tissue acts as auto antigen-reacts with circulating antibodies formed against strep antigens)
3. In situ immune complex formation against anti strep antibodies and glomeruli
4. Direct complement activation
RISK FACTORS

Throat infection: Winter or early spring
Pyoderma: late summer or fall

Overall risk of infection: 15%, regardless of site

Risk of infection after pyoderma: 25%

Asymptomatic carriers: 20%, may thus occur in absence of prodrome

Peak incidence in pre-school children. Clinically apparent GN occurs in < 2% of children infected with strep infection
CLINICAL MANIFESTATIONS

- Abrupt onset
- Age 4-12 years, M>F
- Latent period: Throat infection: 1-2 weeks
  Skin infection: 3-6 weeks

HEMATURIA
- Smoky brown or Cola colored
- Glomerular: dysmorphic RBC, casts in freshly spun urine

PROTEINURIA
- Mild to moderate but nephrotic range is rare

OLIGURIA
- Transient – 50%, Anuria rare
**EDEMA : 85%**  
- Mild : periorbital or pedal  
- Severe : hypertension, pleural effusion or ascites  
- Adolescents : more likely face and legs

**HYPERTENSION: in 80%**  
- Headache, Somnolence  
- Changes in mental status  
- Anorexia, Nausea , Convulsions
• **HYPERTENSIVE EMERGENCY**: 10%
  - BP > 30% increased for age & sex
  - Evidence of encephalopathy
  - Heart failure or pulmonary edema

• **AZOTEMIA**: varying degrees

• **CIRCULATORY CONGESTION**: 20%
  - Dyspnoea, Orthopnoea
  - Cough, Tachycardia, Gallop rhythm
  - Basal creps, CCF, Pulmonary edema
PSGN: ATYPICAL PRESENTATION

Pulmonary edema

Congestive cardiac failure

Hypertensive encephalopathy

Renal failure

Nephrotic syndrome
INVESTIGATIONS

• **URINE**
  - Dysmorphic or crenated RBC and RBC casts
  - Moderate proteinuria ; 5-10% → nephrotic range (Lasts for approximately 5 month)
  - Leukocyte or granular or hyaline casts

• **BLOOD**
  - Transient elevation of urea and creatinine
  - Low complement S.C3 in >90% - in first 2 weeks(normalises in 6-8 weeks)
  - Serum CH50 is commonly depressed, C4 is most often normal or mildly depressed in PSGN.
  - ASO titres elevated 1-5 weeks after infection in 80%, four fold rise, Return to normal after several months
  - The best single antibody titer to document cutaneous streptococcal infection is the antideoxyribonuclease B level

• **Chest Xray** may show pulmonary congestion, cardiomegaly
• **Tubular function** is preserved, or mildly reduced
Clinical features of Acute Glomerulonephritis

**Decreased Serum complement (C3, CH 50)**

**Systemic diseases**
- Lupus nephritis (focal 75%, diffuse 90%)
- Subacute bacterial endocarditis (90%)
- Shunt nephritis (90%)
- Essential mixed cryoglobulinemia (85%)
- Visceral abscess, Renal diseases
- Acute postinfectious GN (90%)
- Membranoproliferative GN Type I (50–80%)

**Normal S.C3**

**Systemic diseases**
- Polyarteritis nodosa, Hypersensitivity vasculitis,
- Henoch-Schönlein purpura
- Goodpasture syndrome

**Renal diseases**
- IgA nephropathy, RPGN
  - Type I (anti-GBM disease)
  - Type II (immune complex CGN)
  - Type III (pauciimmune CGN)
- Postinfectious GN (nonstreptococcal)

**Serologic evidence of an antecedent streptococcal infection (ASO, anti–DNase B, streptozyme test)**

**Positive and/or return of low serum C3 complement to normal by 6–8 wk**
- Acute poststreptococcal GN

**Negative or failure of low serum C3 complement to return to normal by 6–8 wk**
- Lupus nephritis (ANA+, Anti ds DNA Ab)
- Essential mixed cryoglobulinemia (cryoglobulin, hepatitis C virus)
- Shunt nephritis, Visceral abscess (blood culture)
- Membranoproliferative GN (C3NF)
- Bacterial endocarditis, Post infectious GN (non streptococcal)
MANAGEMENT - GENERAL

- Salt restricted diet, low K
- Fluid intake ↓ (600ml/m2+ previous days output)
- Frusemide or loop diuretics for prompt diuresis in fluid overload, volume dependent hypertension, cardiovascular congestion
- Hypertensive emergencies → Anti hypertensives
  – Ca channel blockers
  – Loop diuretics
  – ACE inhibitors
MANAGEMENT- SPECIFIC

Pulmonary edema
– Aggressive diuresis, Oxygen, Morphine, Ventilation

Hyperkalemia
– Oral/iv Restriction, K binding resins
– Nebulised Salbutamol, Glucose insulin
– Calcium infusion

Dialysis
– Fluid overload
– Severe azotemia
– Electrolyte abnormalities
DAILY MONITORING

Clinical: Edema, JVP, BP
Fluid intake and output
Weight
Respiratory status
Neurological status
ECG if hyperkalemic

Biochemical: Urine microscopy
Blood Urea, Creatinine
Electrolytes
MOST IMPORTANT IN ACUTE NEPHRITIS

Clinical diagnosis

Antecedent streptococcal infection +

Serological markers of immune mediated inflammation
**RPGN**

**If Suspected:**
- Is a medical emergency-can progress rapidly to ESR
- Requires histopathological confirmation
- Aggressive immunosuppressive treatment

**Options for treatment:**
- Oral steroids
- iv Methyl Prednisolone
- iv Cyclophosphamide
- Plasmapheresis
- Haemodialysis
RPGN- epithelial cell proliferation inside the Bowmans capsule causing crescent formation and compression of underlying glomerular tuft
OUTCOME - PROGNOSIS

- Usually self limiting, good prognosis - mortality < 1%
- Recovery in 7-10 days
- S.C 3 returns to normal in 6-8 weeks
- Hypertension and hematuria may resolve over weeks
- Proteinuria may last for months
- Microhematuria for years
- Renal Biopsy rarely needed
- ESRD occurs < 2%

• Majority have life long protection
• Recurrent infection: 0.7-7%
• LONG TERM FOLLOW ADVOCATED
INDICATIONS- RENAL BIOPSY

• ATYPICAL PRESENTATION
• Nephrotic range proteinuria in acute stage
• Normal serum complement
• Progressively increasing S creatinine
• Prolonged hypocomplementemia > 3 m
• Ongoing macrohematuria
• Long lasting proteinuria
• Persistent azotemia
• Associated symptoms of systemic disease
INDICATIONS- RENAL BIOPSY

- Postinfectious GN and secondary causes
- Hepatitis B infection
- Shunt Nephritis
- Infective endocarditis
- Associated with HSP
SUMMARY

• Immune mediated condition
• Most common- prototype: PSGN
• Self limiting- rarely progresses to ESRD or recurs
• Complete recovery occurs in >95% of children
• Pathology governs treatment in atypical or severe cases. Outcome is variable
• In secondary forms – more specific treatment may needed
THANK YOU