Postinfectious Glomerulonephritis

Dr Ramnath Balasubramanian
Post streptococcal glomerulonephritis mainly affects:

A. Adults > 60 years old
B. Children between 5 - 12 years old
C. Children < 2 years old
D. Both A & B above
Introduction

“Immune mediated glomerular injury that occurs as a result of host response to an extra-renal infection”

Post streptococcal GN, one of the oldest renal diseases – “the dropsy that follows scarlet fever”

The risk of PSGN is increased in older patients (greater than 60 years of age) and in children between 5 and 12 years of age.

PSGN is uncommon in children less than three years of age.

PSGN is twice as frequent in males as in females.
The changing epidemiology

• Overall reducing incidence over the last 4 decades
• Estimated global incidence 472,000 cases per year
  16000 from developed countries
• Italian registry data – 0.3 cases per 100,000 patient years
• Much higher in LMIC countries - >200 cases/mill pop /yr
• AKI related to PIGN 5-30%
• Much wider spectrum of infectious agents
Nature Rev Neph:2009
Changing Trends

**Before**
- Acute poststreptococcal glomerulonephritis (APSGN)
- Pathogenic agents mainly group A streptococcus
- Age group - pediatric
- Prognosis - complete recovery >95% of patients

**Current**
- Post Infectious glomerulonephritis (PIGN)
- Pathogenic agent: includes staph and gram negative bacteria
- Age group – older
- Prognosis - complete recovery in 50-60% of patients
## Etiology

<table>
<thead>
<tr>
<th>Bacterial</th>
<th>Viral</th>
<th>Fungal</th>
<th>Parasites</th>
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<tbody>
<tr>
<td>Streptococcus groups A, C, G</td>
<td>Coxackie virus</td>
<td>Coccidioides immitis</td>
<td>Plasmodium malariae</td>
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<td>Streptococcus viridans</td>
<td>Echovirus</td>
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<td>Plasmodium falciparum</td>
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<td>Staphylococcus (aureus, epidermidis)</td>
<td>Cytomegalovirus</td>
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<td>Schistosoma mansoni</td>
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<td>Pneumococcus</td>
<td>Epstein–Barr virus</td>
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<td>Schistosoma haematobium</td>
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<td>Neisseria meningitidis</td>
<td>Hepatitis B, C</td>
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<td>Toxoplasma gondii</td>
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<td>Mycobacteria</td>
<td>HIV</td>
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<td>Filarisis</td>
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<td>Salmonella typhi</td>
<td>Rubella</td>
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<td>Trichinosis</td>
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<td>Klebsiella pneumoniae</td>
<td>Measles</td>
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<td>Escherichia coli</td>
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<td>Yersinia enterocolitica</td>
<td>Vaccinia</td>
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<td>Legionella</td>
<td>Parvovirus</td>
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<td>Brucella melitensis</td>
<td>Influenza</td>
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<td>Treponema pallidum</td>
<td>Adenovirus</td>
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<td>Corynebacterium bovis</td>
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<tr>
<td>Actinobacilli</td>
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<tr>
<td>Bartonella henselae</td>
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<tr>
<td>Orientia tsutsugamushi (scrub typhus)</td>
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<td>PSGN &gt;95%</td>
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Pathogenesis of PSGN

“Nephritogenic strains”
M Proteins
Nephritis associated plasmin receptor (NAPlr)
- 92% of patients in convalescence of PSGN
- Glomerular deposition of NAPlr

Streptococcal Pyrogenic exotoxin B (SPeB)
- America and Europe
Nephritogenic streptococcus GAPDH (NAPIr)

↓

Mesangial and GBM binding

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Plasmin entrapment and sustained activity
Inflammatory reactivity

↓

Immune complex penetration through Damaged GBM formation

Nephritogenic streptococcus GAPDH (SpeB)

↓

Anti-SpeB antibodies

↓

SpeB and Anti-SpeB binding

↓

Circulating SpeB-antiSpeB deposition In situ SpeB-anti-SpeB formation

Immune Complex-Mediated Glomerulonephritis
PSGN and Complements

- Mannose binding lectin (MBL) recognises Strep cell wall polysaccharides
- Predominantly alternate pathway activation
- Initially some classical pathway activation – Low C1q, C4
- Crescentic GN association with normal complement levels
Clinical Features

Subclinical form – 4-5 times more common than GN

- 24% of streptococcal sore throat
- 1-2 weeks post throat infection, 3-4 weeks post pyoderma

Acute nephritic syndrome “classical presentation”

- macroscopic haematuria (30-40%)
- hypertension (60-80%)
- oedema (80%)
- oliguria (>50%)

Nephrotic syndrome – 2 to 4%

HSP like rash
ASO titres for the diagnosis of Post streptococcal glomerulonephritis

A. Highly sensitive
B. Highly specific
C. Both A & B
D. None of the above.
If complement levels are persistently low after an episode post streptococcal glomerulonephritis, the following conditions need to be considered EXCEPT

A. Lupus
B. Membranous nephropathy
C. Membranous glomerulonephritis
D. IgA nephropathy
ASOT
- Highly sensitive >97% but specificity 80%
- Titres higher in sore throat Vs pyoderma
- Peak at 3 weeks after presentation

Consider alternative diagnosis
- Normal complement level: rule out IgA nephropathy
- Low complement level after 1–2 months: consider SLE, MPGN
- Nephrotic-range proteinuria
- Rising proteinuria, RPGN
- Age <2 years
- Extra-renal manifestations
## Pathology

### Indications for Biopsy

**Early stage phase**
- Rapid progressive course
- Hypertension >2 weeks
- Depressed GFR† >2 weeks
- Normal complement levels
- Non-significant titres of antistreptococcal antibodies
- Extra-renal manifestations
- Nephrotic syndrome

**In recovery**
- Depressed GFR >4 weeks
- Hypocomplementaemia >12 weeks
- Persistent proteinuria >6 months
- Persistent microscopic haematuria >18 months
diffuse mesangial and endocapillary hypercellularity, and a large number of polymorphonuclear neutrophils (hematoxylin and eosin stain).
Treatment

• Antibiotics for treatment
• Fluid and supportive management
• Antibiotics for prophylaxis of PSGN
• Antihypertensive agents
• Immunosuppressants
Antibiotics in PSGN

- Treatment to reduce antigen load – Penicillin / Erythromycin
- Antibiotics for prevention
- No global agreement on treatment on Group A streptococcal pharyngitis
Supportive care

- Fluids – aim for euvolemia
- Salt restriction
- Diuretics
- Antihypertensives
Immunosuppressants

- Corticosteroids are suggested for severe crescentic GN based on anecdotal evidence only

Crescentic glomerulonephritis with more than 30% of the glomeruli involved

A short course of intravenous pulse steroid therapy is recommended (500 mg to 1 g/1.73 m² of methylprednisolone od for 3-5 d).
Special subtypes of PIGN

Endocarditis associated GN
- Previously seen with sub-acute infection with Strep viridans
- Now restricted to adult IV drug users
- Limited data in children

IgA dominant PIGN
- Variant of PIGN – staph
- Consider IgA and HSP

Shunt nephritis
- Associated with VA shunt
- Immunological reaction with activation of classical com pathway
Prognosis

• No hypertension or renal impairment. Proteinuria 3.1% Microhaematuria 6.3%

• Hypertension twice more prevalent than in controls. No significant difference in renal function, haematuria or proteinuria.

• Children in LMIC – much worse prognosis
• Long term outcome studies scarce
• Excellent long term prognosis
Summary

• PIGN still a major cause of acute GN
• Infection associated GN a better term?
• Changing epidemiology
• Multiple streptococcal antigens identified and immune complex deposition most accepted mechanism
• Evidence base for treatment poor
• Excellent long term outcome
Post-infectious glomerulonephritis

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