Crescentic Glomerulonephritis

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Vice president for students affairs, Mansoura University,
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A twelve-year old boy presented to ER by 4 days history of dark-colored urine, oliguria. His blood pressure is 150/100. UA reveals RBCs 100/HPF, proteinuria ++, and granular cast. Serum creatinine is 3mg/dL. Over the next 10 days, he becomes anuric and serum creatinine rises to...

**Acute nephritic syndrome**

**Rapidly progressive**
WHAT IS YOUR DIAGNOSIS?

Rapidly progressive glomerulonephritis
WHAT IS THE SUGGESTED INVESTIGATION?

Renal Biopsy
WHAT IS YOUR DIAGNOSIS?

Crescentic glomerulonephritis
Rapidly progressive glomerulonephritis

Crescentic glomerulonephritis
AGENDA

- What is meant by crescentic GN...?
- Pathogenesis
- Classification and causes
- Pathology
- Causes
- Epidemiology
- Work up
- Treatment
- Outcome
- Take home Messages
WHAT IS MEANT BY CRESCENTIC GN....?
PATHOGENESIS
CLASSIFICATION AND CAUSES
PATHOLOGY

EM

Normal glomerulus

Active hypercellular crescent (Gaps in glomerular basement membrane)
Immune complex GN

- **Post infectious GN.** Poststreptococcal nephritis, infective endocarditis, shunt nephritis, visceral abscesses, Staphylococcus aureus sepsis, other infections: human immunodeficiency virus, hepatitis B and C, syphilis, legionella, mycoplasma, tuberculosis, leprosy
- **Systemic disease.** SLE, HSP, cryoglobulinemia, mixed connective tissue disorder, juvenile rheumatoid arthritis, Behcet's syndrome, relapsing polychondritis, mixed connective tissue disease, dermatomyositis
- **Primary GN.** IgA nephropathy, membranoproliferative GN, membranous nephropathy, C1q nephropathy

Pauci-immune crescentic GN

- **Microscopic polyangiitis,** Wegener's granulomatosis, renal limited vasculitis, Churg Strauss syndrome
- **Medications:** penicillamine, hydralazine, hydrocarbons, propylthiouracil

Anti glomerular basement membrane (GBM) GN

- Anti-GBM nephritis, Goodpasture's syndrome, postrenal transplantation in Alport syndrome

Idiopathic crescentic GN
EPIDEMIOLOGY
TABLE 31-16 Relative Frequency of Immunopathologic Categories of Crescentic Glomerulonephritis (CGN) in Different Age Groups (in Percent)*

<table>
<thead>
<tr>
<th>IMMUNOPATHOLOGIC CATEGORY</th>
<th>ALL AGES (n = 632)</th>
<th>1-20 (n = 73)</th>
<th>21-60 (n = 303)</th>
<th>&gt;60 (n = 256)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anti–glomerular basement membrane CGN</td>
<td>15</td>
<td>12</td>
<td>15</td>
<td>15</td>
</tr>
<tr>
<td>Immune complex CGN</td>
<td>24</td>
<td>45</td>
<td>35</td>
<td>6</td>
</tr>
<tr>
<td>Pauci-immune CGN†</td>
<td>60</td>
<td>42</td>
<td>48</td>
<td>79</td>
</tr>
<tr>
<td>Other</td>
<td>1</td>
<td>0</td>
<td>3</td>
<td>0</td>
</tr>
</tbody>
</table>
## EPIDEMIOLOGY

<table>
<thead>
<tr>
<th>Condition</th>
<th>SPNSG (n=50)</th>
<th>Srivastava et al (n=43)</th>
<th>Niaudet Levy (n=41)</th>
<th>Jardim et al (n=30)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Immune complex disease</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Unspecified</td>
<td>26</td>
<td>2.3</td>
<td>4.8</td>
<td>-</td>
</tr>
<tr>
<td>Systemic lupus erythematous</td>
<td>18</td>
<td>2.3</td>
<td>2.4</td>
<td>3.3</td>
</tr>
<tr>
<td>Poststreptococcal GN</td>
<td>12</td>
<td>25.5</td>
<td>12.1</td>
<td>6.6</td>
</tr>
<tr>
<td>Henoch-Schönlein purpura</td>
<td>14</td>
<td>6.9</td>
<td>34.1</td>
<td>30</td>
</tr>
<tr>
<td>Membranoproliferative GN</td>
<td>4</td>
<td>-</td>
<td>21.9</td>
<td>23.3</td>
</tr>
<tr>
<td><strong>Vasculitis</strong></td>
<td>6</td>
<td>-</td>
<td>7.3</td>
<td>16.6</td>
</tr>
<tr>
<td><strong>Idiopathic crescentic GN</strong></td>
<td>14</td>
<td>60.4</td>
<td>7.3</td>
<td>13.3</td>
</tr>
<tr>
<td><strong>Antiglomerular basement disease</strong></td>
<td>6</td>
<td>2.3</td>
<td>7.3</td>
<td>6.6</td>
</tr>
<tr>
<td><strong>Others</strong></td>
<td>-</td>
<td>2.3</td>
<td>2.4</td>
<td>-</td>
</tr>
</tbody>
</table>
WORK UP
• Blood levels of urea, creatinine, electrolytes, calcium, phosphate

• Urinalysis: proteinuria; microscopy for erythrocytes and leukocytes, casts
Renal biopsy (light microscopy, immunofluorescence, electron microscopy)
Complement (C3, C4, CH50)

Low level
PSAGN, SLE, MPGN
Diagnosis

ASO, anti-DNase and anti-NDsae

Recent streptococcal infection
Diagnosis

ANA and anti-dsDNA

SLE
ANCA
Pauci-immune GN
Anti-GBM (IgG) antibodies

Anti-GBM nephritis or Goodpasture's syndrome
• Blood levels of cryoglobulin, hepatitis serology
Radiographs, CT scan for chest, sinuses (patients with Goodpasture's syndrome, Wegener's granulomatosis)
TREATMENT
PSAGN Vs other causes

- Are there differences between APSGN and other causes?
- When to start the specific treatment?

Induction phase

- What is the duration of induction phase?
- What is the suggested protocol to be used?

Maintenance Phase

- When to shift?
- What is the suggested protocol to be used?
PSAGN Vs other causes

- Are there differences between APSGN and other causes?
- When to start the specific treatment?

**Whom to treat?**

1. Crescents involving $\geq 50\%$ glomeruli.
2. Acute kidney injury

**Medication?**

1. Methylprednisolone
   - 3 to 6 IV pulses of methylprednisolone followed by tapering doses of oral steroids for 6 months.

2. Cyclophosphamide
   - Orally for 3 months.
   - or by IV monthly for 6 months.
**PSAGN Vs other causes**

- Are there differences between APSGN and other causes?
- When to start the specific treatment?

**Induction phase**

- What is the duration of induction phase?
- What is the suggested protocol to be used?

**Maintenance Phase**

- When to start?
- What is the suggested protocol to be used?
Duration: 3–6 months

Protocol:

1. Prednisone:
   - Methylprednisolone 15–20 mg/kg (maximum 1 g) IV daily for 3–6 doses
   - Prednisone 1.5–2 mg/kg/day PO for 4 weeks; taper to 0.5 mg/kg daily by 3 months; 0.5–1 mg/kg on alternate day for 3 months

2. Cyclophosphamide
   - IV: 500–750 mg/m2 every 3–4 weeks for 6 pulses OR
   - Oral: 2 mg/kg/day

3. Plasmapheresis (double volume) on alternate days for 2–weeks

4. Agents for refractory disease: Intravenous immunoglobulin, TNF-α antibody (infliximab), anti CD20 (rituximab)
Duration: 2-5 years

Protocol:

1. Prednisone 0.5-1 mg/kg on alternate days; later taper
2. Azathioprine 1.5-2 mg/kg/day for 12-18 months
3. Consider mycophenolate mofetil (1,000-1,200 mg/m²/day), if disease activity is not controlled
## Treatment of crescentic glomerulonephritis

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<tr>
<th>Induction phase (3–6 months)</th>
<th>Maintenance phase (2–5 year)</th>
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<td>Methylprednisolone 15–20 mg/kg (maximum 1 g) IV daily for 3–6 doses</td>
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### Agents for refractory disease

|                                                                                           |
| Intravenous immunoglobulin, TNF-α antibody (infliximab), anti CD20 (rituximab) |
• Evidence-based data are limited and specific treatment guidelines for children are based on data from case series and prospective studies in adults mainly.
Evidence-based clinical practice guidelines for rapidly progressive glomerulonephritis 2014

Yoshihiro Arimura, Eri Muso, Shoichi Fujimoto, Midori Hasegawa, Shinya Kaname, Joichi Usui, Toshiko Ihara, Masaki Kobayashi, Mitsuyo Itabashi, Kiyoki Kitagawa, Junichi Hirahashi, Kenjiro Kimura, Seiichi Matsuo

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Renal biopsy is useful in determining the treatment strategy for RPGN. It is important to evaluate and examine the histological parameters that determine the response to therapy and affect the renal prognosis.
CQ 8. Is initial therapy with corticosteroids alone recommended for improving renal function and survival in patients with RPGN?

- Corticosteroid alone → effective
- Corticosteroid + immunosuppressive → more effective
- Initial therapy with corticosteroids alone is recommended only in cases in which the use of immunosuppressive agents is not desirable.

Recommendation grade: C1
In patients with anti-GBM antibody glomerulonephritis presenting with RPGN, high doses of corticosteroids may improve renal function and survival. However, the combined use of immunosuppressive agents is more effective; therefore, initial therapy with corticosteroids alone is recommended, in combination with plasmapheresis, in cases in which the use of immunosuppressive agents is not desirable.
Adding intravenous pulse corticosteroid therapy to oral corticosteroids is recommended when the decline of renal function is very rapid, or when severe systemic complications are present.
Is initial therapy with immunosuppressive agents recommended for improving renal function and survival in patients with RPGN?

CQ 10. Is initial therapy with immunosuppressive agents recommended for improving renal function and survival in patients with RPGN?

Recommendation grade: B
In patients with ANCA-positive RPGN, the addition of immunosuppressive agents to corticosteroids in the initial therapy has been shown to improve renal function and survival.

Recommendation grade: C1
In patients with anti-GBM antibody-positive RPGN, the addition of immunosuppressive agents to corticosteroids in the initial therapy may improve renal function and survival. We recommend immunosuppressive agents with corticosteroids as the initial therapy for these patients.
Which is recommended for improving renal and patient survival in RPGN, oral cyclophosphamide or intravenous pulses of cyclophosphamide?

There are no differences in renal and patient survival between oral cyclophosphamide and intravenous pulses of cyclophosphamide.
If the standard therapy is insufficient, the addition of plasmapheresis to immunosuppressive therapy as the initial therapy may improve renal function and survival.
Is rituximab recommended for improving renal function and survival in patients with RPGN?

No evidence to support that treatment with rituximab improves renal function and survival; however, it could be considered if there is no other treatment available.

**Recommendation grade: not graded**

In patients with anti-GBM antibody disease presenting with RPGN, there is no evidence to support that treatment with rituximab improves renal function and survival.
Limited evidence that IVIg improves renal and patient survival in RPGN, IVIg can be used as an alternative option for patients with concurrent complications such as severe infections when it is advisable to avoid the standard therapy with high-dose steroids and immunosuppressant (off-label use).
Low-dose corticosteroids have been shown to improve renal function and survival.

Recommendation grade: B
In patients with anti-GBM antibody glomerulonephritis presenting with RPGN, low-dose corticosteroids have been shown to improve renal function and survival. We recommend corticosteroids as maintenance therapy for these patients.
The addition of immunosuppressive agents to corticosteroids in the maintenance therapy has been shown to improve renal function and survival.

**Recommendation grade: C1**

In patients with anti-GBM antibody-positive RPGN, the addition of immunosuppressive agents to corticosteroids in the maintenance therapy may improve renal function and survival. We recommend the use of immunosuppressive agents with corticosteroids as maintenance therapy for these patients.
OUTCOME

Almost to 60-70% recover renal function

Determinates of outcome:

+ The severity of renal failure at presentation
+ Renal histology
+ The promptness of intervention
+ The underlying disease
TAKE HOME MESSAGES
TAKE HOME MESSAGES

- RPGN and crescentic GN are two faces of a coin
- The histologic marker is the presence of crescentic, the clinical correlate is RPGN
- Diagnosis of crescentic GN needs the integration of serologic, pathologic and clinical views
TAKE HOME MESSAGES

- It is necessary to make an accurate and rapid diagnosis as treatment strategies vary and delay in instituting treatment results in irreversible disease.
- Evidence based data is limited and specific treatment guidelines for children are based on data from case series and prospective studies in adults.
- The course is largely determined by the severity of renal failure at presentation, the promptness of intervention, renal histology and the underlying disease.
Renal biopsy is useful in determining the treatment strategy.

The treatment strategy is similar in ANCA-positive and ANCA-negative patients.

The addition of immunosuppressive agents to corticosteroids improves renal survival.

All of the above.

In the treatment of RPGN:
Patients with circumferential crescents have more indolent course than those with non-circumferential one

Pauci-immune GN is the most prevalent pathological type in children

The histological type dose not affect the outcome of the disease

None of the above
Thank You