C3 Glomerulopathy

Current Care

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The following includes a list of current (within the last 24 months) affiliations:

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<tr>
<th>Affiliation / Financial Interest</th>
<th>Organization</th>
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<tr>
<td>Associate Director</td>
<td>Molecular Otolaryngology and Renal Research Laboratory</td>
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<td>NIH</td>
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<td>Site Investigator</td>
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My conflicts are managed by a University of Iowa mandatory conflict plan. Both prior and current relationships are on record at the University of Iowa’s Conflict in Research Office: [https://coi.research.uiowa.edu/](https://coi.research.uiowa.edu/)
Objectives

• Review current evaluation and therapy of C3 Glomerulopathy

• Review treatment guidelines for C3 Glomerulopathy

• Efficacy of current treatment approaches to C3 Glomerulopathy
Current Therapeutic Approach

1. Supportive
   a. Blood Pressure Control
      i. Direct pressure related damage to renal blood vessels
      ii. Blockade of renin effects
   b. Urine protein control
   c. Base-line exam
      a. Eye Exam (10% will have Drusen)

2. Diagnostic Workup

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**Functional assays**
- CH50, AP50, FH function

**Quantification of complement components and regulators**
- C3, C4, FI, FH, FB, Properdin

**Measurement of complement activation**
- C3d, Bb, sMAC

**Autoantibodies**
- Anti-FH, anti-FB, nephritic factors (C3, C4, C5)

**Genetic testing**
- C3, CFH, CFI, CFB, CFHR-5, MLPA

**Plasma cell disorders**
- Serum free light chains, serum and urine electrophoresis, and Immunofixation

**Immunofluorescence studies on kidney biopsy specimen**
- IgA, IgG, IgM, C1q, C3, fibrinogen, kappa, lambda, C4d (usually bright C3 negative or minimal Ig, negative C4d)
### Treatment of C3 Glomerulopathy

#### All Patients
- Optimal blood pressure control
- Optimal nutrition for both normal growth in children and healthy weight in adults
- Lipid control

#### Moderately Active Disease
- Urine protein over 500 mg/24 h despite supportive therapy or
- Moderate inflammation on renal biopsy or
- Recent increase in serum creatinine suggesting risk for progressive disease

#### Severe Disease
- Urine protein over 2000 mg/24 h despite immunosuppression and supportive therapy or
- Severe inflammation represented by marked endo- or extracapillary proliferation with or without crescent formation despite immunosuppression and supportive therapy or
- Increased serum creatinine suggesting risk for progressive disease at onset despite immunosuppression and supportive therapy

#### Manage other disease related features

#### Balancing steroid effect with side-effect

- Prednisone
- Mycophenolate mofetil

- Methylprednisolone pulse dosing as well as other anti-cellular immune suppressants have had limited success in rapidly progressive disease
- Data are insufficient to recommend eculizumab as a first-line agent for the treatment of rapidly progressive disease

Current Therapeutic Approach

1. Mycophenolate mofetil and prednisone
   a. Cell-Mediated Immune Suppression

2. Terminal Complement Pathway (TP) Blockade
   1. Anti-inflammation – Anti-anaphylotoxin
   2. Neutralizing effect of TP
- 26 Patients

- Median duration 14 months of eculizumab
  - 6 (23%) with global response
  - 6 (23%) with partial response
  - 14 (23%) no response

- Uncontrolled

Current Therapeutic Approach

1. Mycophenolate mofetil and prednisone

2. Terminal Complement Pathway (TP) Blockade
Moving Forward

• Clear understanding of underlying drivers of disease in a given patient
  – i.e. understanding the role of the terminal complement pathway in disease

• Better understanding of role of “inflammation” in C3 Glomerulopathy manifestations
  – “Secondary” effects of complement dysregulation

• Controlled trials
  – Patient enrollment
    • Patient Tolerance - Safety
  – Positive Outcomes
Thank You

Good Health to All of You!
I’m very thankful to have Two “Work” Families