Key Takeaways for Clinicians in the Management of C3 Glomerulopathy

**Diagnosis**

C3G is diagnosed on kidney biopsy with a membranoproliferative pattern of injury on light microscopy and C3 deposition at least 2 orders of magnitude greater than any other immune reactant on immunofluorescence.

Differential diagnosis of C3G:
- Infection related glomerulonephritis and post-infectious glomerulonephritis should be ruled out. In patients ≥ 50 years of age at presentation, evaluate for presence of monoclonal protein.

Clinical phenotype of C3G:
- Usually follows a chronic indolent course with persistent alternative complement pathway activation.

Extra-renal manifestations of C3G:
- Acquired partial lipodystrophy and retinal drusen are reported as direct consequence of complement activation.

Laboratory Investigations for C3G:
- Serum/plasma levels of complement proteins should be measured in all patients. Low C3 is seen in up to 75% cases of C3G. C3 nephritic factor, Factor H autoantibodies and free light chains should be assayed.

Genetic analysis in C3G:
- No clear benefit of genetic analysis except in kidney transplantation for possible donor evaluation.

**Treatment**

All patients should have optimal blood pressure control with renin angiotensin aldosterone system inhibitors. Adequate lipid control should be achieved.

For patients with moderate disease:
- Includes patients with 1) urine protein > 500 mg/24 hours despite supportive therapy, 2) moderate inflammation on biopsy, 3) recent increase in serum creatinine. Should be given prednisone and mycophenolate mofetil.

For patients with severe disease:
- Includes patients with 1) urine protein > 2000 mg/24 hours despite supportive therapy and immunosuppression, 2) severe inflammation on biopsy, 3) recent increase in serum creatinine. For moderate-to-severe disease, such patients can be treated with MMF and glucocorticoids. If this fails, eculizumab should be considered. Non-responders should be considered for a clinical trial where available.

Kidney transplantation in C3G:
- No specific data available. Carries high risk of histological recurrence (90%) with no known preventive strategies.

---

**References**