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Marked Renal C3 Deposition Defines a Distinct Clinicopathologic Phenotype in ANCA-Associated Glomerulonephritis

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Objectives : Complement activation is increasingly recognized as a critical amplifier of inflammation in ANCA-associated glomerulonephritis (ANCA-GN). However, the clinicopathologic and prognostic implications of marked glomerular C3 deposition remain incompletely understood. We investigated whether marked renal C3 deposition identifies a biologically distinct phenotype and whether it is associated with adverse renal outcomes.
Methods : Among 121 patients with ANCA-GN reviewed across four hospitals between 2015 and 2025, 110 patients with complete data were included in the final analysis. Renal C3 deposition was graded by immunofluorescence and categorized as no/trace or marked (>1+). Baseline clinical and histopathologic characteristics were compared between groups. Renal survival was defined as dialysis-free survival and evaluated using Kaplan–Meier analysis and Cox proportional hazards models. Treatment response was also assessed.
Results : Sixteen patients (14.5%) exhibited marked C3 deposition. Compared with the no/trace group, these patients had lower serum C3 levels (92 [80–108] vs. 103 [87–117] mg/dL; $p = 0.018$), a higher proportion of non-MPO ANCA serotype ($p = 0.071$), and a greater crescent ratio ($p = 0.094$), indicating a more severe crescentic burden. Treatment response did not significantly differ between groups ($p = 0.083$), although refractory disease was numerically more frequent in patients with marked deposition. Dialysis-free survival was significantly reduced in the marked group (log-rank $p = 0.049$), and Cox analysis demonstrated an approximately twofold increased risk of progression to dialysis (hazard ratio ≈ 2.1).
Conclusions : Marked renal C3 deposition delineates a clinicopathologic subset of ANCA-GN characterized by enhanced crescent formation and impaired renal recovery. These findings support the concept that prominent C3 deposition reflects active complement-mediated injury and may help identify patients who could derive greater benefit from complement-targeted therapeutic strategies. Further prospective studies are warranted to clarify its role in risk stratification and treatment selection.