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Hypocomplementemia at Diagnosis of Antineutrophil Cytoplasmic Autoantibody Glomerulonephritis Is an Independent Risk Factor for a Worst Outcome

The Authors Reply: We appreciate the opportunity to respond to the report by Tampe *et al*.[1] regarding the prognostic significance of C3 hypocomplementemia in patients with pauci-immune antineutrophil cytoplasmic autoantibody glomerulonephritis.[2] Notably, this group of investigators, in agreement with our findings, revealed that 13.2% of patients had low serum C3c at diagnosis, while these patients had higher probability of experiencing requirement of kidney replacement therapy or death.[1] Low serum C3c levels were associated with worse renal function, reflected by median glomerular filtration rate, higher urinary protein-to-creatinine ratio, and higher antineutrophil cytoplasmic autoantibody renal risk score at diagnosis.[1] Although we do not know the precise reason why a relatively small proportion of patients with antineutrophil cytoplasmic autoantibody vasculitis present with low serum complement, and how this is connected with a worst outcome, it is becoming clear that this subgroup of patients follows a different pathway, in terms of pathophysiology and outcome, despite administration of standard therapy. One might speculate that either delayed diagnosis or a different pathogenetic background might explain this observation. In any case, its interpretation points toward an individualized approach in patients with antineutrophil cytoplasmic autoantibody vasculitis, and more importantly given the knowledge of the crucial role of complement activation in some of these patients, complement blockage, using C5a receptor inhibitor avacopan or the monoclonal C5a antibody IFX-1, should probably be used in clinical practice in conjunction with all or part of the current therapeutic scheme.

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