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Autoantibodies targeting complement receptors 3a and 5a are decreased in ANCA-associated vasculitis

Sebastian Klapa[a,*], Andreas Koch[b], Anja Kerstein[a], Christian Karsten[c], Harald Heidecke[d], Markus Huber-Lang[e], Peter Lamprecht[a], Gabriela Riemekasten[a], Antje Müller[a]

[a] *Department of Rheumatology & Clinical Immunology, University of Lübeck & Institute for Experimental Medicine Christian-Albrechts-University Kiel c/o German Naval Medical Institute, Kronshagen, Germany*
[b] *Institute for Experimental Medicine Christian-Albrechts-University Kiel c/o German Naval Medical Institute, Kronshagen Germany*
[c] *Institute for Systemic Inflammation Research, University of Lübeck, Germany*
[d] *CellTrend GmbH, Luckenwalde, Germany*
[e] *Department of Orthopaedic, Trauma, Hand, Plastic and Reconstruction Surgery, University of Ulm*
[*] *Corresponding author, email: sebastian.klapa@uksh.de*

Introduction: Necrotizing crescentic glomerulonephritis (NCGN) is a pathogenic hallmark of full-blown ANCA-associated vasculitis (AAV). In AAV, NCGN is characterized by scantly deposited immune complexes and involvement of the complement system. The relevance of the latter in AAV is reflected by elevated amounts of circulating C5a and, foremost, by protection from NCGN through blockade of C5aR1. In contrast, little if any is known about autoantibodies recognizing complement receptors 3a and 5a in AAV patients.

Methods: To examine the presence of autoantibodies directed against complement receptor C3a (C3aR) and C5a (C5aR1) in AAV, sera of patients with AAV [granulomatosis with polyangiitis (GPA), n=49 and microscopic polyangiitis (MPA), n=10] were measured by Elisa in comparison to healthy controls (HC, n=127). In addition, amounts of circulating C3a and C5a were determined by Elisa. Clinical parameters (BVAS, VDI, therapy) and disease marker (ESR, CRP, creatinine, anti-PR3, anti-MPO) were gathered at the time of serum sampling.

Results: Unlike MPA, in GPA lower titers of anti-C3aR were observed in comparison to HC. In addition, the concentration of anti-C5aR1 was decreased in both, GPA and MPA when compared to HC. In particular, GPA patients without a history of therapy using cyclophosphamide and/or rituximab exhibited a negative correlation between the concentration of anti-C5aR1 and the disease activity (BVAS).

Conclusion: The results may give a hint that anti-C3aR and anti-C5aR1 antibodies play distinct roles in GPA and MPA. Further, anti-C5aR1 might be of diagnostic value to monitor the clinical progress of GPA.