Alternative Complement Pathway in Anca-Associated Glomerulonephritis as a New Target for Treatment

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Submission: March 10, 2017; Published: April 24, 2017
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Introduction

The Anti-neutrophil cytoplasmic antibody (ANCA)-associated vasculitides are characterized by systemic vasculitis in combination with the presence of anti-neutrophil cytoplasmic antibodies [1]. ANCA-associated glomerulonephritis is considered “pauci-immune” with absent or mild glomerular tuft staining for immunoglobulin (Ig) and/or complement in renal biopsies. Because of this relative paucity of complement in vessels, complement system was not initially envisioned as an important participant in the pathogenesis of ANCA vasculitis and ANCA glomerulonephritis [2]. We recently published a paper were we evaluated the prevalence and clinical significance of immune deposits in ANCA-associated glomerulonephritis. The results showed that in a total of 53 patients, typical pauci-immune GN was found in 39 patients (73.5%). In 14 patients (26.4%) examination revealed substantial deposition of Ig or complement in the mesangium and/or along the glomerular capillary wall. The only difference comparing both groups was significantly higher proteinuria in patients with immune deposits. C3 deposition on the capillary wall was the most frequent finding (64.2%), followed by C3+IgG (21.4%) and IgG alone (14.2%). Normal serum complement C3 and C4 levels were observed in 50 patients (94.33%), only 3 (5.6%) were found to have slightly low levels. We did not find correlation between C3 deposits in renal tissue and levels of C3 in peripheral blood. One possible explanation could be that there is not immune complex deposition, but rather expression of activation of the alternative complement pathway, without real consumption of C3 [3].

In spite of these results, ANCA glomerulonephritis is still not consider an immune complex-mediated disease [11]. Besides that most patient with ANCA vasculitis are pauci immune, the fact that up to 30% of patients have some degree of immune deposits, mainly C3, opened a new theory about the role of complement in the pathogenesis of the disease, with an important role in the activation of primed neutrophils by the component C5a and the perpetuation of the inflammatory phenomenon thought the alternative complement pathway [3].

In terms of treatment, this new theory promoted new trials to test new drugs that block the C5a receptor to prevent the activation of the alternative pathway [12].

Conclusion

In conclusion, now we have a new conception about the pathogenesis of ANCA vasculitis, we now are aware that some patients will have some degree of immune deposits in renal biopsies and most important, we will have the chance to use a new drug to block this pathway and improve the prognosis of the disease.

References


Keywords: ANCA vasculitis, Alternative complement pathway, Renal biopsy


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