Publication of the Month

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Pathophysiology of ANCA-Associated Small Vessel Vasculitis

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Background: The antineutrophil cytoplasmic autoantibody (ANCA)-associated vasculitides (AAV) include Wegener's granulomatosis (WG), microscopic polyangiitis (MPA), its renal limited from, idiopathic necrotizing crescentic glomerulonephritis, and Churg-Strauss syndrome (CSS). These small vessel vasculitides are characterized by necrotizing inflammation of the wall of the small vessels, frequently in conjunction with the presence of ANCA. ANCA in AAV are directed to either proteinase 3 (PR3) or myeloperoxidase (MPO). In the right clinical context, the specificity of anti-PR3 and anti-MPO for AAV is extremely high. The strong association of anti-PR3 and anti-MPO with AAV has led to the assumption that ANCA are directly involved in the pathogenesis of these diseases.

Summary: Data from clinical studies and from in vitro and in vivo experimental studies are presented in this review. This data will provide insight into the pathophysiologic pathways involved in lesion development of AAV. This has already led to more focused and specific methods of treatment and will lead to even better disease management in the future.

In vitro experimental data point to the pathogenetic pathways involved in lesion development, in which neutrophils, the alternative pathway of the complement system, and endothelial cells play a major role, in addition to the autoantibodies. In vivo experimental studies strongly support a pathogenic role for anti-MPO, but an animal model for anti-PR3 is lacking. In anti-PR3–associated WG, T cells seem to play a major role, as well. Finally, microbial factors seem to be involved in disease induction and possibly in disease expression.

Conclusions: Clinical data support, but certainly do not prove, that anti-PR3 and anti-MPO are involved in the pathogenesis of AAV. Although great progress has been made in the understanding of AAV, further studies are needed to fully elucidate the etiopathogenesis of these diseases.

Comment: Highly sensitive and specific ANCA tests are a prerequisite not only for diagnostic purposes but also for studying the pathogenic role of anti-PR3 and anti-MPO. In December 2010 Phadia completed the package of new highly sensitive ANCA tests with EliA MPO^S and EliA PR3^S. Both tests are calibrated against the new CDC ANCA reference samples and results are given in International Units (IU/ml), facilitating the comparability of different study results.