ANCA-Related Glomerulonephritis

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ANCA glomerulonephritis and small vessel vasculitis are a group of disorders that have many common clinical and pathological features in common. Yet, they can be differentiated on the basis of phenotypic features with respect to granulomatous inflammation involving the respiratory tract (Wegener’s granulomatosis), eosinophil rich granulomatous inflammation involving the respiratory tract (Churg-Strauss syndrome), and necrotizing vasculitis with few or no immune deposits (microscopic polyangiitis). From the clinical perspective, these disorders are characterized by a relapsing and remitting course. The nature of the lesions may either be focal or diffuse, and they typically involve a number of capillary beds. These may include diseases of the kidney with or without dermal, respiratory, neural, gastrointestinal, or other extrarenal manifestations of these diseases.

The serology of small vessel vasculitis has been substantially improved by the evaluation of ANCA. In the current era, ANCA must include both immunofluorescence and antigen-driven testing. ANCA testing may turn out to be most important in its negative predictive value, although its positive predictive value for necrotizing and crescentic glomerulonephritis is quite high. Much has been learned about ANCA antigens including myeloperoxidase and proteinase 3. These target antigens are more than just of serologic importance for they may be involved with the pathogenesis of vasculitis as well.

The pathogenesis of these disorders is most likely associated with ANCA. There are a number of clinical observations in addition to association alone that raise the possibility that ANCA are involved in the pathogenesis of these diseases. The ANCA titer correlates with disease activity. There are certain drug treatments that can induce ANCA concurrent with the development of vasculitis. There are a number of in vitro observations that suggest ANCA cause vascular injury. These include the ability of ANCA to activate neutrophils and monocytes resulting in endothelial cell damage.

The most important new observation is an animal model of ANCA-induced glomerulonephritis and vasculitis in which antibodies or splenocytes are transferred into RAG-2 mice with the development of necrotizing and crescentic glomerulonephritis and small vessel vasculitis.

The treatment of ANCA-associated disorders requires both anti-inflammatory and immunosuppressive therapy. Our approach includes the use of intravenous Solu-Medrol followed by oral prednisone and then either oral or IV cyclophosphamide. The key questions at present are how long one should treat a patient and whether maintenance therapy is required. Thus, a current effort has been to study the predictors of relapse to determine if there are those individuals who do not require long-term treatment in contrast to those who may require persistent maintenance. Are there alternative treatment approaches to small vessel vasculitis? While the use of methotrexate, azathioprine, mycophenolate mofetil, and soluble TNF receptor antagonists have all been tried, it is not currently clear as to their overall usefulness. Until the precise pathogenesis of these disorders is elucidated, the use of prednisone and cyclophosphamide will remain a mainstay.