특별 강연 II

IgA-Nephropathy: How can Better Insight Into the Pathogenesis Result in Better Therapy?

Jürgen Floege

University Hospital, RWTH Aachen, Aachen, Germany

Immunoglobulin-A nephropathy (IgAN) is the most common glomerulonephritis worldwide. For example, in Japan, full-blown IgAN has been detected in about 1.5% of all allograft kidneys at the time of transplantation. Genetic and environmental modifiers as well as generic progression factors (e.g. hypertension) must play a major role in determining who will become clinically overt and who will progress. In patients with clinically overt IgAN and/or progressive disease, it is now relatively well established that the pathogenesis involves six major steps: 1) Increased occurrence of IgA1 with poor galactosylation in the circulation. This might relate to migration of mucosal B-cells to the bone marrow, where they produce "correct" poorly galactosylated IgA. Modulation of mucosal immunity may offer new therapeutic options. 2) Generation of IgG antibodies against poorly galactosylated IgA1. This could lay the foundation for immunosuppression while detection of such IgG autoantibodies may accommodate the non-invasive monitoring of IgAN. 3) Mesangial deposition and/or formation of IgG-IgA1 or IgA1-IgA1 complexes. 4) Activation of mesangial IgA receptors and/or complement, both of which lend themselves to therapeutic interference. 5) Mesangial cell damage & activation of secondary pathways, such as overproduction of platelet-derived growth factor (PDGF), which can be specifically targeted. 6) Activation of pathomechanisms which are not specific for IgAN and that drive glomerulosclerosis and tubulointerstitial fibrosis. While at present our therapeutic armamentarium is still largely limited to supportive care and immunosuppression in some instances, these new insights can be expected to yield novel, perhaps individualized therapeutic options in primary and recurrent IgAN.