KSN 2017 Abstract

Lupus Nephritis

Anthony CHANG

Pathology, University of Chicago, United States

Since its inception over 40 years ago, the classification of lupus nephritis has focused entirely on glomerular alterations. This remains true for the most recent 2003 International Society of Nephrology/Renal Pathology Society (ISN/RPS) lupus nephritis classification. The NIH activity and chronicity indices are widely used in conjunction with the lupus nephritis classification and 5 of the 6 parameters for activity focus on the glomerular compartment while one parameter exists for interstitial inflammation.

Several studies have identified the importance of interstitial inflammation, which may be a better therapeutic target given that interstitial fibrosis and tubular atrophy may be less reversible. Our group found that interstitial inflammation was superior to any glomerular parameter after multivariate analysis of a cohort of 68 lupus nephritis patients and the degree of interstitial inflammation correlated with renal outcomes. We also generated antibodies from CD38+ or Ki-67+ B cells isolated from lupus nephritis patients by laser capture microdissection and expression cloning. Many antibodies revealed cytoplasmic immunoreactivity and most of these were confirmed to bind directly to vimentin, which was highly expressed in severely inflamed regions of the kidneys. In addition, high anti-vimentin antibody serum titers correlated with the presence of severe tubulointerstitial inflammation. Although interstitial inflammation often correlates with the extent of glomerular injury in lupus nephritis, there are several lines of evidence that these processes may be distinct. First, rare cases of lupus patients with prominent tubulointerstitial immune complex deposition without significant glomerular deposits have been reported. Second, in-situ immune processes can occur in lupus nephritis kidneys. An increase in myeloid and plasmacytoid dendritic cells has been observed in lupus nephritis kidneys. Ectopic germinal center formation also may be found in a subset of lupus patients, which has been observed in the target organs of other autoimmune disorders. Analysis of antibody sequences from the plasma cells isolated from these organized lymphoid structures demonstrates both clonal expansion and somatic hypermutation and provides circumstantial evidence that such immune processes may be occurring to facilitate the targeting of local antigens. Finally, the IgG subclass composition of immune complex deposits often differs between glomeruli and the tubulointerstitium within a given lupus nephritis kidney biopsy.

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Renal vascular lesions are common and include, in descending order of frequency, atherosclerosis, thrombotic microangiopathy, noninflammatory necrotizing vasculitis and rarely true vasculitis. Accelerated atherosclerosis is a well recognized phenomenon in the setting of autoimmunity, especially lupus. Noninflammatory necrotizing vasculitis represents prominent vascular immune complex deposition. The finding of thrombotic microangiopathy in the setting of lupus raises the clinical consideration of antiphospholipid antibody syndrome, but other clinical entities including but not limited to hemolytic uremic syndrome, thrombotic thrombocytopenic purpura, malignant hypertension, or scleroderma, can also be associated with this injury. Of interest, the β2-glycoprotein I (β2-GPI) plays a role in the inhibition of complement. Therefore, autoantibodies against β2-GPI may predispose to the formation of thrombi in a similar manner as atypical hemolytic uremic syndrome. Therefore, incorporating both tubulointerstitial and vascular changes provides a more accurate prediction of the renal outcomes in lupus patients.