THE KOREAN SOCIETY OF NEPHROLOGY
APCN & KSN 2024
June 13(Thu) - 16(Sun), 2024 Coex, Seoul, Korea
Promoting Sustainable Kidney Health: The Asia-Pacific and Beyond

Submission No. : GN03-0002
Session Title : Glomerulonephritis 3 (Pathology)
Session Topic : Renal Pathology
Date & Time, Place : June 15 (Sat) / 10:30-12:00 / Room 1 (GBR 101 - 102)

Histologic Classification of IgA Nephropathy: It's Role in Patient Care

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The Oxford classification of IgA nephropathy (IgAN) was the first histological classification of a kidney disease to be developed using an evidence-based approach. Five lesions were found to be of independent prognostic value: mesangial hypercellularity (M), endocapillary hypercellularity (E), segmental glomerulosclerosis (S), tubular atrophy/interstitial fibrosis (T), and crescents (C). Active inflammatory glomerular lesions (endocapillary hypercellularity and crescents) predict outcome only in patients not receiving steroid/immunosuppressive therapy. T score is the best predictor of renal survival, reflecting the stage of disease at the time of diagnosis. Tubulointerstitial inflammation correlates with outcome and tubulointerstitial macrophages play a role in fibrosis. Segmental glomerulosclerosis (S1) shows morphological heterogeneity. Podocytopathic features are associated with higher levels of proteinuria and more rapid progression to end stage disease. Study of the VALIGA patient cohort identified four morphological subgroups of S1 with progressively worse renal survival. There is an interaction between therapy and endocapillary hypercellularity and crescents; patients with these lesions benefit from immunosuppression. Similarly, podocytopathic segmental sclerosis in IgAN is associated with improved outcome following steroid therapy. Endocapillary hypercellularity (E1) reflects glomerular inflammation; a retrospective study of response to steroid therapy in patients at risk of progression demonstrated that the number of glomerular macrophages is the most powerful predictor of response to therapy. The reproducibility of M, E and C scores is generally poor between pathologists working in different units and this impacts on the clinical value of the classification. The poor reproducibility of E score can be overcome by immunostaining for CD68, a marker of monocyte/macrophages. Quantification of glomerular CD68-positive cells is highly reproducible and correlates closely with E score. The clinical value of histological classification in patients receiving new agents, including complement-directed therapy,

requires evaluation. It is likely that the Oxford Classification will evolve as new evidence emerges, and with introduction of new therapies.

Keywords: IgA nephropathy, Oxford Classification