

IMMUNOGLOBULIN FREE LIGHT CHAINS IN SITU IN PATIENTS WITH CHRONIC KIDNEY DISEASE

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BACKGROUND AND AIMS: Monoclonal FLC have pro-inflammatory effects on PTEC as well as co-precipitating with Tamm-Horsfall protein (THP) in distal tubules as casts. Polyclonal FLC have not been studied in the kidney in situ, but are potent activators of some non-renal cells. Serum polyclonal FLC levels progressively increase with worsening CKD. This study was aimed to assess the presence of FLC in the kidney in CKD.

METHODS: Renal biopsy specimens from 9 patients with established CKD due to ischaemic nephropathy were analysed. Immunofluorescence staining was performed using directly conjugated antibodies against κ -FLC, λ -FLC and THP.

Periodic acid methenamine-silver stained sections from these 9 patients and 23 others with ischaemic nephropathy were examined. Image analysis software was used to calculate chronic damage index (CDI) for each biopsy, as the ratio of total scarred area to total cortical area, and cast numbers were counted. A cast index was calculated as the ratio of tubules containing casts in each biopsy to the total number of tubules visible.

RESULTS: κ and λ FLC were detected within PTEC of all 9 patients. Casts stained positive for κ and λ FLC as well as THP. Tubules showing intracellular FLC were devoid of casts, indicating these were proximal tubules. In tubules containing casts, there was no intracellular FLC, indicating they were distal tubules. Staining for intact immunoglobulins was negative in all 9 biopsies.

Cast numbers negatively correlated with CD34 expression, indicating that cast precipitation is associated with an ischaemic microenvironment. There was a positive correlation with macrophage infiltration, as well as CDI. Non-statistically significant relationships were seen with ACR and FLC positive tubules.

CONCLUSION: We propose that as CKD progresses and nephron numbers decline, the remaining nephrons are exposed to increasing concentrations of FLC. The potential for PTEC uptake of FLC decreases as renal injury progresses. The increased delivery of FLC to the distal nephron may then promote cast formation.