Chemokine ligand 14 could be a potent biomarker of CKD progression

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Objectives: Chemokine ligand 14 (CCL14), a ligand for CCR1, has been known as a M2 polarizing marker and chemotactic cytokine, which is expressed by fibroblast, monocyte, etc. Although it was first isolated from the hemofiltrate of patients with chronic renal failure, its expression pattern in chronic kidney disease have never been investigated.

Methods: To elucidate concentration change of CCL14 in chronic kidney disease, we performed urine proteomic analysis using three patients’ random urine per each CKD1 and 5. For validating tissue expression of CCL14, kidney biopsy tissues of three control, nine CKD 3, and eight CKD 5 patients were evaluated by immunohistochemistry. Among CKD 3 group, patients with GFR decrease more than 5 ml/min/1.73 m² within a year were considered to have rapid progression. For in vitro study, primary cultured human tubular epithelial cells (hTECs) and glomerular endothelial cells (GECs) were treated with rTGFβ for inducing fibrosis, and CCL14 expression level was measured using western blotting.

Results: In urine proteomics analysis, we discovered CCL14 showed a 122-fold increase in CKD 5 patients’ urine comparing to CKD 1 (p<0.001). In other hands, in human kidney biopsy tissue, CKD 3 patients with rapid progression showed higher expression level of CCL14 (17.33±4.13) compared to non-progressive CKD 3 (10.12±3.60) (p=0.032), control (12.48±2.49) (p=0.019), and CKD 5 (9.63±5.52) (p=0.049). C-reactive protein was adversely lower in progressive CKD 3 patients compared to others (p=0.017), and interstitial inflammation or fibrosis pattern was not different (p=0.861). In in vitro assay, CCL14 expression was increased 2 fold by treating rTGFβ in GEC cells.

Conclusions: CCL14 expression tends to increase in patients with progressive CKD. Moreover, its expression is increased by a rTGFβ-enriched fibrotic environment. Our results suggest CCL14 could be a biomarker of CKD progression that pre-existing inflammatory marker or pathologic variables could not predict.