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Glomerular glucocorticoid receptor expression associates with treatment response and prognosis in patients with IgA nephropathy

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Objectives : Corticosteroid is a potential therapeutic option in patients with IgA nephropathy (IgAN) who have persistent proteinuria of ≥ 1g/day after 3-6 months of maximal supportive care. Responsiveness to steroid is highly variable and unpredictable in patients receiving steroid treatment. Glucocorticoid receptor (GCR) is present in glomerular cells such as mesangial cells and podocytes. However, it is unknown on the association between GCR and steroid responsiveness in management of glomerular diseases. Therefore, this study aimed to evaluate whether steroid responsiveness may differ depending on GCR expression level in patients with IgAN.

Methods : Among 504 patients of biopsy-proven IgAN between 2010 and 2015, 78 patients had received steroid treatment. After excluding patients who did not give an informed consent and had estimated glomerular filtration rate (eGFR) of < 30 ml/min/1.73 m2, nephrotic syndrome, and inadequate biopsy samples, a total of 35 patients were included in the analysis. Glomeruli were obtained from biopsy tissues by manual microdissection. Glomerular mRNA expression of GCR was assessed by real-time polymerase chain reaction. Complete (CR) was defined as random urine protein-to-creatinine ratio (UPCR) < 0.3 g/g creatinine and partial (PR) remission was defined as a ≥ 50% reduction of proteinuria from baseline and UPCR of ≥ 0.3 g/g creatinine. Disease progression was defined as a ≥ 30% decrease in eGFR during follow-up period.

Results : The mean age of study patients was 43.9 years and 74.3 % were men. All patients responded to steroid treatment; CR and PR occurred in 14 (40.0%) and 21 (60.0%) patients, respectively. There were no significant differences in

baseline eGFR and proteinuria level between CR and PR groups. The mRNA expression of GCR was significantly higher in the patients with CR than those with PR (P = 0.008). Immunohistochemal study also confirmed the enhanced expression of GCR in the former. During a median follow-up of 21.2 months, disease progression occurred only in 1 patient (7.1%) in CR group, as compared to 10 patients (47.6%) in PR group (P = 0.013).

Conclusions : This study shows that higher expression level of glomerular GCR is associated with a higher probability of steroid-induced CR and better renal outcome in IgAN.

Keywords : IgA nephropathy, Glucocorticoid receptor, Steroid responsiveness, Real-time polymerase chain reaction