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Clinical features and outcomes of idiopathic membranous nephropathy in Korea

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Membranous nephropathy (MN) is a major cause of nephrotic syndrome in adults. In Korean GlomeruloNEphritis sTudy (KoGNET), a retrospective cohort of patients receiving renal biopsy from 1979 to 2018 from 18 centers in Korea, MN ranks as second (9.3%) most common GN after IgA nephropathy (34.2%). In this topic, clinical features and outcomes of idiopathic MN (iMN) as well as treatment results, especially with immunosuppressive (IS) agents will be presented. The results are summarized as follows:

1) In an analysis of 1,776 patients with idiopathic MN, 1,075 (60.5%) were male. The mean age of patients was 53.0 ± 14.7 years and there were 428 (24.1%) patients over 65 years old. At the time of renal biopsy, 755 (42.5.0%) and 266 (15.0%) had hypertension and diabetes, respectively. Eight hundred seventy one (49.0%) had nephrotic range of proteinuria and mean serum albumin level was 2.7 ± 0.8 g/dL. Compared to the younger group, more patients had hypertension and diabetes in the elderly group. Upon clinical presentation, nephrotic syndrome was more common, and hemoglobin and serum albumin levels were lower in the elderly group. Complete or partial remission (CR or PR) rates were 48.5%, 63.8%, and 68.0% at 6 months, 12months after biopsy, and last follow-up, respectively. Remission rate were not significantly different at last follow-up in the elderly group compared to the younger group. In Cox proportional hazard regression, older age (HR 0.98 [0.97–0.99]), elevated hemoglobin level (HR 0.82 [0.72–0.93]), high serum albumin level (HR 0.66 [0.44–0.99]), and high estimated GFR (HR 0.96 [0.95–0.97]) at biopsy were good predictors of renal outcomes. Older age (HR 1.04 [1.01–1.10]) and presence of hypertension at biopsy (HR 2.76 [1.30–5.88]) were significant risk factors for patient survival.

2) Regarding a treatment strategy, IS therapy should be restricted to patients with high risk for progression given the natural course of iMN. Cyclophosphamide and steroid have been suggested as initial IS therapy in 2012 KDIGO recommendation. However, due to the side effects of alkylating agents, Calcineurin inhibitors (CNIs) and/or Rituximab (RTX) were suggested as alternative therapies in high-risk patients. Although 2012 KDIGO guideline argues against the use of mycophenolate mofetil (MMF) monotherapy in iMN, in a small randomized controlled study for Korean patients with high-risk iMN (n=39), MMF with low dose corticosteroid was not an inferior treatment option compared to treatment with CsA and low dose corticosteroids.

In a retrospective analysis from a single center, 15 iMN patients resistant to other IS therapies were treated with RTX. RTX was administered as fixed dose of 375 mg/m^2 iv. twice at interval of 2 weeks. The average age of patients was 54 (range 24-75) years and 13 were male (87%). The median eGFR, serum albumin level, and spot urine protein-to-creatinine ratio at baseline were 37.0mL/min/1.73m^2 (IQR, 28.0-66.5), 2.2g/dL (IQR, 1.9-2.9), and 6.6g/g (IQR, 5.9-12.5), respectively. For median follow-up of 20 months, 8 patients (53%) had achieved CR or PR. In responder group (n=8), median eGFR increased from 31.5 to 61.5 mL/min/1.73m^2, serum albumin level increased from 2.3 to 4.2 g/dL during the period. Anti-phospholipase A2 receptor antibody (antiPLA2R-ab) was positive in 7 among 8 tested patients. Among 7 patients with positive antiPLA2R-ab, the titer decreased to average 12.3% in 5 of 7 (71.4%) patients. The optimal dosage of RTX for treatment of iMN is still disputable, but modified dose of RTX in this study had achieved CR or PR in 53 % of high-risk iMN patients with resistance to other IS therapies. Optimal dosage or protocol of RTX for treatment of iMN, especially in Asian patients needs to be evaluated in future studies.