

PROGRESSION IN PRIMARY MEMBRANOUS NEPHROPATHY IS ASSOCIATED WITH PLASMINOGEN ACTIVATOR INHIBITOR-1 GENE POLYMORPHISM

C-H Chen^{1,3}, C-H Cheng¹, K-H Shu¹, M-C Wen², M-J Wu¹, F-J Tsai³

¹Department of Internal Medicine, ² Pathology, Taichung Veterans General Hospital; ³Institute of Clinical Medicine, China Medical University, Taichung, Taiwan

BACKGROUND: Plasminogen activator inhibitor type 1 (PAI-1) activity plays an important role in renal fibrosis. This study was conducted to determine the association of PAI-1 gene polymorphism 4G/5G with membranous nephropathy (MN) in clinical manifestations and progression.

METHODS: We recruited 92 MN patients as study group. The PAI-1 genotype results were interpreted in relation to the clinical manifestations of MN.

RESULTS: After follow-up of 6.9 ± 4.9 years, creatinine clearance in MN patients with 4G/4G genotype was significantly lower than that in patients with 4G/5G or 5G/5G genotype (41.7 ± 26.9 , 59.7 ± 41.8 and 75.0 ± 27.6 mL/min, respectively, $p=0.006$). Coronary artery diseases were more prevalent in patients with 4G5G genotype (12/29%) and 4G4G genotype (3/10%) as compared with those with 5G5G genotype (1/5%) ($p=0.024$). Higher incidence of peripheral vascular events was also found in patients with 4G5G (18/44%), and 4G4G (6/20%) as compared with those with 5G5G genotype (3/14%) ($p=0.021$). The disease progression was seen more frequently in patients with 4G4G (11/37%), and 4G5G (12/30%) as compared with those with 5G5G genotype (2/9.5%, $p=0.023$). The deterioration of renal function was associated with the histological stage, degree of glomerulosclerosis, degree of tubulointerstitial fibrosis and severity of intimal fibroplasia of vessels in renal biopsy.

CONCLUSIONS: However, the carriage of the 4G allele was associated with renal deterioration and increased cardiovascular as well as other vascular events in MN patients. This novel and unique finding should prompt a specific consideration in the treatment of MN patients with the 4G4G genotype.

Keywords: Plasminogen Activator Inhibitor, Gene Polymorphism, Primary Membranous Nephropathy