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More Severe Mitochondrial Injury at The Time of Diagnosis is Associated with Poor Prognosis in Minimal Change Disease

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Objectives: We hypothesized that the pathogenesis of minimal change disease (MCD) may be associated with mitochondrial injury and that the degree of mitochondrial injury at the time of diagnosis may serve as a prognostic marker in MCD

Methods: We retrospectively enrolled MCD patients who were followed up for more than 5 years and IgA nephropathy (IgAN) patients as controls (n = 20 each). Focusing on the stimulator of interferon genes (STING) pathway activated by mitochondrial injury, immunohistochemical (IHC) staining for STING was performed on kidney tissue at the time of diagnosis. The IHC stain site and signal intensity for STING were analyzed. Time-averaged proteinuria (TA-proteinuria) was calculated as the average of the mean of proteinuria measurements were obtained by 24-hour urine collection every 6 months. A relapse after treatment was defined as proteinuria >3.5 g per 24 hours after complete or partial remission

Results: In patients with IgAN and MCD, kidney tissue from 13 patients each showed positive IHC staining for STING. While various kidney structures including glomerulus and tubulointerstitium were stained in IgAN patients, the glomerulus was exclusively stained in MCD patients. MCD patients were divided into the high (n = 6) and low (n = 14) intensity subgroups according to the signal intensity based on 2+ and more or less, respectively. TA-proteinuria and frequency of relapses during the follow-up period were higher in the high intensity group than in the low intensity group (1.18 ± 0.54 vs. 0.57 ± 0.45 g/day, p = 0.022; and 0.72 ± 0.60 vs 0.09 ± 0.22 episodes/year, p = 0.022, respectively)

Conclusions: These findings suggest that more severe mitochondrial injury, as represented by a high signal intensity of IHC stain for STING at the time of diagnosis, could be used as a valuable prognostic marker to predict poor prognosis in MCD

Figure 1. Representative images of IHC staining for STING on kidney tissue obtained from MCD and IgAN patients

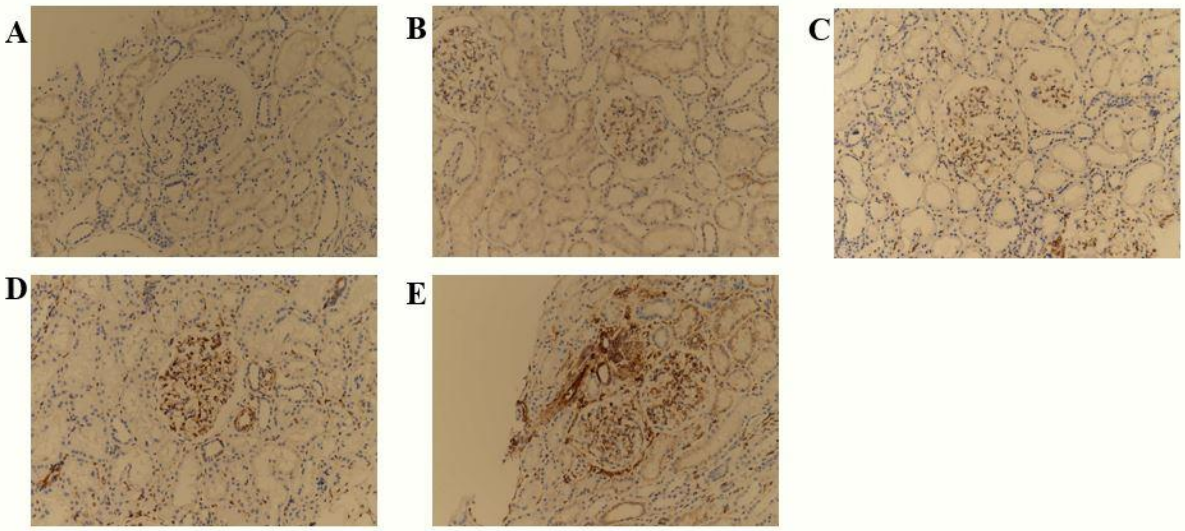

Figure 1. Representative images of immunohistochemistry staining for STING on kidney tissue obtained from MCD and IgAN patients. MCD patients were classified into negative (A), 1+ (B), 2+ (C), and 3+ (D) according to the IHC signal intensity. To compare with MCD patients, image of IHC stain for STING of most characteristic IgAN patient were presented (E).