Morphological Subtypes and Their Clinicopathological Associations of Podocytic Infolding Glomerulopathy: Retrospective Nationwide Cohort Study of 93 Cases

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Abstract

Background:

Podocyte infolding glomerulopathy (PIG) is a rare disease of the glomerulus and was first described in 2008. Despite an increasing number of case reports and cohort studies being published worldwide, the diagnostic morphological criteria remain insufficiently defined, leading to diagnostic ambiguity. Therefore, we investigated the morphological definition of PIG by first clarifying its subtypes.

Methods

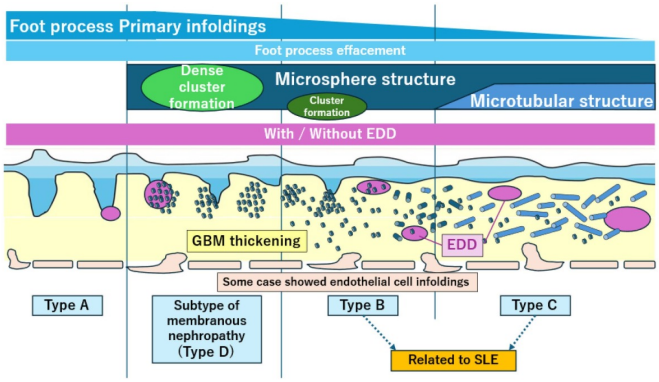
A nationwide retrospective cohort study was conducted. Clinical data and transmission electron micrographs (TEM) were collected from patients diagnosed with PIG between 1991 and 2025, from 69 institutions in Japan. The TEM findings were systematically re-evaluated with a focus on podocytic infolding and the patterns of microspheres or microtubules in the glomerular basement membrane (GBM) in conjunction with the clinical findings.

Results

Ninety-three cases fulfilled the diagnostic criteria for PIG. Based on TEM findings, the cases were classified into four morphological subtypes: Type A: primary podocyte infolding without the presence of microspheres or microtubules (n = 21); Type B: the presence of microspheres (n = 34); Type C: the presence of microtubules (n = 38); and Type D: dense clusters of microspheres (n = 10)□Figure□. Types B and C were observed in younger female patients and showed a high prevalence of systemic lupus erythematosus (SLE). In contrast, types A and D were more prevalent in older male patients and were not associated with SLE.

Conclusions

This study established TEM-based morphological criteria for PIG, clarifying four subtypes. These findings improve diagnostic accuracy and demonstrate the heterogeneity of PIG.



References

1. Joh K, Taguchi T, Shigematsu H, Kobayashi Y, Sato H, Nishi S et al. Proposal of podocytic infolding glomerulopathy as a new disease entity: a review of 25 cases from nationwide research in Japan. Clin Exp Nephrol. 2008;12(6):421-31.