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NUP107 mutations in children with steroid-resistant nephrotic syndrome

Eujin Park*[1], Yo Han Ahn[2], Hee Gyung Kang[1,3], Il Soo Ha[1], Hae Il Cheong[1,3]

[1]Department of Pediatrics, Seoul National University Children's Hospital, [2]Department of Pediatrics, Kangnam sacred heart hospital, [3]Research Coordination Center for Rare Diseases, Seoul National University Hospital, Seoul, Korea, Republic Of

Background: The *NUP107* gene is a novel gene associated with autosomal recessive steroid-resistant nephrotic syndrome (SRNS) with focal segmental glomerulosclerosis (FSGS) in children. The frequency of *NUP107* mutations in children with SR-FSGS remains unknown.

Methods: Nine families with two siblings affected by childhood-onset SRNS or proteinuria were recruited. FSGS was confirmed by a kidney biopsy in at least one affected sibling in all families. In addition, 69 sporadic pediatric cases with biopsy-proven SR-FSGS who were not responded to any treatment were also included. All coding exons with flanking introns of the *NUP107* gene were amplified using polymerase chain reaction and directly sequenced.

Results: Biallelic *NUP107* mutations were detected in four pairs (44.4%) of siblings of the familial cases and three (4.3%) sporadic cases. All affected patients harbored p.Asp831Ala mutation in one allele and a truncating or abnormal splicing mutation in the other allele. The *NUP107* mutations-positive patients revealed earlier onset age (39.4±13.1 versus 76.8±50.0 months, P=0.027) and more rapid progression to ESRD (at the ages of 58.9±23.4 versus 123.1±62.7 months, P<0.001) than mutations-negative patients. None of the eight mutations-positive cases, who underwent kidney transplantation, had recurrence of FSGS in the graft kidney, while 35.3% of mutations-negative cases had recurrence of FSGS.

Conclusion: An unexpected high incidence of *NUP107* mutations was revealed in Korean children with SR-FSGS. Initial genetic screening for children with SR-FSGS should include the *NUP107* gene, at least in Korea. Further research is necessary to determine the incidences of *NUP107* mutations in other countries.

Keywords: End-stage renal disease, Focal segmental glomerulosclerosis, NUP107 gene mutation, Steroid-resistant nephrotic syndrome