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Mitochondrial Cytopathies in Children with Steroid-Resistant Focal Segmental Glomerulosclerosis and Sensorineural Hearing Loss

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Background: The phenotypic combination of steroid-resistant focal segmental glomerulosclerosis (SR-FSGS) and sensorineural hearing loss (SNHL) has been mainly reported in patients with mitochondrial cytopathies, including primary coenzyme Q10 (CoQ10) deficiency.

Methods: From 1999 to 2015, a total of 10 unrelated Korean pediatric patients with biopsy-proven SR-FSGS and SNHL were included in this study from our hospitals. In all patients, the 3243A>G mutation in *MT-TL1* was screened. We performed Sanger sequencing of other candidate genes in the following order: *COQ6*, *COQ2*, *PDSS2*, *ARHGDIA*, *ADCK4*, and *INF2*.

Results: The mean age at the onset of SR-FSGS was 28.3±14.3 months. Nine patients progressed to ESRD at the mean age of 59.9±53.6 months, and seven underwent kidney transplantation without recurrence of FSGS. Five patients harbored biallelic *COQ6* mutations, and two carried a heterozygous *COQ6* mutation. One patient presented multi-organ involvement, including biopsy-proven mitochondrial myopathy, although the underlying genetic defect was not detected. Two *COQ6* mutations, c.189_191delGAA and c.782C>T, were detected repeatedly in multiple patients. Renal biopsy for the patients carrying *COQ6* mutations revealed FSGS—of either a not-otherwise-specified variant or a collapsing variant—with variable degrees of glomerular sclerosis, whereas abnormal mitochondrial proliferation in podocytes was a constant finding.

Conclusion: Primary CoQ10 deficiency, particularly that caused by *COQ6* mutations, should be considered in children presenting with both SR-FSGS and SNHL. Although primary CoQ10 deficiency is a rare disorder, an early diagnosis is essential because the condition is treatable when CoQ10 supplementation is started at the early stage. We recommend early kidney biopsy because detection of abnormal mitochondrial proliferation in podocytes might provide an earlier diagnostic clue as compared with biochemical and/or genetic diagnoses.

Keywords: Coenzyme Q10 deficiency, COQ6 mutation, Mitochondrial cytopathy, Mitochondrial proliferation in podocyte, Sensorineural hearing loss, Steroid-resistant focal segmental glomerulosclerosis