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COQ6 mutations in children with steroid-resistant focal segmental glomerulosclerosis and sensorineural hearing loss

*Hae il CHEONG

Department of Pediatrics, Seoul National University Children, Korea,South

Steroid-resistant focal segmental glomerulosclerosis (SR-FSGS) is a highly heterogeneous disease entity both phenotypically and genetically. The phenotypic combination of SR-FSGS and sensorineural hearing loss (SNHL) has been mainly reported in patients with mitochondrial cytopathies, including primary coenzyme Q10 (CoQ10) deficiency.
During the period from 1999 to 2015, there had been 15 unrelated children with phenotypic combination of SR-FSGS and SNHL in our hospital. Among them, two patients were diagnosed as MYH9-associated nephropathy, one as MELAS syndrome, and two as non-genetic diseases. We performed mutational analyses, mainly focusing on mitochondrial cytopathies, in the remaining 10 patients and found six (M:F = 2:4) patients with biallelic COQ6 mutations. Then, we conducted retrospective phenotype analyses of these six patients. The median age at the onset was 29 months (range 15–47 months). All six patients progressed to end stage renal disease (ESRD) within a median of 13 months (range 1–27 months) after the onset. Renal biopsies revealed FSGS with variable degrees of glomerular sclerosis, whereas abnormal mitochondrial proliferation in podocytes was a constant finding. None of the five patients who underwent kidney transplantation developed recurrence of FSGS.
In 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. In fact, after this study, we could make relatively early diagnosis in three additional patients with COQ6 mutations solely on the basis of abnormal mitochondrial proliferation in podocytes without clinical evidences of SNHL. In addition, in one of the patients, CoQ10 supplementation resulted in remission of proteinuria.