Mutation spectrum of genes associated with steroid-resistant nephrotic syndrome in Chinese children

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Abstract

Approximately 20% of children with idiopathic nephrotic syndrome do not respond to steroid therapy. More than 30 genes have been identified as disease-causing genes for steroid-resistant nephrotic syndrome (SRNS). Few reports were from the Chinese population. The coding regions of genes commonly associated with SRNS were analyzed to characterize the gene mutation spectrum in children with SRNS in central China. The first phase study involved 38 children with five genes (NPHS1, NPHS2, PLCE1, WT1, and TRPC6) by Sanger sequencing. The second phase study involved 33 children with 17 genes by next generation DNA sequencing (NGS, 22 new patients, and 11 patients from first phase study but without positive findings). Overall deleterious or putatively deleterious gene variants were identified in 19 patients (31.7%), including four NPHS1 variants among five patients and three PLCE1 variants among four other patients. Variants in COL4A3, COL4A4, or COL4A5 were found in six patients. Eight novel variants were identified, including two in NPHS1, two in PLCE1, one in NPHS2, LAMB2, COL4A3, and COL4A4, respectively. 55.6% of the children with variants failed to respond to immunosuppressive agent therapy, while the

resistance rate in children without variants was 44.4%. Our results show that screening for deleterious variants in some common genes in children clinically suspected with SRNS might be helpful for disease diagnosis as well as prediction of treatment efficacy and prognosis.

Keywords: Nephrotic syndrome, Steroid-resistant, Gene mutation, SRNS, NGS