S-C26

신-결손 증후군의 임상-유전학적 연구

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A Clinico-genetic Study of Renal-coloboma Syndrome in Children

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Background : Renal-coloboma syndrome (RCS) is a rare autosomal dominant disorder caused by the PAX2 gene mutations, and clinically characterized by renal and ocular involvement, typically bilateral renal hypoplasia and optic disc coloboma, respectively.

Methods : The phenotype and genotype of six children with RCS were analyzed. The clinical findings were retrospectively reviewed by pediatric nephrologists and ophthalmologists. All coding regions of the PAX2 gene were amplified by polymerase chain reaction and were directly sequenced.

Results : A common mutation, c.619insG, was detected in five patients including two siblings and one novel mutation, R104X, in one. The renal phenotype (bilateral hypoplastic kidneys with progressive renal dysfunction) was similar among the patients, but vesicouretral reflux, which is one of the common manifestations of RCS, was not detected in any patients. The ocular manifestations showed wide variability ranging from subtle optic disc anomalies to microphthalmia. In one family with two affected siblings, unaffected parents had no mutation in their peripheral blood DNA, suggesting germline mosaicism in one of the parents. An intragenic microsatellite marker study revealed that the mutation was of maternal origin. This is the second report of a familial case of RCS with suspected germline mosaicism.

Conclusion : Both inter- and intra-familial phenotypic variability, especially of ocular manifestations, of RCS were confirmed, and c.619insG mutation in PAX2 is predominant in Korean children with RCS. The possibility of germline mosaicism should be considered during molecular diagnosis and genetic counseling for the PAX2 gene mutations.