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Novel Variations in KIRREL1 Gene and Infantile Onset Nephrotic Syndrome

Dear Editor,

More than 58 monogenic genes associated with steroid resistant nephrotic syndrome (SRNS) have been described to date.[1] Kin of IRRE-Like protein 1 (KIRREL1) has been described as an nephrotic syndrome type 1 (NPHS1) like Ig superfamily cell adhesion molecule.[2] We report two heterozygous missense mutations in the KIRREL1 gene leading to SRNS in a child with infantile nephrotic syndrome.

A 2-year-old male, a case of infantile-onset SRNS born out of a nonconsanguineous marriage, diagnosed at the age of 11 months was reported positive for the KIRREL1 gene mutation on exons 12 and 15. A mislocalization of both KIRREL1 mutants c.1513G>A (p.Ala505Thr) and c.1918C>T (p.Arg640Cys) was noted, which have not been reported previously as pathogenic variants. This was also confirmed by Sanger sequencing, as seen in Figure 1. Given the condition we found in our case of two different mutations in the same gene is classified as compound heterozygosity, it is difficult to ascertain any definite relationship between our findings and the clinical presentation. The child was started on Tacrolimus and ACE-I inhibitors and discharged. On 1-year follow-up, the child is in complete remission. There were no extrarenal manifestations or syndromic features in the child.

A direct interaction between NPHS1 and KIRREL1 because of their co-localization at the slit diaphragm has been described.[3] KIRREL1 is necessary for the rearrangement of the actin cytoskeleton of the slit diaphragm.[4] Previously, mutations in the KIRREL1 gene from two unrelated families were reported in children who presented at the ages of 5 and 14 with SRNS, respectively, which were p.Arg440Cys and p.Ser573Leu.[1] Patients with this mutation achieved complete remission upon treatments with tacrolimus,

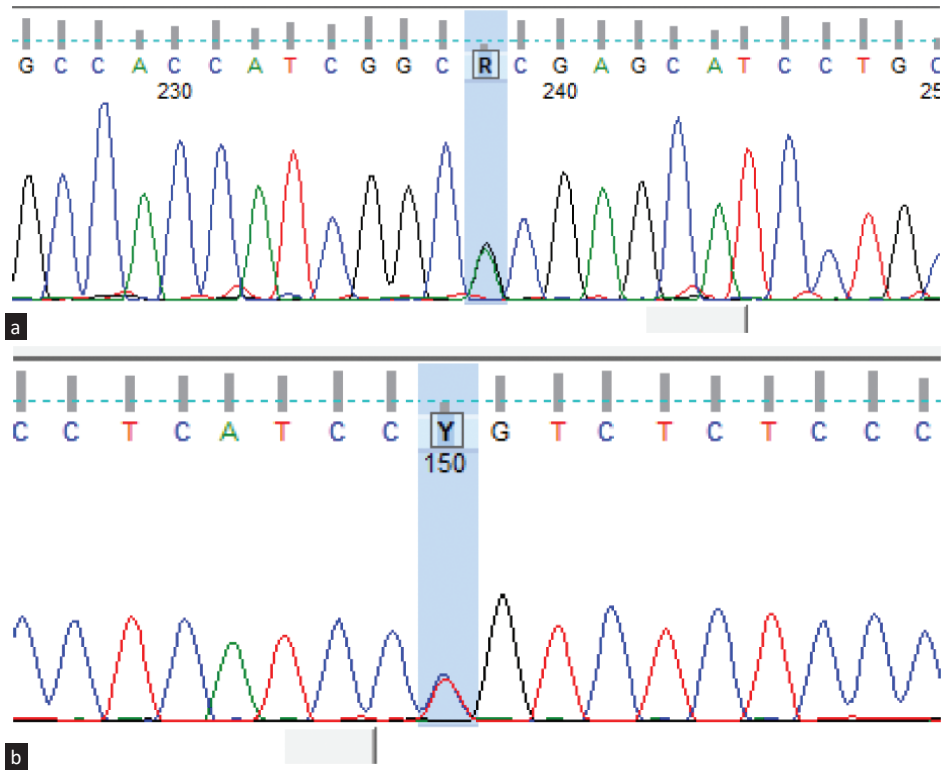

Figure 1: (a) Sanger sequencing data (electropherogram) shows a nucleotide change at c.1513G>A (p.Ala505Thr) in the KIRREL1 gene. (b) Sanger sequencing data (electropherogram) shows a nucleotide change at c.1918C>T (p.Arg640Cys) in the KIRREL1 gene.

CCB, and ACE-I; however, they can progress to CKD.[1] For genotype-treatment relationships, further research is needed.

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Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent.

Conflicts of interest

There no conflicts of interest.

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