KSN 2020
FULLY VIRTUAL MEETING

Abstract Type : Poster
Abstract Submission No. : PO-1642

Defects of CRB2 and TNS2 genes identified in autosomal dominant form of adult onset focal segmental glomerulosclerosis

Hyeyun Jeong[1], Hyeong Dae Park[2], Dong Ho Yang[1], Yu Ho Lee[1], Jinkun Bae[3], MinJi Sung[1], Jaehee Kim[1], Hyun-Ju An[1], Sang Ho Lee[4], So-Young Lee[1]
[1]Department of Internal Medicine-Nephrology, Bundang CHA General Hospital, Korea, Republic of
[2]Department of Graduate School of Medicine, CHA University, Korea, Republic of
[3]Department of Emergency Medicine, Bundang CHA General Hospital, Korea, Republic of
[4]Department of Internal Medicine-Nephrology, Kyung Hee University Medical Center, Korea, Republic of

Case Study:

Introduction

Focal segmental glomerulosclerosis (FSGS) is a syndrome that arises after podocyte injury from diverse causes. To identify causes of FSGS, previous studies showed that some podocyte-specific gene mutations were associated with primary FSGS. In this study, we investigated the gene linked with familial FSGS through whole exome sequencing (WES) of father and his son.

Case

A 65 year old man was admitted for peripheral pitting edema with proteinuria over 10 years. His son was also diagnosed with FSGS and on HD treatment. The Laboratory test showed normal creatinine (0.8 mg/dL), elevated total cholesterol (263 mg/dL), lower normal serum albumin level (3.6 mg/dL) and protein 4+ in urinalysis. The patient underwent renal biopsy, and FSGS was identified.

DNA was isolated from blood samples from patient, his wife, and his son using the DNA purification kit according to the manufacturer's protocol. Whole exome sequencing was performed on the three family members. The obtained sequences of patient and his son were aligned to the reference genome of patient's wife, and single-nucleotide polymorphisms were detected.

Result

The patient and his son carried heterozygous mutations of CRB2 in exon 10 on chromosome 9 and TNS2 in exon 1 on chromosome 12. WES showed that c.C3329>T (predicting p.T1110M) in CRB2 and c.C38>T (predicting p.A13V) in TNS2 gean were inherited to his son. The CRB2 protein regulates podocyte cell polarity, and its heterozygous mutation was carried in FSGS patient. Although TNS2 function is unclear, its mutation is associated with murine podocyte foot process and 6 different mutations have been detected in families with nephrotic syndrome.

Conclusion

We reported the case of FSGS patient carrying 2 heterozygous mutations, and genetic test using WES revealed that these mutations located in CRB2 and TNS2 gene inherited through parental line.

Figure 1. Renal biopsy finding

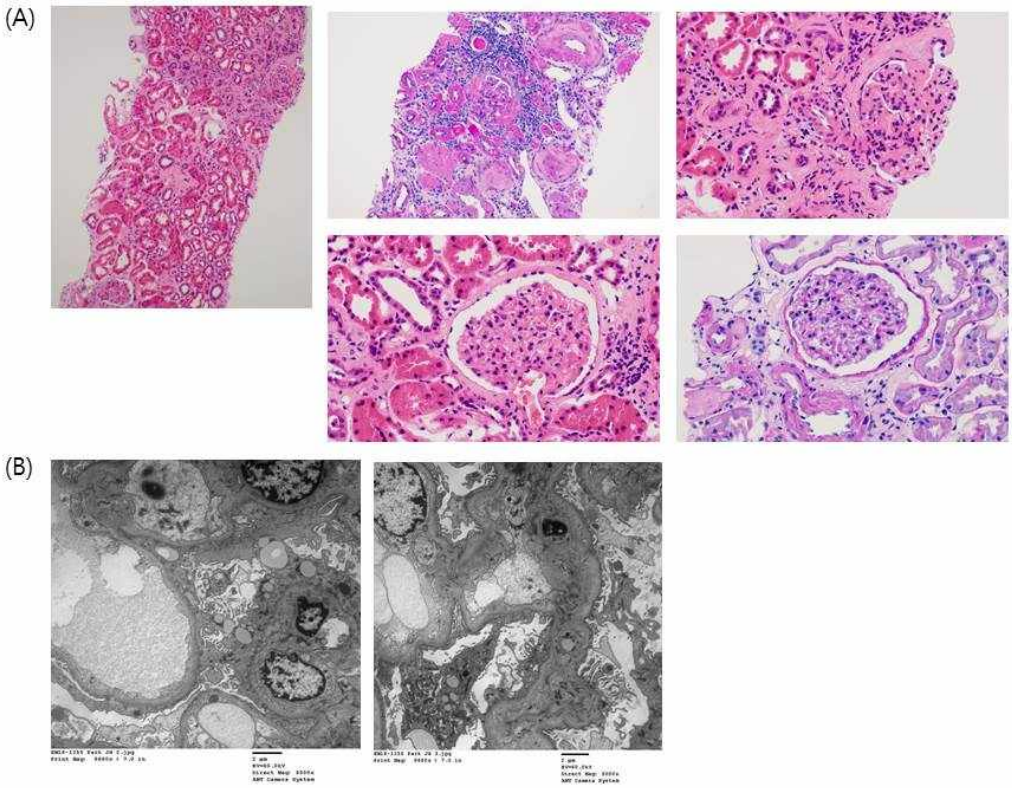

Figure 1. Light microscopic fining (A) and Electron microscopic fining (B) of patient

Figure2. the result of WES and exon structure

(A)

Position	rsID	Ref	Alt	Function	Gene	Phenotype	Info.
Chr9:126136139	rs73571431	C	T	Nonsynonymous	CRB2	FSGS type9	NM_173689:exon10:c.C3329T:p.T1110M (Hetero)
Chr12:53444007	rs749029842	C	T	Nonsynonymous	TNS2	Nephrosis	NM_170754:exon1:c.C38T:p.A13V (Hetero)

(B)

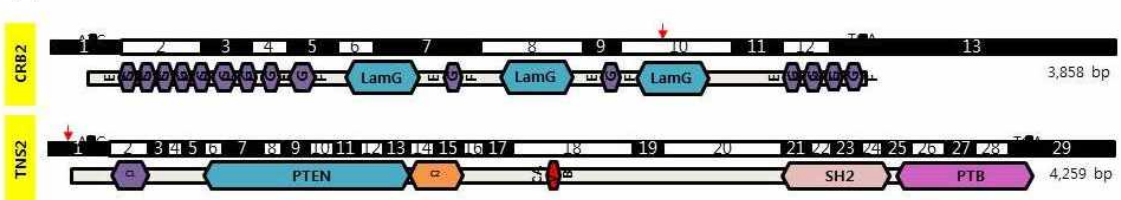

Figure 2. The result of whole exome sequencing (A) and exon structure of human CRB2 and TNS2 (B)