Genetic Rarity: The First Case Report of *TMPRSS3* Mutation Coinciding with Multicystic Dysplastic Kidney

Dear Editor,

A 9-month-old male born to a non-consanguineous marriage was admitted with complaints of fever, lethargy, and reduced urine output. There was a history of two infant deaths in the family. He had hypoglycemia and severe hypernatremic dehydration. Physical examination revealed signs of dehydration. Blood gas analysis and renal function revealed severe metabolic acidosis and hypernatremia, and urea and creatinine levels were 144 and 3.5 mg/dL, respectively. His clinical and laboratory parameters improved with supportive management, and the hemogram and peripheral blood smear findings were normal. Urinalysis demonstrated nephrotic range proteinuria and microscopic hematuria. A sonogram of the abdomen and kidney–ureter–urinary bladder demonstrated a multicystic dysplastic kidney (MCDK) on the left side. He had persistent hypertension, which was managed with enalapril. Ocular and auditory evaluation did not reveal any abnormality. Genetic analysis was performed to look for inborn error of metabolism. It revealed a heterozygous variant (c.413C>A, p.Ala138Glu) in the *TMPRSS3* gene, pathogenic as per the American College of Medical Genetics and Genomics, and confirmed with Sanger sequencing [Figure 1, Supplementary Files]. Genetic counseling and surgical options were explained to the parents. Screening of the family members was normal.

Mutations in *TMPRSS3* are usually associated with autosomal recessive deafness in infants in heterozygous state.[1] *TMPRSS3* mutations have been reported to express themselves with nonsyndromic hearing loss previously in the heterozygous state.[2] Though the expression of *TMPRSS3* in the human kidneys has been less studied, this mutation has also been seen to play a role in pseudo-hypoaldosteronism type 1 and Liddle syndrome.[3] A splice variant of *TMPRSS3*, *TMPRSS3f*, has also been found in the kidneys of mice, which share 89% identity with the human *TMPRSS3f*.[4] So, it is likely that a mutation in *TMPRSS3* might produce structural renal anomalies along with deafness.

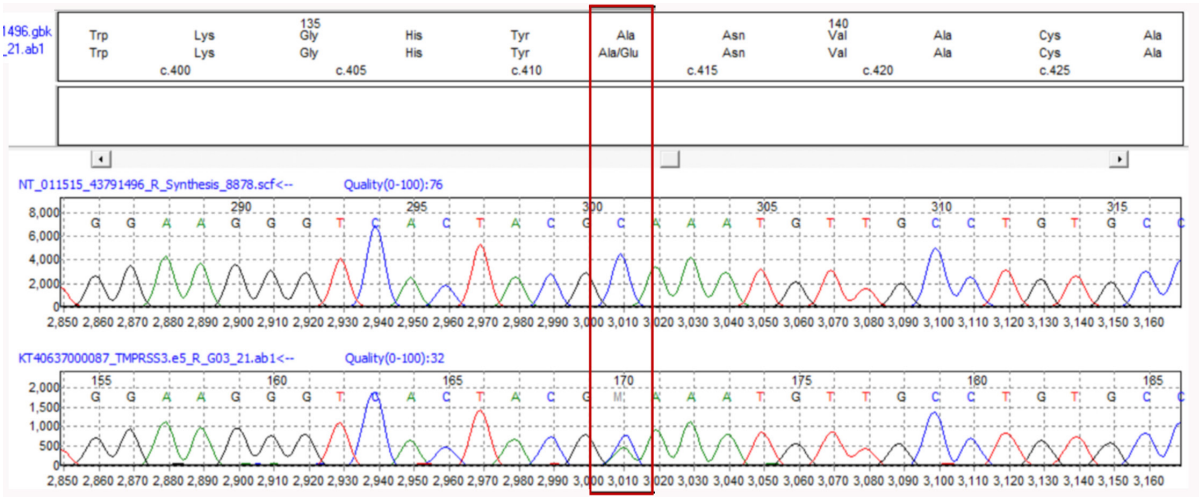

Figure 1: Sanger sequencing data (electropherogram) for the provided sample showing nucleotide change at chr21: c.413C>A,, (p.Ala138Glu) in *TMPRSS3* gene. Red, green, black, and blue colored peaks show thymine, adenine, guanine, and cytosine bases, respectively. The red rectangle in the image highlights a specific nucleotide change in DNA sequencing data (electropherogram).

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We thank all the residents and staff who were involved in the care of this patient.

Declaration of patient consent

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

Conflicts of interest

There are no conflicts of interest.

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References

1. Cambio AJ, Evans CP, Kurzrock EA. Non-surgical management of multicystic dysplastic kidney. BJU Int 2008;101:804–8.
2. Shao A, Chan SC, Igarashi P. Role of transcription factor hepatocyte nuclear factor-1β in polycystic kidney disease. Cell Signal 2020;71:109568.
3. Chen TJ, Song R, Janssen A, Yosypiv IV. Cytogenomic aberrations in isolated multicystic dysplastic kidney in children. Pediatr Res 2022;91:659–64.
4. Scott HS, Kudoh J, Wattenhofer M, Shibuya K, Berry A, Chrast R, *et al.* Insertion of beta-satellite repeats identifies a transmembrane protease causing both congenital and childhood onset autosomal recessive deafness. Nat Genet 2001;27:59–63.

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