CASE STUDY

Strand Clinical Exome Test: Accurate Diagnosis of Inherited Disorders

Introduction

Congenital nephrotic syndrome, usually manifesting as steroid-resistant nephrotic syndrome, can result in end-stage renal disease in children at a fairly early age. Usually, the onset of renal failure is evident from 0-3 months of age (Liebeskind, 2014).

Rescue from early onset renal disease has proven to be difficult. An understanding of the genes involved in hereditary nephrotic syndrome has led to the conclusion that modification of the sialylation status of angiopoietin-like- 4 protein may help to reduce the severity of symptoms like proteinuria (Macé & Chugh, 2014).

More than 30 different genes have been linked with idiopathic pediatric nephrotic syndrome (Wang et al., 2017). Genetic diagnostic tests like the Strand Clinical Exome Test can be used very effectively to understand mutations that have caused nephrotic syndrome, quite accurately.

Gender : Male

Age : 2.5 years

Location: Mumbai

Diagnosis: Congenital Nephrotic Syndrome

Strand Test: Clinical Exome Test

Conclusion :

- A VUSD mutation was identified in the *NPHS1* gene
- Congenital Nephrotic Syndrome confirmed

Patient Profile

Tanmay Gupta*, presented with proteinuria and build-up of ascites fluid in his abdomen when he was around 6-7 months old. His parents, Shivani* and Pramod Gupta*, consulted Dr. Kamini Mehta, a pediatric specialist in Mumbai.

They had lost an earlier child, following the development of similar symptoms and were anxious when Tanmay showed the same signs.

Dr. Kamini Mehta diagnosed the disorder as nephrotic syndrome, based on clinical investigations. Given that the onset of the disease was early, she suspected this to be a case of hereditary nephrotic syndrome. In addition, Tanmay was administered immunosuppressants as part of the treatment regimen. Dr. Mehta wanted to understand the genetic nature of the condition, and if required, remove Tanmay off immunosuppressants. The couple was advised to undergo genetic counselling, a complimentary service provided by Strand, and was then advised to provide Tanmay's blood sample to be tested using the Strand Clinical Exome Test.

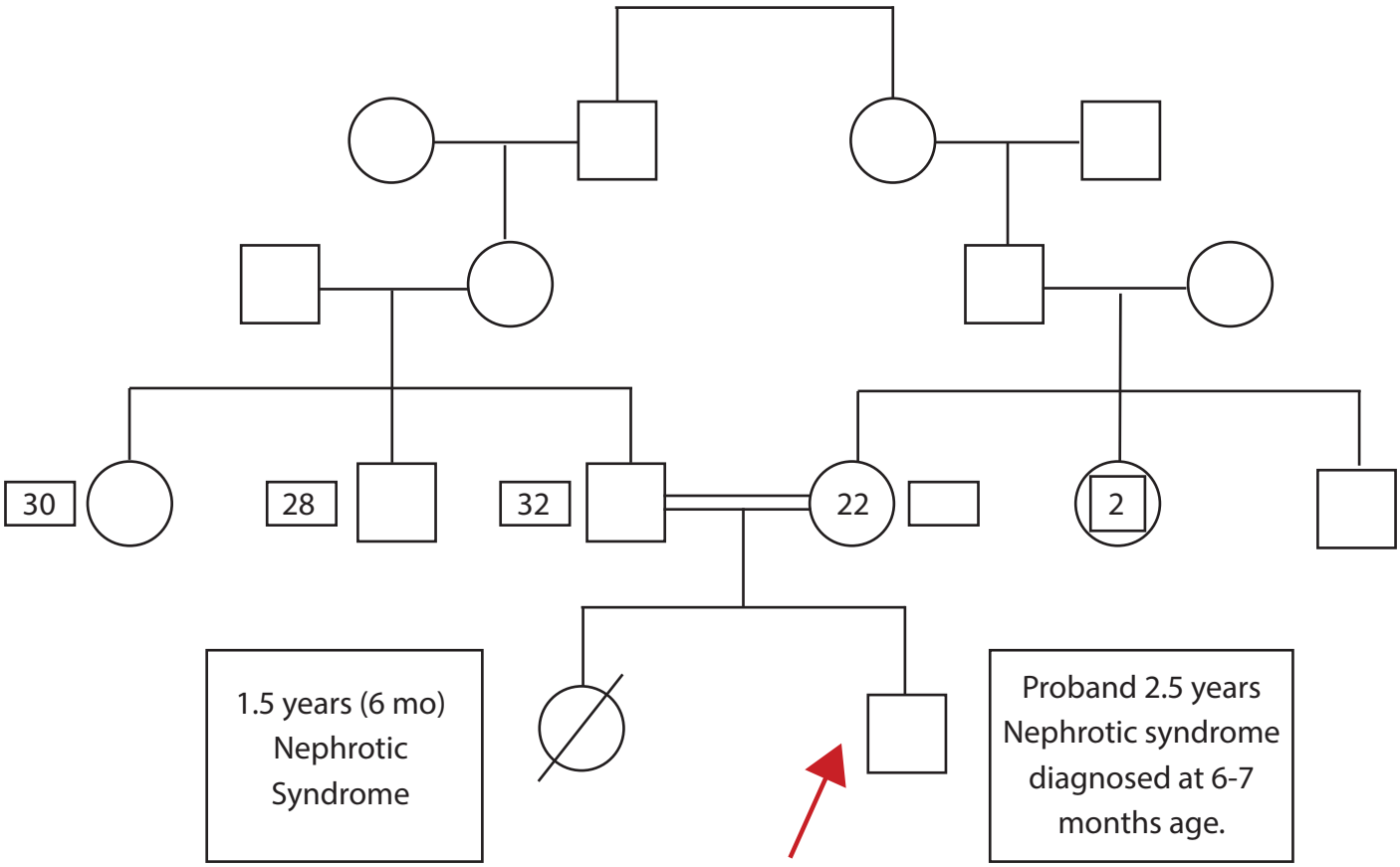
Family History

Shivani and Pramod are a consanguineous couple. Shivani's paternal grandmother and Pramod's maternal grandfather are siblings. Therefore, Shivani and Pramod are second cousins to each other. Consanguineous marriages are known to have a greater risk of incidence of inherited genetic disorders for the children.

The Strand Clinical Exome Test is a comprehensive genetic test that can identify genetic variants involved in several inherited disorders.

* Name changed to protect patient privacy

Family Tree - Pre-Test Genetic Counselling



Results of Genetic Testing

A 'variant of unknown significance with a probable damaging effect (VUSD)' was identified in Tanmay's genome.

Key Findings

Gene	Variation	Zygosity	In heritance	Clinical significance
NPHS1	chr3:37038149delA c.156delA p.Glu53ArgfsTer4	Homozygous	Recessive	Variant of Uncertain Significance with Probable Damaging Effect (VUSD)

This is a variant in the *NPSH1* gene. Tanmay is homozygous for this mutation.

RESULT **VUS** **A 'variant of unknown significance with a probable damaging effect (VUSD)' in the *NPSH1* gene was identified**

Key Interpretations

- The likelihood of hereditary nephrotic syndrome evident in a 7-month-old child was confirmed using the Strand Clinical Exome Test.
- The proband is homozygous for this VUSD variant of the *NPSH1* gene.Germline mutations in *NPHS1* have been associated with inherited nephrotic syndrome. (Genetics Home Reference)
- The proband's parents were advised to undergo mutation-specific testing* (MST). MST can help to evaluate the status of other children in this family and asses their risk of renal failure. A confirmation of their status as heterozygous carriers would allow for estimation of risk of bearing more children with the same genetic profile as the proband.
- Genetic testing also helped in making a decision about taking the child off immunosuppressants.

Strand Clinical Exome Test

The Strand® Clinical Exome Test is a Laboratory Developed Test (LDT) that was developed at the Strand Center for Genomics and Personalized Medicine at Strand Life Sciences. The test covers ~4500 genes and is a comprehensive test for inherited disorders.

References

Liebeskind, D. S. (2014). Nephrotic syndrome. In Handbook of clinical neurology (Vol. 119, pp. 405–415). http://doi.org/10.1016/B978-0-7020-4086-3.00026-6

Wang, Y., Dang, X., He, Q., Zhen, Y., He, X., Yi, Z., & Zhu, K. (2017). Mutation spectrum of genes associated with steroid-resistant nephrotic syndrome in Chinese children. Gene, 625, 15–20. http://doi.org/10.1016/j.gene.2017.04.050

Genetics Home Reference

The parameter marked with an * are not accredited by NABL and CAP.

Strand Life Sciences Pvt. Ltd.
5th Floor, Kirloskar Business Park, Bellary Road, Hebbal, Bangalore - 560 024
Phone: 1800-1022-695, support.strandx@strandls.com, www.strandls.com

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