

CASE STUDY

Solving the Metabolic Riddle: Genetic Analyses Reveal the Cause Behind Hypoglycaemia and Seizures Evident in a Child

Patient Profile

A 9-year-old girl, Arpita*, was brought to a prominent hospital in Bangalore for a consultation with a renowned endocrine specialist. Generalized seizures and hypoglycaemia were her principal health issues. In addition to these symptoms, she also suffered from vomiting, hepatomegaly and increased sensorium. Blood tests showed that she had high serum lactate levels as well. Episodes of hypoglycaemia and seizures had started when Arpita was 1.5 years old.

The doctors handling the case advised a liver biopsy as well as genetic tests to understand whether inherited genetic mutations were the cause of Arpita's health issues.

Family Tree- Pre-Test Genetic Counselling

Arpita's father's mother and mother's father were siblings. Essentially, her parents were cousins and therefore were in a consanguineous marriage. Given this family history, her physician prescribed the Strand Clinical Exome Test to ascertain whether an inborn error of metabolism was present in the child.



Gender: Female

Age: 9 years

Diagnosis: Hypoglycaemia and generalized seizures. Genetic testing advised.

Key Findings:

- Mutation in Fructose- 1,6-bisphosphate gene (*FBP1*) identified
- Proband homozygous
- Parents advised to test themselves as well as proband's sibling
- Detailed analysis of mutant gene was enabled by Strand NGS and Sanger sequencing offered as

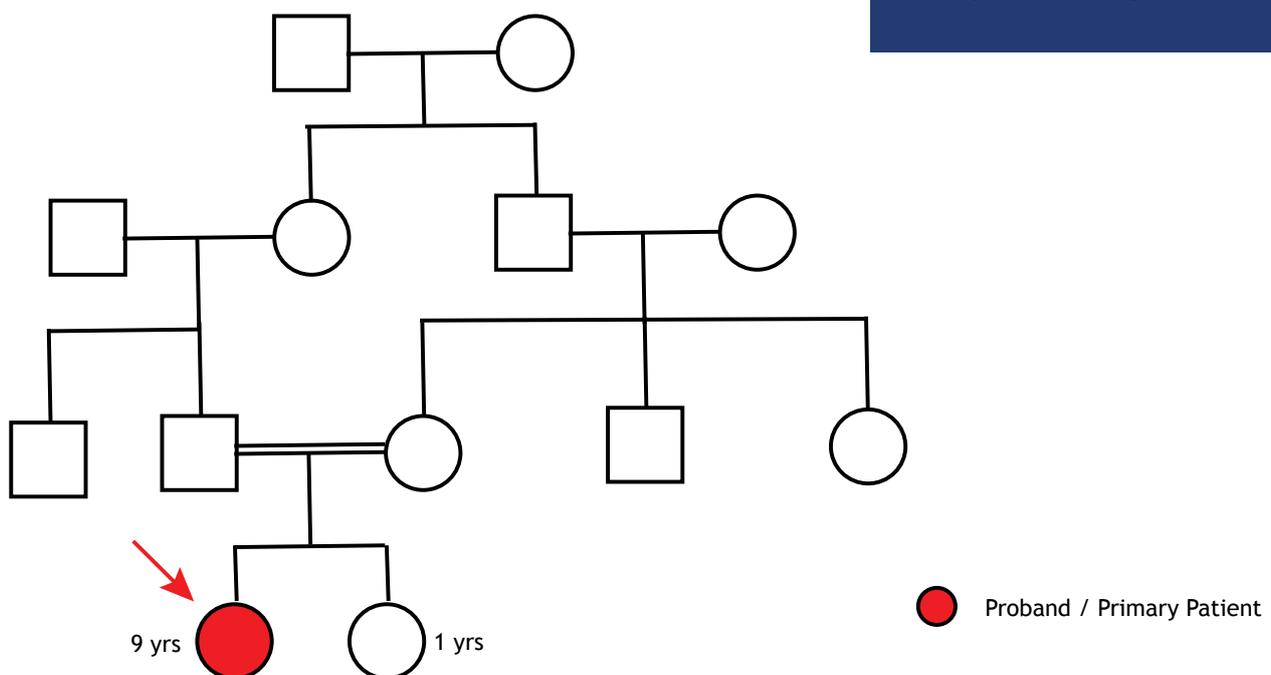


Figure 1. Arpita's Family Tree

*Name changed to protect patient privacy

Results of Genetic Testing

Arpita was found to be homozygous for a mutation in the *FBP1* gene. This gene codes for an enzyme, fructose-1,6-bisphosphatase, that is involved in the synthesis of glucose from substances like lactic acid, amino acids, and glycerol. Deficiency of this enzyme has been linked with metabolic acidosis, ketosis, elevated levels of serum lactic acid, and even coma (Li et al. 2017).

Since Arpita is homozygous for this mutation, bearing two mutant copies of the gene, she suffers from a complete deficiency of the fructose-1,6-bisphosphatase enzyme, manifested as hypoglycaemia and periodic seizures.

RESULT



A homozygous 'pathogenic' variant that results in a 331bp ALU sequence element insertion was detected in exon 2 of the *FBP1* gene

Key Findings

Gene	Variation	Zygoty	Clinical significance
<i>FBP1</i>	chr9:g.97382716_97382717insKT305716.1:g.87_417 c.227_228insKT305716.1:g.87_417 p.Leu77GlyfsTer39	Homozygous	Pathogenic

Strand's Bioinformatics Software Enabled Deep Genetic Analysis

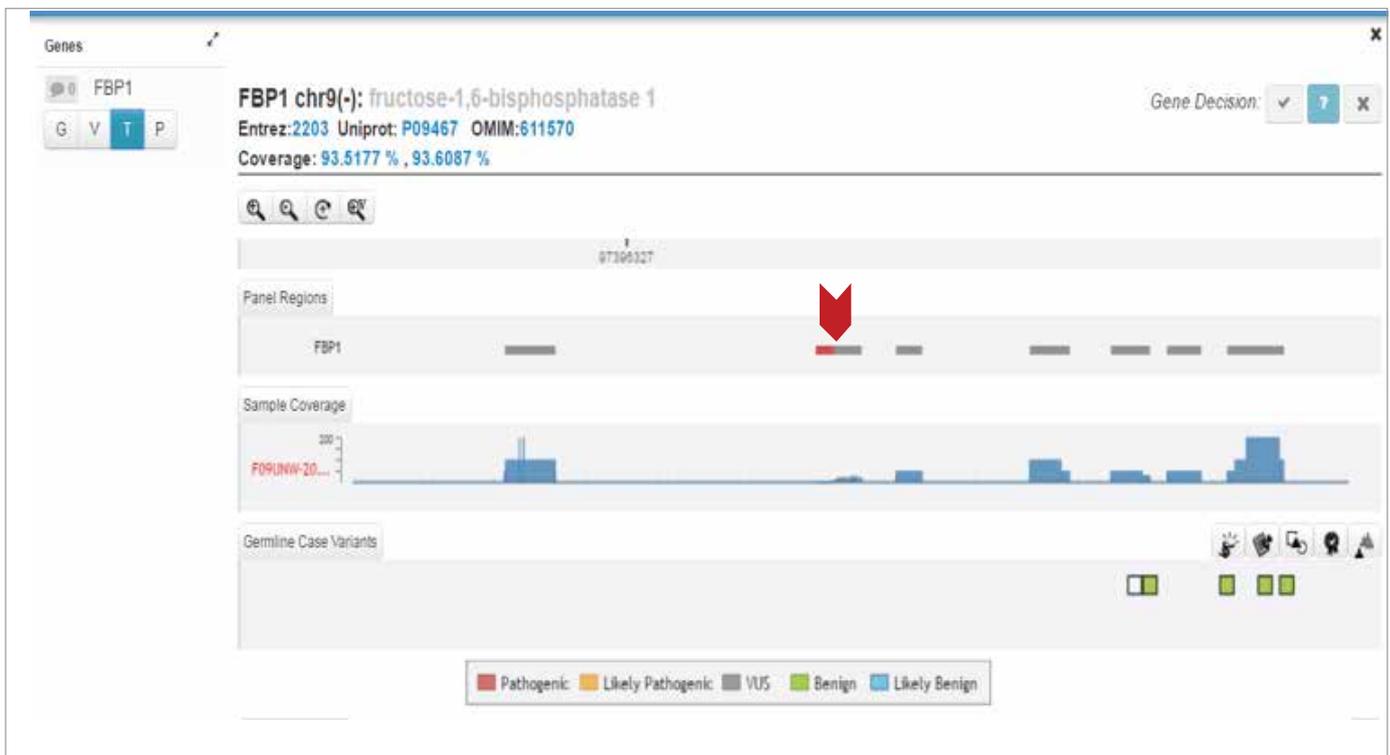


Figure 2. NGS analysis of Arpita's DNA with low readouts of the *FBP1* gene (arrowhead)

Strand Clinical Exome Test

The Strand Clinical Exome test includes genes involved in inherited metabolic disorders. The test is a comprehensive test that can assay for > 4500 genes

References

Li, N. et al., 2017. *Clinical and Molecular Characterization of Patients with Fructose 1,6-Bisphosphatase Deficiency. International journal of molecular sciences*, 18(4). Available at: <http://www.ncbi.nlm.nih.gov/pubmed/28420223> [Accessed May 23, 2017].

