

CASE STUDY

Strand Clinical Exome Test Provides Precise Diagnosis of Infantile Epilepsy

Introduction

Epileptic seizures in infancy and early childhood can present as either febrile or afebrile seizures. Seizures are symptoms of several rare congenital syndromes like Dravet Syndrome, Lennox-Gastaut Syndrome, Benign Myoclonic Epilepsy and others. Although a differential diagnosis can be achieved by comparing and contrasting the symptoms, diagnostic tests like the Strand Clinical Exome test can help to identify underlying genetic defects.

A good understanding of the molecular defects that result in seizures as well as other developmental delays can be useful in managing the child's health better. Physiological symptoms can also vary for different mutations in the same gene (Uddin et al., 2017). Hence, elucidation of the exact genetic variants that are responsible for congenital abnormalities is an important part of diagnosis of these disorders.

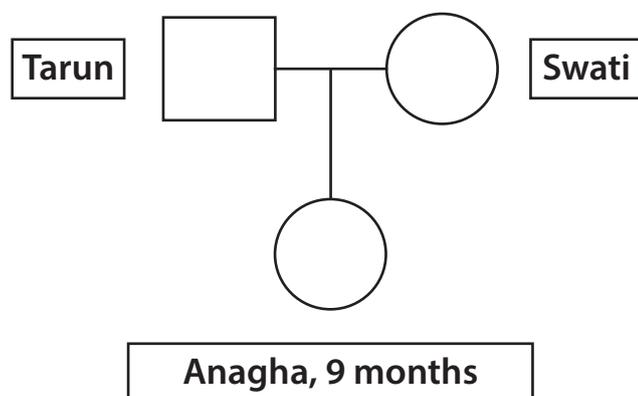
Patient Profile

Anagha*, a 9-month-old girl was referred to Dr. Shekhar Patil, a Pediatric Neurologist at a medical college hospital, Kamothe (Navi Mumbai), for presentation with epileptic seizures. Her seizures were evident from day five post birth and were a significant source of anxiety for her parents.

Family History

Anagha's parents, Swati and Tarun Kolaskar*, are a non-consanguineous couple. Their family history on either side has been unremarkable in terms of having inherited disorders.

Family Tree - Pre-Test Genetic Counselling



Although the family history did not have evidence of congenital developmental deficiencies, *de novo* (new) mutations can arise and cause specific disorders.

The Strand Clinical Exome test was prescribed in order to understand which genes are changed and what are the specific changes in these genes.

This information is useful for arriving at an accurate diagnosis of her epilepsy.



Gender : Female

Age : 9 months

Location: Navi Mumbai, Maharashtra

Diagnosis: Early-infantile epileptic encephalopathy 4 (EIEE4)

Strand Test: Clinical Exome Test

Conclusion :

- Precise diagnosis of pediatric epilepsy
- Therapeutic options suitable for Early-infantile epileptic encephalopathy indicated

* Name changed to protect patient privacy

Results of Genetic Testing

Analysis using the Strand Clinical Exome test led to the identification of a pathogenic variant of the *STXBP1* gene.

RESULT

A pathogenic variant in the *STXBP1* gene was identified in Anagha's genome

Key Findings

Gene	Variation	Zygoty	Inheritance	Clinical significance
<i>STXBP1</i>	chr9:130430405_130430409delCTGGA c.841_845delCTGGA p.Leu281ArgfsTer31	Heterozygous	Dominant	Pathogenic

- ◆ In Anagha's genome, a pathogenic variant of the *STXBP1* gene was identified.
- ◆ This gene produces a syntaxin-binding protein. Syntaxin is a transmembrane receptor expressed in neurons. Syntaxin binding proteins are essential for docking of synaptic vesicles to the plasma membrane, in order to release neurotransmitters.
- ◆ The identified variant (a deletion of 5 nucleotides) is most likely to cause a frameshift mutation, thereby resulting in a truncated (shorter than normal) protein.
- ◆ The resultant deficiency in protein functions is likely to manifest as tonic-clonic seizures, absence seizures and epilepsy.
- ◆ Germline mutations in the *STXBP1* gene are inherited in an autosomal dominant mode. Therefore, the epileptic effects are evident even if Anagha has only one copy of the defective gene.

Treatment Plan

Pediatric epilepsies present with developmental delay as well. Medications that control the seizures may be prescribed for patients with inherited encephalopathies. In cases like Anagha, the possibility of developing specific drugs that can overcome the defect caused by a single gene, has been proposed (Stamberger, Weckhuysen, & De Jonghe, 2017).

If drug development is successful, the identification of the genetic variant using tests like the Strand Clinical Exome test will be immensely useful in the choice of therapy.

Conclusion

- ◆ Anagha, a 9-month-old girl was referred to Dr. Shekhar Patil with presentation of epileptic seizures. Seizures were evident in the infant from the fifth day, post-birth.
- ◆ Anagha's parents are in a non-consanguineous marriage. Given the lack of history of congenital abnormalities in the family, the Strand Clinical Exome test was prescribed for Anagha in order to understand the precise genetic anomaly that caused seizures.
- ◆ The Strand Clinical Exome test facilitated the identification of a pathogenic variant of the *STXBP1* gene in the patient's DNA.
- ◆ A confirmed diagnosis of early-infantile epileptic encephalopathy 4 (EIEE4) was arrived at based on the identified genetic variant of the *STXBP1* gene.
- ◆ The patient's parents were advised about strategies to manage her developmental challenges.
- ◆ Anagha's eligibility for emergent therapies that can be developed against *STXBP1* mutations, has been established.

Strand Clinical Exome Test

The Strand Clinical Exome Test is designed to identify genes that are involved in several inherited and congenital disorders. This is a laboratory-developed test that can identify mutations in >4500 genes.

The performance of this test has been validated in several cases of neuromuscular, neurodevelopmental abnormalities as well as in inherited errors of metabolism.



References

Stamberger, H., Weckhuysen, S., & De Jonghe, P. (2017). STXBP1 as a therapeutic target for epileptic encephalopathy. *Expert Opinion on Therapeutic Targets*, 21(11), 1027–1036. <https://doi.org/10.1080/14728222.2017.1386175>

Uddin, M., Woodbury-Smith, M., Chan, A., Brunga, L., Lamoureux, S., Pellecchia, G., ... Boelman, C. (2017). Germline and somatic mutations in STXBP1 with diverse neurodevelopmental phenotypes. *Neurology. Genetics*, 3(6), e199. <https://doi.org/10.1212/NXG.0000000000000199>



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

#StayAheadOfCancer  

Strand is accredited by



8750941



Certificate No. MC - 2434

Strand ID: RD267316032018