Case Study: Epileptic encephalopathy caused by an STXBP1 mutation

Clinical Overview:
An 11-year-old male presents to clinic with a clinical history of epileptic encephalopathy and infantile spasms with onset at the age of 4 weeks. He was also noted to have autistic features and profound intellectual disability (ID). His parents reported no family history of similar symptoms. Previous genetic testing, including a karyotype, array CGH and for fragile X syndrome were all negative. The GeneDx infantile epilepsy panel, which includes sequencing and deletion/duplication analysis of 38 genes, was ordered. A heterozygous Leu130AspfsX11 mutation in the STXBP1 gene was identified, which supports a diagnosis of epileptic encephalopathy.

Patient Information:
Age: 11 years  Specimen: Blood
Referral diagnosis: Epileptic encephalopathy, autistic features, infantile/epileptic spasms, ID
Family history: No known family history of similar symptoms
Previous Testing: Karyotype: Normal
                      Array CGH: Normal
                      Fragile X syndrome: Normal

Diagnostic Summary:
POSITIVE. Heterozygous Leu130AspfsX11 (c.388_389delCT) mutation in the STXBP1 gene.

Infantile Epilepsy Panel: Sequence analysis and deletion/duplication analysis of 38 genes revealed the heterozygous Leu130AspfsX11 STXBP1 mutation. This mutation was previously reported in a patient with early infantile epileptic encephalopathy, profound intellectual disability, and spastic quadriplegia. Mutations in the STXBP1 gene have been identified in patients with early infantile epileptic encephalopathy, also called Ohtahara syndrome. Most individuals with STXBP1 mutations exhibit clonic spasms with a suppression-burst pattern on EEG, intractable seizures, and severe intellectual disability. The presence of Leu130AspfsX11 in the STXBP1 gene is consistent with the diagnosis of epileptic encephalopathy in this individual.

Diagnostic Implications:
There are many different causes of epilepsy, including genetic disorders, metabolic diseases, and structural brain abnormalities. Knowing the genetic cause of an individual’s seizures can clarify the prognosis, assist in treatment and management of the patient, and predict the risk of a disease in family members. Mutation-specific testing for the STXBP1 mutation can be performed on the parents of this child to determine if the mutation had newly occurred in the child or was inherited from one of the parents, which allows the family to be provided with a more accurate recurrence risk.

References: