Case Study: GLUT1 deficiency caused by an SLC2A1 deletion

Clinical Overview:
A 9-year-old female presents to clinic with history of seizures and dyskinesia since birth, microcephaly and intellectual disability (ID). Her parents reported no family history of similar symptoms. She has been previously tested for GLUT1 deficiency through gene sequencing performed at another laboratory. The GeneDx infantile epilepsy panel, which includes sequencing and deletion/duplication analysis of 38 genes, was ordered. A heterozygous partial gene deletion of SLC2A1 was detected and a diagnosis of GLUT1 deficiency was established. Studies have shown that large deletions and duplications in SLC2A1 account for 11-14% of GLUT1 deficiency syndrome.1, 4

Patient Information:
Age: 9 years  Specimen: Blood
Referral diagnosis: Epileptic encephalopathy, autistic features, infantile/epileptic spasms, ID
Family history: No known family history of similar symptoms
Previous Testing: SLC2A1 sequencing: Negative

Diagnostic Summary:
Infantile Epilepsy Panel: Sequence analysis and deletion duplication analysis of 38 genes revealed a heterozygous partial gene deletion including exon 3 and part of exon 4 of SLC2A1. Both partial and complete SLC2A1 gene deletions have been identified in patients with glucose transporter type 1 deficiency syndrome (Glut1-DS).1, 2 Glut1-DS is characterized by reduced cerebrospinal fluid (CSF) glucose in the presence of normal blood glucose due to impaired glucose transport across the blood-brain barrier.3 In the majority of cases, patients present with seizures in the first 2 years of life and demonstrate delayed neurologic development, dysarthria, acquired microcephaly, and complex movement disorders. Mutations in SLC2A1 are inherited in an autosomal dominant manner and ~90% of cases are de novo (arising new in that individual and not inherited from either parent).4

Diagnostic Implications:
There are many different causes of epilepsy, including genetic disorders, metabolic diseases, and structural brain abnormalities. Knowing the specific cause of an individual’s seizures can guide the appropriate treatment. In individuals with SLC2A1 mutations, a ketogenic diet often improves seizure control and reduces paroxysmal events, although cognitive impairment persists.3, 4 Additionally this individual’s parents can now have mutation-specific testing to assess if this deletion was inherited or has occurred de novo. In the latter case, the risk of having another child with GLUT1 deficiency is very low but not zero due to the possibility of germline mosaicism in one of the parents.

References: