Wolcott Rallison syndrome caused by a novel mutation in EIF2AK3 gene.

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Objectives:

Wolcott-Rallison syndrome (WRS) is an autosomal recessive disorder characterized by early-onset diabetes, skeletal dysplasia, and growth retardation. Some patients of WRS may develop central hypothyroidism, hepatic dysfunction, renal insufficiency or central nervous system abnormalities. This is a very rare disorder and, less than 100 cases have been described till 2009. Mutations in the eukaryotic translation initiation factor 2α kinase (EIF2AK3) gene are responsible for this disorder. The objective of this case report is to present a case of Wolcott-Rallison syndrome caused by a novel mutation in EIF2AK3 gene, which has never been reported previously.

Methods:

A 5-month-old female child was brought to our hospital with complaints of multiple episodes of multi-focal tonic clonic seizures for last 1 day. She was the first in birth order, born out of non-consanguineous marriage, delivered at term with weight appropriate for gestational age, without significant perinatal problems. There was no significant family history. On routine investigations patient was found to have persistent hyperglycemia.
We investigate her further for hyperglycemia and found that her C-peptide levels are inappropriately low (<0.30 ng/mL) for her blood sugar levels. Considering the possibility of infantile diabetes, her blood samples were sent to Royal Devon and Exeter NHS foundation trust, Exeter, UK, for genetic testing. Analysis of exons 1, 6, 7, 9, 11, 14, 16 and 17 of the EIF2AK3 gene (AF110146.1) was done by Sanger sequencing. She was found homozygous for a novel EIF2AK3 missense mutation, p.R1064Q, at exon 17.

Results:

The mutations in the gene encoding EIF2AK3 are responsible for Wolcott Rallison syndrome. Our patient was found to be homozygous for a novel missense mutation (p.R1064Q)) in exon 17 of the EIF2AK3 gene. Her mother and father were also confirmed as heterozygous carriers.

Conclusions:

The results of genetic study are consistent with the diagnosis of Wolcott Rallison syndrome caused by a novel mutation in EIF2AK3 gene. This mutation has not been reported previously but *in silico* evidence suggests that it is likely to be pathogenic.

References:

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Diabetes

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