INTRODUCTION

NGLY1 enzyme deficiency is a rare congenital disorder of glycosylation (NGLY1-CDG) involving multisystemic neurodevelopmental disorder where affected individuals show developmental delay, epilepsy, hyperkinetic movement disorder, intellectual disability, hypo- or alacrimia, elevated liver transaminases that may spontaneously resolve in childhood, and poor growth due to feeding difficulties. He were present a cause of NGLY1-CDG having a novel mutation and renal agenesis in addition to the previously reported cases.

CASE SUMMARY

We described male case aged 3 years 9 months, was followed by our department with neuromotor developmental delay, hypotonia and epilepsy microcephaly, hypertransaminasemia, alacrimia and unilateral renal agenesis. He was born at 32 weeks and 1350 g and hospitalized in the neonatal intensive care unit for one month. Parents are 3rd degree relatives. In his antenatal history, was found to have unilateral renal agenesis. And in the postnatal abdominal ultrasonography, VCUG (Voiding Cystourethrogram) and MAG3 scintigraphy, there was right renal agenesis and left grade hydroureteronephrosis. When he was one month of age Ureteroneocystostomy was performed. At presentation, we noted dysmorphic features (low-set ears, palpebral fissure, small face, high-arched palate, small size in the hands and feet compared to the body), microcephaly, central hypotonia, choreo-athetoid movement in the upper and lower limbs, corneal ulceration due to absence of tears. He is on sodium valproate, levetiracetam, clonazepam therapy for epilepsy. The EEG demonstrated features of epileptic activity.
Brain MRI imaging demonstrated thin corpus callosum and triventricular hydrocephalus. Ophthalmic examination, there was corneal ulceration and hyperopia. In otoacoustic examination, bilateral hearing impairment was observed more severe on the left side. Elevated serum transaminases (AST 85 U/L (N < 52) ALT = 29 UIL (N < 29) ) were first noted at the age of 7 months. Liver volume was normal. Infectious causes of serum transaminases elevation were not found. Transaminase elevation continued until the age of 3.5 and then it resolved spontaneously. Urine organic analysis, acylcarnitine profile by tandem mass spectrometry analysis, serum transferrin electrophoresis, blood ammonia and lactate, serum amino acids, and urinary glycosaminoglycans were normal. Electromyelography was normal. Whole exome sequencing revealed a novel variant in the NGLY1 gene in a homozygous state( p.Q346(c.1036C>T)) and both parents were heterozygous for the same gene (figure 1.2.3). NGLY1 deficiency was confirmed by the identification of the oligosaccharide in the urine of the patient. We provide treatment for specific symptoms to our patient.

Figure 1. IGV visualization of the patient

Fugure 2,3. IGV visualition of the parents (dady and mamy)
DISCUSSION

NGLY1 deficiency is a rare autosomal recessive congenital disorder of N-linked deglycosylation related to N-Glycanase deficiency. This disease is the only one disorder of N-linked deglycosylation while more than 100 different congenital disorders have been reported for glycosylation.1

The pathogenesis of N-glycanase 1 deficiency remains unknown, but a cytosolic accumulation of misfolded glycoproteins as well as a dysregulation of the endoplasmic reticulum-associated degradation (ERAD) pathway were described. The clinical features of NGLY1-CDDG include a significant developmental disability, abnormal involuntary movements, alacrimia or poor tear production, hypotonia, microcephaly, as well as elevated serum transaminases.2 As of April of 2021, fewer than 100 individuals with NGLY1 deficiency have been identified. There are no standardized treatment protocols or guidelines for affected individuals.3

The treatment of NGLY1 deficiency is directed toward the specific symptoms that are apparent in each individual.3

Our patient described in this case had similar symptoms to other clinical cases that were reported in the literature. Unlike the literature, we detected a novel mutation and renal agenesis in our patient. This variant is important as it expands the phenotype and genotype data suspected to be associated with NGLY1 deficiency.

REFERENCES