

CASE REPORT

A 3-year-old patient presents with global developmental delay, significant hypotonia, and sporadic involuntary movements. Parents report an absence or severe reduction of tears, frequent respiratory infections, and episodes of mild seizures since infancy. Neurologic examinations reveal poor head control, microcephaly, and a marked movement disorder suggestive of dystonia.

Phenotypically, the child shows limited motor skills, delayed milestones in walking and speech, and an inability to form complex words. Laboratory findings reveal elevated liver enzymes and subtle vacuolization in hepatic cells on biopsy. No definitive abnormality has been identified on routine metabolic screening.

Genetically, suspicion for an autosomal recessive disorder led to targeted gene panel testing. Heterozygous variants in the NGLY1 gene on chromosome 3p24.2 were identified but not fully confirmed in both alleles due to incomplete sequencing data. The NGLY1 gene encodes N-glycanase, central to the glycoprotein degradation pathway. Definitive confirmation requires repeat analyses, possibly whole-exome sequencing, to identify or confirm compound heterozygous or homozygous loss-of-function mutations.

Prior medications included standard antiepileptics (levetiracetam) for seizure control and baclofen for neuromuscular spasticity. Past empirical treatments included multiple nutritional supplements aimed at improving mitochondrial function, although mild improvements were noted only transiently.

Current management focuses on supportive care, with continued use of levetiracetam and a trial of triheptanoin for potential metabolic benefit. Occupational and physical therapy sessions are conducted weekly to enhance mobility and reduce developmental regression. Ophthalmologic evaluation for possible tear production augmenting therapies is ongoing.

Differential diagnoses considered so far include congenital disorders of glycosylation, mitochondrial encephalomyopathies, and other lysosomal storage diseases. The overall clinical and biochemical findings have pointed increasingly toward a congenital disorder of deglycosylation, yet final confirmation is pending definitive genetic results.

Next steps not yet undertaken include advanced molecular testing with validated whole-exome or genome sequencing and assessment of NGLY1 protein function via fibroblast assays. Additional metabolic profiling, including measurement of deglycosylated substrates, may provide further clarity. A referral to a specialized metabolic genetics team and the consideration of expanded newborn screening data could offer additional diagnostic insights. Ultimately, identifying a biallelic pathogenic variant in NGLY1 will be critical for definitive diagnosis and to guide future targeted therapies and family counseling.