Mitochondrial Complex 1 Deficiency Nuclear Type 4 in a Toddler: A Case Report of NDUFV1 Gene Mutation

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Introduction

The most common deficiency in oxidative phosphorylation disorders is isolated complex I, and while this deficiency can arise from mutations in both nuclear and mitochondrial genes, there is no clear genotype-phenotype correlation (1, 2, 3). In most cases, the causative mutations are found in nuclear-encoded genes, with the NDUFV1 gene being one such example. (4,5) Patients associated with mutations in the NDUFV1 gene can present with a range of clinical manifestations, including recurrent vomiting, strabismus, muscular hypotonia, myoclonic epilepsy, psychomotor regression, infantile myoclonic epilepsy, spasticity, macrocephaly, cerebellar ataxia, and ptosis. Neuroimaging may reveal brain atrophy and potentially progressive macrocytic leukodystrophy. The course of this disease is typically severe, and some patients may succumb at a young age due to metabolic complications (6)(7).

Case

A male patient aged 1 year and 8 months presented to us with vomiting and subsequent neurodevelopmental delay that began in the 10th month of life. Upon reviewing the patient's medical history, it was learned that he was born via cesarean section at 38 weeks weighing 3700 grams and had no health problems until the 10th month of life. The family history revealed that the mother, father, and two male siblings were healthy with no known affected individuals in the family. On physical examination, the patient's height was between the 10-25th percentiles, while his weight and head circumference were between the 3-10th percentiles. The patient was unable to sit or walk without support, and other system examinations revealed no significant findings. Routine laboratory tests were also unremarkable. The patient, who exhibited normal neuromotor development in the first 10 months of life but later showed skill loss and inability to acquire new skills, was requested to undergo genetic testing for neurodegenerative diseases. Genetic analysis revealed pathogenic variants in the NDUFV1 gene (NM_007103.4:c.1156C>T, NM_007103.4:c.632C>T). After segregation analysis, these variants were shown to be compound heterozygous, and the patient was diagnosed with Mitochondrial Complex 1 Deficiency Nuclear Type 4. The patient was initiated on mitochondrial cocktail therapy and was followed up by the departments of pediatric metabolic diseases, pediatric cardiology, and ophthalmology

Conclusions

In children showing healthy neuromotor development, any developmental halt or loss of acquired abilities should prompt consideration of neurodegenerative and neurometabolic diseases, with mitochondrial diseases included in the differential diagnosis.

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