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Abstract Topic: - Clinical Genetics

Abstract Title: - Exploring the clinical and genetic profile of mitochondrial DNA depletion syndrome: A case series

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Aims: - To explore the clinical and genetic profile of mitochondrial DNA depletion syndrome

Methods: - The cross-sectional study was conducted in the Pediatric Neurology unit of a tertiary care hospital. Children with mitochondrial disorders were reviewed for presence of DNA depletion defects. Case records were reviewed and the data regarding the presentation, family history, biochemical profile, radiological features, and molecular genetic studies was collected.

Results: - We report 3 cases with SUCLG1 gene mutation. The age of symptom onset was six months in all cases. The common clinical presentations were global developmental delay (100%), generalized dystonia (100%), and impaired vision (33.3%). There was no history of seizures in any case. Biochemical analysis revealed high levels of urine methylmalonic acid (MMA), plasma lactate, and methyl malonyl carnitine in all cases. Brain magnetic resonance imaging showed symmetrical altered SI areas in bilateral basal ganglia, periventricular areas and atrophy of bilateral corpus striatum. Genetic analysis identified a common novel homozygous missense variant (c.358G>C; p.Val120Leu) in SUCLG1 gene. The in-silico prediction of the variant was deleterious by PolyPhen-2 and damaging by LRT, SIFT and Mutation Taster2.

Conclusions: - The diagnosis of mitochondrial disorders with diverse phenotype has always been challenging. MDDS associated with SUCLG1 gene can be detected biochemically by elevated plasma lactate and methylmalonic acid. Mass spectrometry-based analysis of metabolites may potentially reduce the time to diagnosis and management.

Keywords: - We report 3 cases with SUCLG1 gene mutation. The age of symptom onset was six months in all cases. The common clinical presentations were global developmental delay (100%), generalized dystonia (100%), and impaired vision (33.3%). There was no history of seizures in any case. Biochemical analysis revealed high levels of urine methylmalonic acid (MMA), plasma lactate, and methyl malonyl carnitine in all cases. Brain magnetic resonance imaging showed symmetrical altered SI areas in bilateral

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