A Novel Pathogenic Variant in the SLC6A8 Gene Presenting as Isolated Adult-Onset Dystonia in a Female: A Case Report

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Background

Creatine Transporter Deficiency (CTD) is the most common form among Creatine Deficiency Disorders (CDD), a group of rare neurometabolic conditions affecting brain energy metabolism. CTD is X-linked inherited and is caused by pathogenic variants in the SLC6A8 gene, which encodes the creatine transporter responsible for cellular creatine uptake. Affected individuals, mostly young males, may present with intellectual disability, speech and language delay, seizures, behavioral disturbances, or motor symptoms such as hypotonia, ataxia, and sometimes dystonia. While cognitive deficits are well described, movement disorders remain underreported and not fully understood.

Materials

We report a 39-year-old female patient who presented with isolated cervical dystonia, without developmental delay, intellectual disability, epilepsy, or a positive family history for neurogenetic disorders.

Methods

The patient underwent neurological examination, blood and cerebrospinal fluid (CSF) analyses, and brain MRI. Genetic testing was performed through exome sequencing and in silico genes panel including major genes associated with dystonia.

Results

Neurological examination revealed a dystonic head posture with rightward rotation and torsion, ipsilateral shoulder elevation, and sustained contraction of the right trapezius and sternocleidomastoid muscles. Blood tests, CSF analysis, and brain MRI were unremarkable. Genetic analysis identified a heterozygous null variant, c.1016+2T>C, in the SLC6A8 gene. This splice-site variant is absent from population databases such as gnomAD and may disrupt normal splicing, potentially causing a truncated protein. According to ACMG criteria, it is classified as pathogenic.

Discussion

CTD is most diagnosed in males with severe intellectual disability, while heterozygous females are often asymptomatic or mildly affected, typically presenting with non-motor symptoms such as mild intellectual disability. Thereby, isolated cervical dystonia in an adult female carrying a pathogenic SLC6A8 variant is highly unusual. It is plausible that disruption of cerebral creatine homeostasis impairs energy metabolism within basal ganglia circuits, contributing to motor manifestations. Importantly, CTD is potentially treatable, with supplementation strategies - such as creatine, arginine, and glycine - under investigation; therefore, it is a condition that should be considered in clinical practice, despite its rarity.

Conclusions

This case expands current genetic knowledge and the clinical spectrum of SLC6A8-related CTD, showing that it can present as isolated dystonia in adult females. It underscores the relevance of genetic testing even in the absence of cognitive or developmental abnormalities and emphasizes the importance of evaluating CTD in the diagnostic workflow, as it represents a potentially treatable condition.

References:

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