Expanding the clinical spectrum of AADC deficiency. Report of two Argentinian teenager siblings with an attenuated phenotype

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BACKGROUND
• Aromatic L-amino acid decarboxylase (AADC) deficiency is an autosomal recessive neurometabolic disorder which lead to defective synthesis of monoamine neurotransmitters.
• Symptom onset typically occurs during the first months of life and is characterized by early onset hypotonia, oculogyric crises, dystonia, impaired development, and autonomic dysfunction.
• Only few cases with a milder course have been reported.

CASES
We describe 2 teenage brothers with AADC deficiency due to compound heterozygous DDC gene pathogenic variants (c.201+5G>C and c.206C>T p). Both siblings presented with almost normal acquisition of early developmental milestones but with a mild course of neurodevelopmental features during childhood.

1) Index case, age 13, has a behavioral phenotype consistent with hyperactive-impulsive type of ADHD. He also had abnormal mild dyskinetic movements, excessive hands sweating and sleep problems since toddler. He showed sporadic oculogyric crisis since age 2 y.o specially when tired.

2) Older brother, age 15, never presented oculogyric crisis, but he has always been observed due to motor clumsiness, tics and excessive drooling.

Both attend normal school. Formal cognitive assessment is pending.

AADC deficiency diagnosis was made by whole exome sequencing and confirmed by plasma enzymatic assay (see table).

Urinary organic acids were abnormal in both patients: ↑ VLA / VNA

Treatment: Methylphenidate, dopamine agonists and melatonin treatment led to some clinical improvement in Case 1. Case 2 is not receiving any medication.

REFERENCES