AADC deficiency is a severe disease

AADC deficiency typically presents early and can lead to the need for lifelong care, with life-limiting motor and autonomic dysfunction, developmental delay leading to premature death.1-4

Patients usually do not develop full head control or the ability to sit unassisted or stand.

AADC deficiency affects patients of any gender, ethnic origin or geographical region.

AADC deficiency is an enzyme required for biosynthesis of dopamine and serotonin.

AADC deficiency can manifest with a broad spectrum of symptoms. The most common are1-3:

- In the autosomal recessive disease AADC deficiency, mutations in the dopa decarboxylase (DDC) gene result in reduced AADC enzyme activity, leading to severe combined deficiency of the neurotransmitters dopamine, serotonin, norepinephrine, and epinephrine.
- The result is an increase in L-dopa, 3-OMD, VLA, and 5-HTP; and a decrease in the neurotransmitter metabolites HVA and 5-HIAA.

AADC deficiency can affect patients of any gender, ethnic origin, or geographic region.

AADC deficiency has been reported in individuals of Asian, Caucasian, Arabic, Iranian, and Jewish ethnic origin.4

Aromatic-L-amino acid decarboxylase (AADC) deficiency:

AADC deficiency can also be attributed to a number of other conditions2,8-11 especially those that present with movement disorders, especially oculogyric crisis.6,8,11

Despite symptom onset during infancy, diagnosis is typically delayed2,3

AADC deficiency can be difficult to diagnose, especially in patients with other conditions.2,8-11

Many of the most common symptoms of AADC deficiency can also be attributed to a number of other conditions such as cerebral palsy and epilepsy, resulting in potential misdiagnosis.2,3,4,6,7

However, the presence of the following should prompt investigation of AADC deficiency:

- Autonomic symptoms that are not typical of other conditions:2,3
  - Normal EEG and neuroimaging; one study showed that only a small proportion of patients with AADC Deficiency had an abnormal EEG, MRI, or CT.

AADC deficiency can affect patients of any gender, ethnic origin, or geographic region.2,3

AADC deficiency can also be attributed to a number of other conditions.2,8-11

Early identification of AADC deficiency can help improve the care and management of patients.

The diagnostic pathway for suspected AADC deficiency2-5

Perform3:
- CSF neurotransmitter metabolite panel
- Plasma enzyme activity assay

Interpret4:
- Reduced HVA, 5-HIAA, and MHPG; elevated 3-OMD, L-dopa, and 5-HTP; and normal pterins in CSF
- Low plasma AADC enzyme activity
- Increased urinary VLA

Confirm with genetic testing5:
- Mutation(s) in the DDC gene

Conclusions:

AADC deficiency is a rare and devastating disorder of the central nervous system that typically presents early and may require lifelong care.2,3,4,5 It can cause hypotonia, developmental delay, movement disorders and autonomic symptoms.2,3

Earlier identification can help improve the care and management of patients with AADC deficiency.2,3 However, AADC deficiency may be misdiagnosed or undiagnosed.1,3

Hypotonia is the most commonly reported symptom of AADC deficiency. It is therefore necessary to consider testing for AADC deficiency in patients with unexplained hypotonia.

References: