DISEASE BURDEN OF AROMATIC L-AMINO ACID DECARBOXYLASE (AADC) DEFICIENCY: SIGNS AND SYMPTOMS

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1. Background and objective

- AADC deficiency is a rare neuro-metabolic disease associated with a range of symptoms and functional issues including oculogyric crisis, hypotonia, or failure to thrive among other motor, cognitive and autonomic symptoms[1].
- The aim of this study was to assess the burden of AADC deficiency in a multi-country patient cohort in Europe.

2. Methods

- A case study questionnaire was developed based on information from literature and expert input including questions around patient characteristics, disease course, signs and symptoms and motor milestone achievement.
- Physicians experienced in the management of patients with AADC deficiency were asked to complete the questionnaire based on the information available in medical records and their knowledge of their patient(s).

3. Results

- Eleven interviews with clinicians in France, Italy and Spain were conducted providing information on 20 individuals with AADC deficiency aged 3-40 years (Table 1).
- Patients with AADC deficiency were experiencing a wide range of symptoms (Table 2). The most frequent symptoms experienced by these patients included movement disorders (100%), developmental delay (90%), sleeping problems (85%), and gastrointestinal problems (80%).
- Some symptoms varied among the patient groups according to the best motor milestone achieved; however, all signs and symptoms were present in more than one patient group (Table 2).
- Patients who were able to walk assisted or unassisted also experienced symptoms that were more commonly present in patients who had no motor function or full head control only (i.e. hypotonia, poor head control, oculogyric crisis, feeding/swallowing problems (Table 2)).

Table 1. Key Patient Characteristics According to Best Achieved Motor Milestone

	Walking assisted or unassisted (n = 10)	Sitting unassisted or standing with support (n = 2)	No motor function or full head control only (n = 8)	Overall (n = 20)
Time from symptom onset to diagnosis, years				
0 – <2	4 (40)	2 (100)	6 (75)	12 (60)
2 – <6	1 (10)	0	2 (25)	3 (15)
6 – <19	1 (10)	0	0	1 (5)
≥ 19	4 (40)	0	0	4 (20)
Follow-up duration, years, mean (SD)	7.2 (2.4)	2.0 (0)	3.5 (2.9)	5.2 (3.2)
Alive at time of survey	9 (90)	2 (100)	6 (75)	17 (85)
Male sex	6 (60)	2 (100)	4 (50)	12 (60)
Ethnicity				
Caucasian	8 (80)	1 (50)	3 (38)	12 (60)
African	1 (10)	1 (50)	1 (13)	3 (15)
Other	1 (10)	0	3 (38)	4 (20)
Not reported	0	0	1 (13)	1 (5)

Data are n (%) unless otherwise indicated.
SD, standard deviation.

Table 2. Number of patients experiencing each symptom at the time of the survey according to best achieved motor milestone

Symptom	Walking assisted or unassisted (n = 10)	Sitting unassisted or standing with support (n = 2)	No motor function or full head control only (n = 8)	Overall (n = 20)
Movement disorders	**10 (100)**	**2 (100)**	**8 (100)**	**20 (100)**
Dyskinesia	7 (70)	2 (100)	6 (75)	15 (75)
Oculogyric crisis	5 (50)	2 (100)	7 (88)	14 (70)
Dystonia	5 (50)	1 (50)	7 (88)	13 (65)
Myoclonus	4 (40)	0	3 (38)	7 (35)
Hypokinesia and/or bradykinesia	2 (20)	0	4 (50)	6 (30)
Tremor	1 (10)	0	1 (13)	2 (10)
Developmental delay	**8 (80)**	**2 (100)**	**8 (100)**	**18 (90)**
Delayed cognitive development	7 (70)	2 (100)	8 (100)	17 (85)
Delayed speech development	7 (70)	2 (100)	8 (100)	17 (85)
Delayed motor development	5 (50)	2 (100)	8 (100)	15 (75)
Sleeping problems	**8 (80)**	**1 (50)**	**8 (100)**	**17 (85)**
Insomnia	8 (80)	1 (50)	8 (100)	17 (85)
Hypersomnia	1 (10)	0	1 (13)	2 (10)
Gastrointestinal	**8 (80)**	**2 (100)**	**6 (75)**	**16 (80)**
Diarrhea	7 (70)	0	5 (63)	12 (60)
Constipation	1 (10)	2 (100)	3 (38)	6 (30)
Other CNS symptoms	**9 (90)**	**1 (50)**	**5 (63)**	**15 (75)**
Fatigue	8 (80)	0	4 (50)	12 (60)
Dysarthria	3 (30)	0	3 (38)	6 (30)
Epileptic seizures	0	1 (50)	0	1 (5)
Behavioral problems	**7 (70)**	**1 (50)**	**6 (75)**	**14 (70)**
Irritability	4 (40)	1 (50)	4 (50)	9 (45)
Dysphoria/mood problems	7 (70)	0	2 (25)	9 (45)
Excessive crying	0	1 (50)	6 (75)	7 (35)
Muscle tone regulation	**4 (40)**	**2 (100)**	**8 (100)**	**14 (70)**
Hypotonia	2 (20)	2 (100)	8 (100)	12 (60)
Poor head control	2 (20)	0	8 (100)	10 (50)
Hypertonia	0	2 (100)	4 (50)	6 (30)
Upper respiratory tract	**7 (70)**	**0**	**7 (88)**	**14 (70)**
Excessive drooling	6 (60)	0	6 (75)	12 (60)
Nasal congestion	5 (50)	0	1 (13)	6 (30)
General	**6 (60)**	**1 (50)**	**6 (75)**	**13 (65)**
Feeding/swallowing problems	2 (20)	1 (50)	6 (75)	9 (45)
Gastrointestinal problems	2 (20)	1 (50)	5 (63)	8 (40)
Failure to thrive	3 (30)	1 (50)	4 (50)	8 (40)
Contractures	0	0	4 (50)	4 (20)
Depressive disorders	5 (50)	0	1 (13)	6 (30)
Cardiovascular	**6 (60)**	**0**	**2 (25)**	**8 (40)**
(Orthostatic) hypotension	6 (60)	0	2 (25)	8 (40)
Bradycardia	2 (20)	0	0	2 (10)
Skin homeostasis	**2 (20)**	**0**	**6 (75)**	**8 (40)**
Excessive sweating	2 (20)	0	5 (63)	7 (35)
Temperature instability	1 (10)	0	4 (50)	5 (25)
Eyes	**4 (40)**	**0**	**2 (25)**	**6 (30)**
Ptosis	4 (40)	0	2 (25)	6 (30)
Miosis	0	0	1 (13)	1 (5)
Metabolic endocrine	**3 (30)**	**0**	**2 (25)**	**5 (25)**
Hypoglycemia	3 (30)	0	0	3 (15)
Hyperprolactinemia	1 (10)	0	2 (25)	3 (15)
Other symptoms	**5 (50)**	**1 (50)**	**3 (38)**	**9 (45)**

Data are n (%).[a]Results are not mutually exclusive.
CNS, central nervous system.

4. CONCLUSION

- This study shows the high burden of AADC deficiency as described by the broad range of highly debilitating signs and symptoms experienced by patients with this disease.

References

1. Wassenberg T, et al. Orphanet J Rare Dis. 2017 Jan 18;12(1):12.